THE ACTION OF DICOUMAROL ON LABORATORY AND WILD RATS, AND ITS EFFECT ON FEEDING BEHAVIOUR

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(With Plates 1 and 2, and 5 Figures in the Text)

INTRODUCTION

The behaviour of wild rats towards an unfamiliar food presents problems of both practical and theoretical interest (Chitty, 1950; Shorten, 1950; Thompson, 1948). When first eaten the food is often taken in very small amounts; if poison is present its effects soon make the rats stop feeding, and if they recover the rats are often found to be *bait-shy*; that is, they refuse the bait entirely (Rzoska, 1950). As far as rat control is concerned prebaiting with harmless food can overcome this difficulty by inducing rats to feed rapidly on the bait when poison is eventually added (see Barnett, 1948, for a review); and if there are even then a few bait-shy survivors they may be disposed of by a second prebaiting and poisoning with different materials. In large-scale practice, however, this elaborate programme presents considerable difficulties for organizations such as local health authorities, and they are often unable to adhere to it.

Since attempts to find and use very highly toxic substances are unlikely to be profitable (Barnett & Spencer, 1949), the main need is for a poison which does not cause shyness. Given this it would be possible to dispense with prebaiting, and to lay the poison repeatedly without reducing its effectiveness. Chronic baiting, as this procedure might be called, might in some places greatly reduce administrative difficulties, especially if the bait were laid in permanent containers (see Elton, 1950, for a discussion of 'permanent poison points').

It was suggested by Messrs Ward, Blenkinsop and Co. Ltd., in a personal communication, that dicoumarol (3·3′-methylene-*bis*-4-hydroxycoumarin), a blood anti-coagulant, might be used as a rat poison (see also O'Connor, 1948). Since dicoumarol acts slowly, and has little or no ill effect after only a single dose, it seemed to us that it might not set up shyness and so might serve as a poison for chronic baiting. The present paper describes experiments designed to test this possibility.

EXPERIMENTS ON WHITE RATS

Method. Female white rats were mated, and eighteen or nineteen days later were separated from the male and fed on sausage rusk* mixed with its own weight of water and containing 0·04 or 0·08 per cent dicoumarol†. This mixture was

* Sausage rusk is a biscuit meal, used as a filler for sausages.
† Supplied by Ward, Blenkinsop and Co. Ltd.

given in one series of experiments for only one day, in another series continuously until the rats died or the experiment was stopped.

Results. Thirteen rats were given the bait (0·04 per cent dicoumarol) for only 24 hr. Each rat ate approximately 20 g. Four were not pregnant and showed no ill effects; they were killed after 10 days, and examination of the thorax and abdomen showed nothing abnormal. Of the nine pregnant rats two died, 3 and 4 days respectively after administration of the bait. Symptoms before death included paleness of ears, eyes and feet, lassitude and loss of blood from the vagina. Two rats with these symptoms were killed after 2 days; both showed extensive bleeding into the uterus, and one had haemorrhagic patches on the lungs. The remaining five rats survived and produced litters, but of the thirty-three young only thirteen survived (cf. Kraus, Perlow & Singer, 1949).

Fifteen rats were given the bait continuously (six with dicoumarol at 0·08 %). No alternative food was provided. All died except one (not pregnant), which was killed when in a very weak state after 23 days. Seven of these rats were pregnant, and showed uterine bleeding on examination after death; death took place from 4 to 9 days after the first administration of the bait. The seven rats which died, although not pregnant, lived for 9, 11, 12, 13, 15, 16 and 19 days respectively from the beginning of dosing. These, and the one which was killed, all had spontaneous haemorrhages internally (cf. Jürgens, 1948), and some also developed skin petechiae and bleeding round the nostrils and eyes (Pl. 1, figs. 1 and 2; Pl. 2, fig. 1). This variation in susceptibility to dicoumarol is paralleled by the results of clinical studies (Allen, 1947).

OBSERVATIONS IN THE FIELD

Methods. For control in the field dicoumarol was applied in the proportion of 0·13 % in one of three bases: (i) national flour (85 % extraction) plus 10 % castor sugar; (ii) wholemeal; (iii) dry sausage rusk.

Dicoumarol was supplied with bismuth carbonate and chalk in the proportions:

Bismuth carbonate	1 g.
Chalk	5 g.
Dicoumarol	200 mg.

40 g. of this mixture was added to 960 g. of the bait base. The bait was laid in holes, or in containers made of drainpipes 15 in. long, of 3 in. internal diameter, blocked at one end (Pl. 2, fig. 2). Before baiting began a census of the rat population was taken by the method of Chitty & Shorten (1946; see also Chitty, 1950), and a further census was taken when baiting ended. The census method is to lay a surplus of wheat (in these experiments in the drainpipes already mentioned) and to weigh the residues. The amount of wheat eaten each day gives a figure representing the size of the population. All censuses were continued until daily wheat consumption had reached a plateau; the average consumption for the last 3 days was taken to represent the population level.

In three tests the dicoumarol bait was laid once a week and the weight eaten in each period of 7 days was recorded.

Six tests were on *Rattus norvegicus* Berkenhout, the common brown rat. A seventh was on *R. rattus* L., the 'black' rat.

Results. The results of the tests are summarized in Table 1. In the first three (123, 124, 125), in which fresh bait was laid two or three times a week, all the baiting was done in rat holes, and drainpipe containers were used only for census. When bait is laid in holes it is not possible to weigh residues, but it could be seen that in these tests, after an initial period of 1–2 weeks during which all the bait was taken, the amount of bait eaten declined steadily until there was always a surplus present. The holes were generally damp, and the bait, which contained sugar, tended to cake. Two of these tests were failures, while the third gave a kill of 80 % or more.

Table 1. *Field tests*

Test no.	Habitat	Bait base(s)	Period of treatment (weeks)	Baiting interval (days)	Census 1 (g.)	Census 2 (g.)	Percentage estimated killed	Time of year
123	Farm	Flour and sugar	4	2–3	425	280	25–45	Feb.–Apr.
124	Refuse tip	Flour and sugar	4	3–4	1,365	230	80–84	Feb.–Apr.
125	Refuse tip	Flour and sugar	4	2–3	3,050	2,310	22–31	Feb.–Apr.
372(*a*)	Refuse tip	Flour and sugar	7	7	39,770	10,230	73–75	Feb.–May
372(*b*)	Refuse tip	Wholemeal	14	7	10,230†	8,650	9–18	May–Sept.
373	Pig farm	Wholemeal; rusk	7	7	1,490	100	93–94	June–Aug.
374	Farm	Wholemeal; rusk	9	7	8,520	2,660	67–70	June–Aug.
—	Food-store*	Wholemeal	8	Varied	*c.* 240	*c.* 130	*c.* 50	July–Sept.

* The species here was *R. rattus*. † This was census 2 of test 372 (*a*).

In three further tests the bait was laid in the drainpipes used for census, and was replenished only once a week. Residues were weighed, and the weekly take recorded (Text-figs. 1–3). In all three the amount eaten weekly fell steadily at first, and in test 372*a* (Text-fig. 3) it fell throughout the 7 weeks of treatment. In tests 373 and 374 the bait base was changed after 3 weeks, from wholemeal to rusk; in both instances the change was followed by a check in the decline in the amount taken, and in test 374 it rose for 2 weeks and then remained fairly steady.

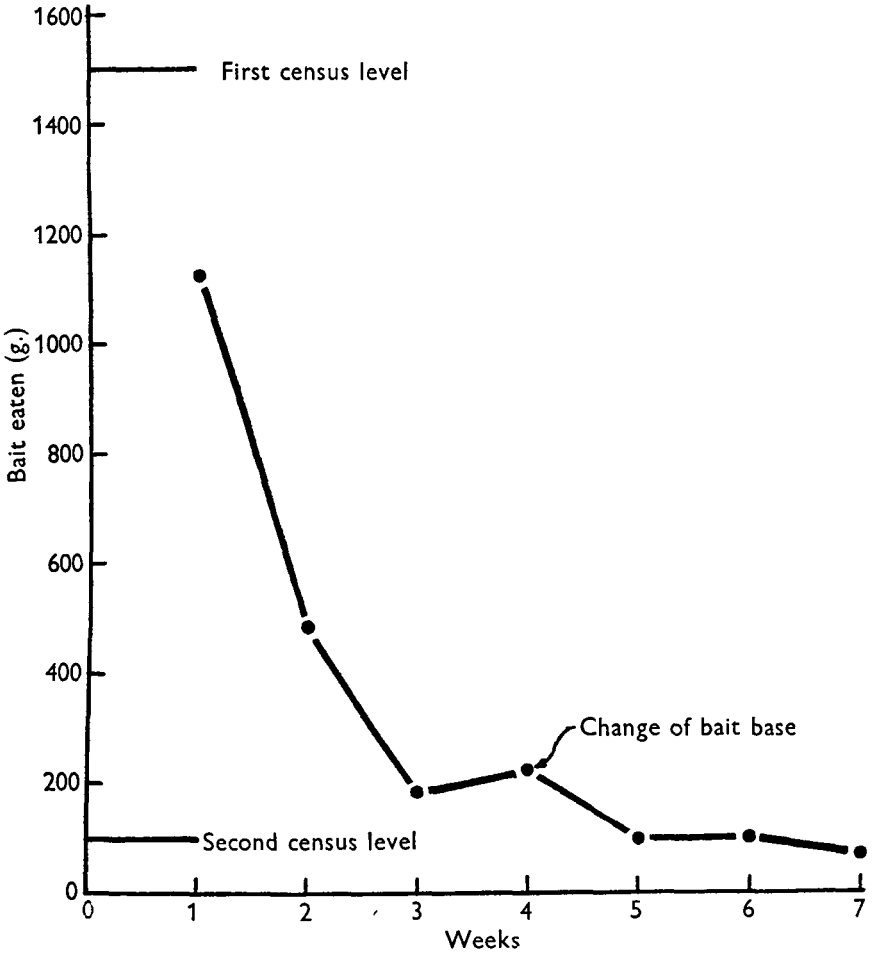
Test 372 was carried out at a tip which had been used in another series of experiments in the previous year. In June 1948 the rat population had been reduced to a level corresponding to a daily wheat take of 960 g. In February 1949 the census figure (Table 1) was 39,770 g. This was the first census of the experiment with dicoumarol, and, since the tip is far from any possible source of invading rats, it illustrates the reproductive capacity of this rat population.

The second census was carried out when 7 weeks of dicoumarol baiting had brought the weekly take of bait to a very low level (Text-fig. 3). This census indicated that about 25 % of the rats remained, and baiting was therefore continued with wholemeal, instead of national flour and sugar, as the bait base. With this base too the weekly take began fairly high and then fell off for 5 weeks (Text-fig. 4); after this it remained steady, but for minor fluctuations, for 9 weeks, when baiting was discontinued. A third census indicated only a slight further reduction of the population resulting from 14 weeks' baiting in the new base.

Text-figs. 1–4 show that in the experiments to which they refer the *weekly* take of bait containing dicoumarol was usually, from the first, less than the *daily*

amount of wheat taken during the census. The dicoumarol bait often showed obvious signs of disturbance by rats, even when little or none had been eaten; it was common to find a good deal of spillage outside the containers (Pl. 2, fig. 2).

The bodies of forty-two rats were found and examined during these experiments. All showed evidence of dicoumarol poisoning in the form of internal haemorrhages. Other bodies were picked up by the occupiers or people working on the various sites but were not examined. There was no evidence of mortality from external injuries.



Text-fig. 1. Test no. 373.

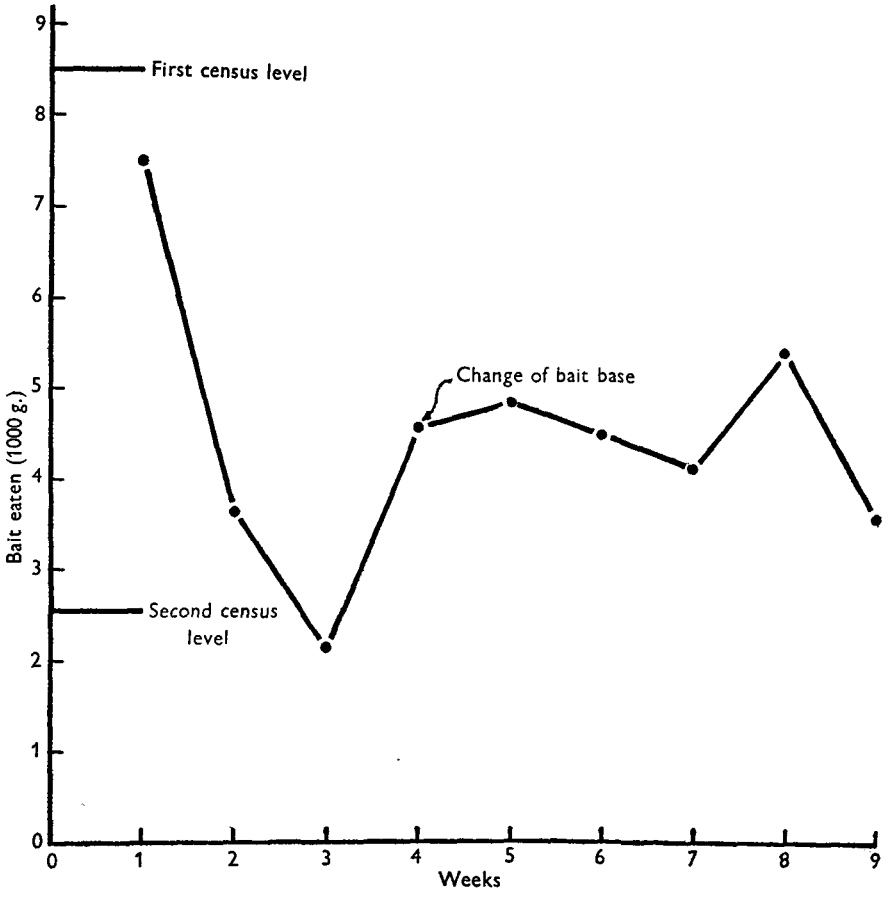
Text-figs. 1–4. Weekly takes of dicoumarol bait, and census levels, in tests at three sites.

In the test on *R. rattus*, which was kindly carried out by Mr J. W. Hancock of Bermondsey Borough Council, observations of take were less regular and detailed. The phenomenon of extensive disturbance of the bait while little was eaten was, however, observed throughout the experiment. Baiting was done for 8 weeks. The censuses indicated a kill of the order of 50 %.

LABORATORY EXPERIMENTS ON WILD RATS

The results of the field tests suggested the need for laboratory experiments on wild rats. Four series of experiments were therefore undertaken, in an attempt to get information on the effects of ingestion of dicoumarol on feeding behaviour.

Series (i). Fifteen wild *R. norvegicus* (eight males and seven females), of weights varying from 110 to 400 g., were trapped in various places. None had previously had dicoumarol. Each rat was kept alone in a small cage, and for 10–12 days was given a choice of wholemeal, or wholemeal containing dicoumarol; seven had



Text-fig. 2. Test no. 374.

dicoumarol in the proportion of 0·032 % by weight, and eight in the proportion of 0·064 %. None of the females was pregnant.

Of those receiving the lower concentration of dicoumarol, three took more plain wholemeal than that with dicoumarol on every day of the experiment, and the remaining four on every day except one. The mean daily take per rat of wholemeal was 14·7 g., and of the dicoumarol mixture 3·2 g. Of the rats receiving the higher concentration of dicoumarol, four preferred wholemeal on every day; one preferred

it on every day except one; and two on every day except two. In this group the mean daily take per rat of wholemeal was 13·1 g., and of dicoumarol mixture 1·7 g.

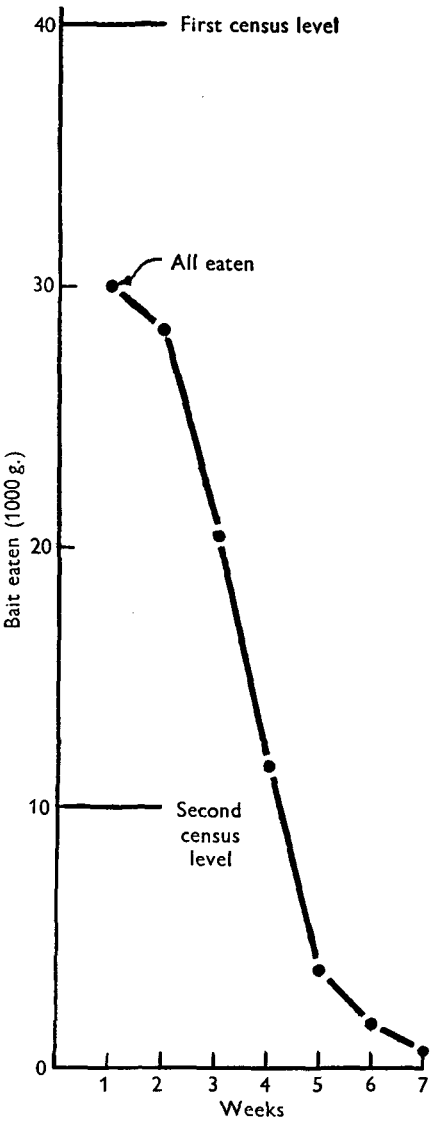
None of these rats died. The main conclusion from this experiment was that the dicoumarol mixture was distasteful to wild rats.

Series (ii). Eleven rats were trapped at two sites where dicoumarol baiting had been going on for 8 and 4 months respectively (test nos. 372 and 374), and were given the same choice as were those of series (i). The experiment went on for 15–18 days, or until the rats died.

Results were similar to those for series (i). Only four rats failed to prefer the plain wholemeal on every day. The mean daily take of wholemeal per rat was 15·2 g., and of dicoumarol mixture 2·25 g. One difference was shown in this series from the preceding one: three of the rats died, after 4, 12 and 15 days of experimental feeding respectively. All three showed the typical internal bleeding of dicoumarol poisoning, and a blackening of the distal part of the spleen due to deposition of haemoglobin (Jürgens, 1948).

Series (iii). A further group of nine rats from the same sites was tested for response to the bait base (wholemeal) in which dicoumarol had been administered during the field experiments. Six rats which had not been exposed to dicoumarol served as controls. All these rats were given a choice between wholemeal and whole wheat.

The mean percentage of wholemeal eaten by each rat in the three groups was as follows:



Text-fig. 3. Test no. 372*a*.

6 control rats	4 rats from site 374	5 rats from site 372
53·1	44·8	40·6

The experimental rats therefore took less wholemeal than the controls, but the difference was not great; moreover, there was marked individual variation, shown in Table 2.

Series (iv). Sixteen wild rats, of 110–460 g. weight, none previously exposed to dicoumarol, were fed as follows:

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(*a*) choice of 85 % extraction flour *or* the same flour + 10 % castor sugar, 6 days.

(*b*) the same, but with dicoumarol (0·032 %) added to the sugar-flour mixture, 3–4 days.

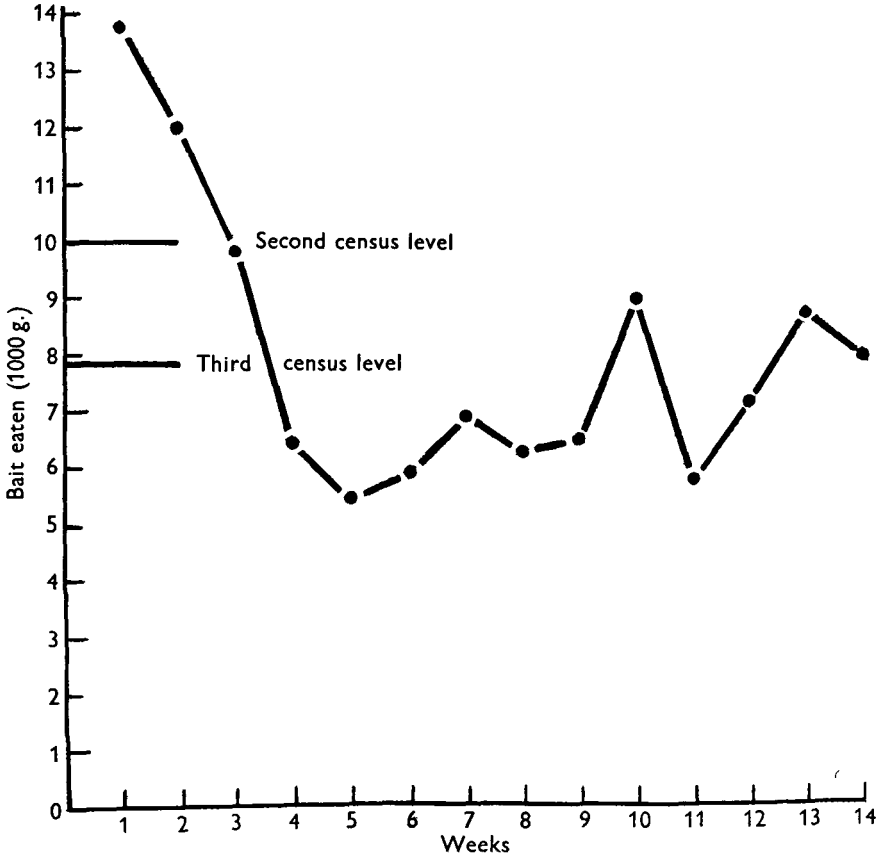
(*c*) flour only, 6 days.

(*d*) as (*a*), 8 days.

Table 2. *Mean daily take in g. of wholemeal and whole wheat of individual rats*

6 controls		4 from site 374		5 from site 372	
Flour	Wheat	Flour	Wheat	Flour	Wheat
9·0	12·4	10·4	12·5	13·0	19·5
14·0	5·0	11·4	11·8	12·5	7·9
7·5	7·2	15·0	10·9	9·0	16·5
14·0	9·5	6·9	19·1	9·5	13·6
3·8	10·6			6·0	17·8
10·1	5·6				

The object was to test whether ingestion of dicoumarol in a sugar-flour mixture would alter the response of the rats to this mixture when it was offered again.



Text-fig. 4. Test no. 372*b*.

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The results are shown in Text-fig. 5. In phase (*a*) the rats, with three exceptions, clearly preferred the sugar-flour. In phase (*b*) the same preference was shown on the whole, despite the presence of dicoumarol. In phase (*c*) the rats had no alternative to flour. In the final phase they had the opportunity of continuing to eat plain flour, or of returning to the mixture with sugar which they had previously preferred.

Of the sixteen rats two now showed a decisive reversal of preference. Another four showed a reversal, but only after an initial period of 2–5 days during which the sugar mixture was preferred. (We have no explanation of this peculiar phenomenon.) With seven rats the results were equivocal: the proportion of plain flour eaten was greater than in phase (*a*), but there was still some degree of preference for sugar-flour. Two rats, both of which had shown anomalous behaviour in phase (*a*), showed a decisive preference for sugar-flour in phase (*d*). Finally, one rat preferred plain flour in phase (*a*); took mainly sugar-flour when it contained dicoumarol in phase (*b*); and in phase (*d*) again preferred plain flour.

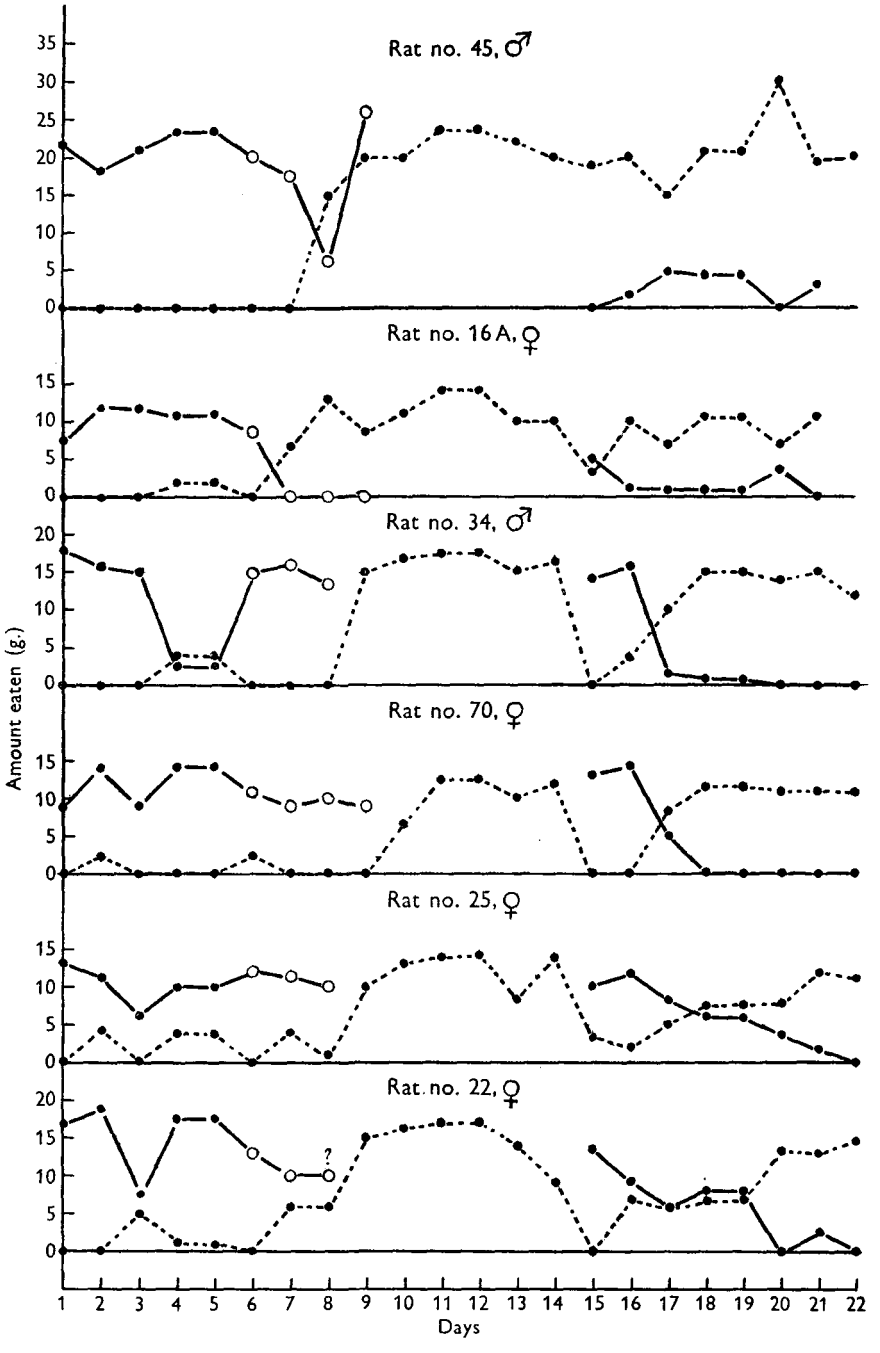
On the whole therefore, despite marked variation among individuals, in this experiment the ingestion of dicoumarol did tend to turn rats away from the bait base which had contained it.

DISCUSSION

This paper describes only a preliminary exploration of the possibilities of chronic baiting. Three questions arise from our present results: (i) What can be concluded on the efficacy of dicoumarol? (ii) What is the significance of the effect of ingestion of dicoumarol on feeding behaviour? (iii) What is the significance of these results for the general problem of chronic baiting? In this discussion only *R. norvegicus* will be considered.

For the first question the best indication comes from tests 372–374. Chronic baiting with dicoumarol in a dry cereal base appears to result, after some weeks, in an equilibrium between the lethal effects of the baiting and breeding by the rat population. This equilibrium is most clearly shown in test 372, which was done on an isolated population of, probably, at least 1600 rats; censuses showed that, after the first 7 weeks of treatment, a further 14 weeks' application of dicoumarol in a different base resulted in a negligible net further reduction.

This equilibrium requires explanation. An early observation was the considerable disturbance of bait, even in the absence of actual consumption; this may be due to a deterrent taste. Later, the laboratory experiments on wild rats decisively confirmed the distastefulness of one mixture containing dicoumarol. However, this does not adequately account for the *change* in the responses of rat colonies to the baits; i.e. for the equilibrium reached after the initial decrease in take. Distastefulness may be expected to reduce the efficacy of a poison, but if a poison causes a steady reduction in the numbers of rats for some weeks it might be expected to continue to do so until there are no rats left. If distastefulness is to be the whole explanation we must suppose that only a minority of the rats refuse the bait, and that only they survive. This, though a possibility, is not supported by



Text-fig. 5*a*.

Text-figs. 5*a–c*. The daily food intake of the sixteen wild rats of series (iv), showing the tendency for a change in the initial preference for sugar-flour, after this base had been given with dicoumarol. ●—●, flour and sugar; ○—○, flour, sugar and dicoumarol; ●– – –●, flour alone.

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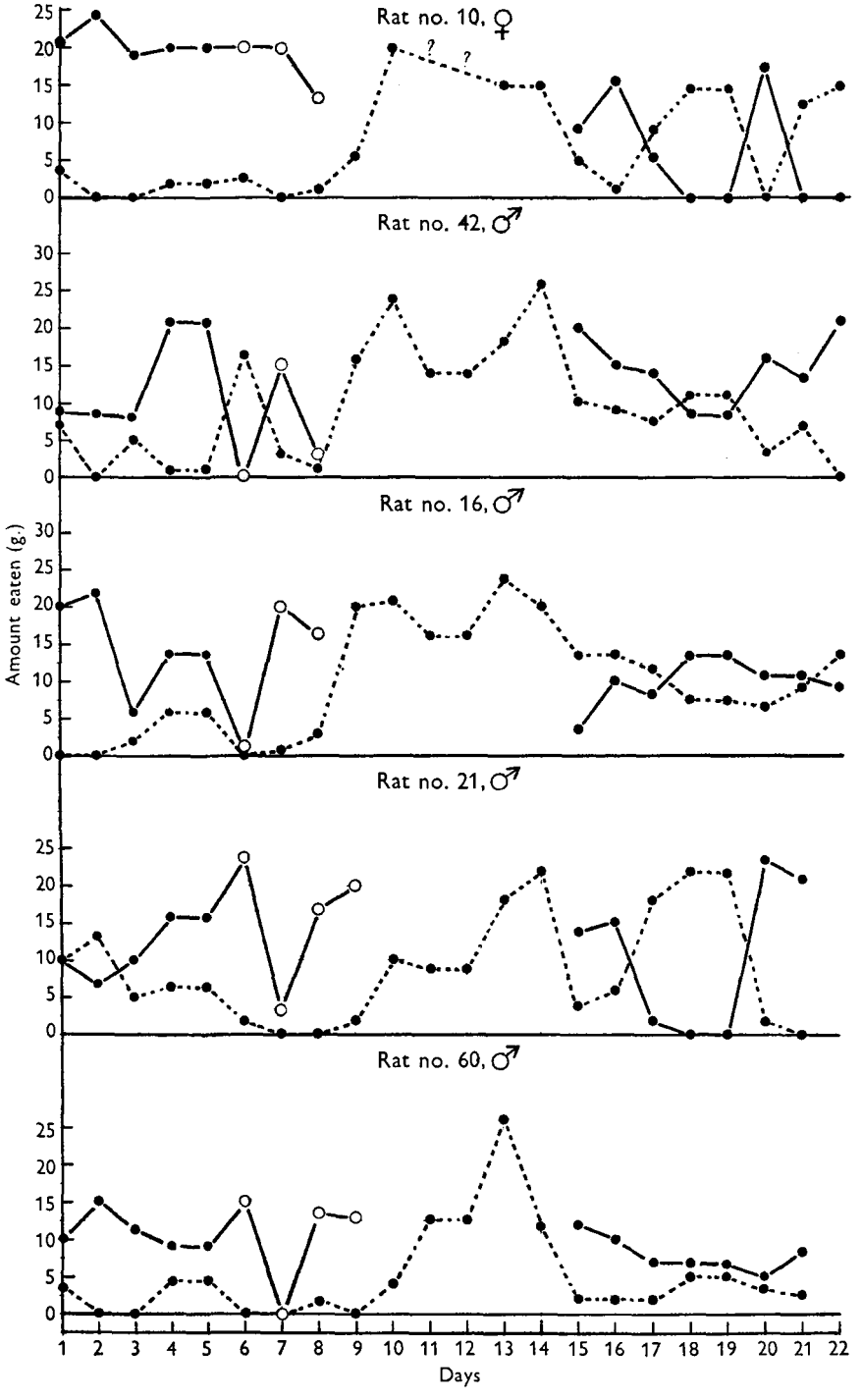

Text-fig. 5*b*.

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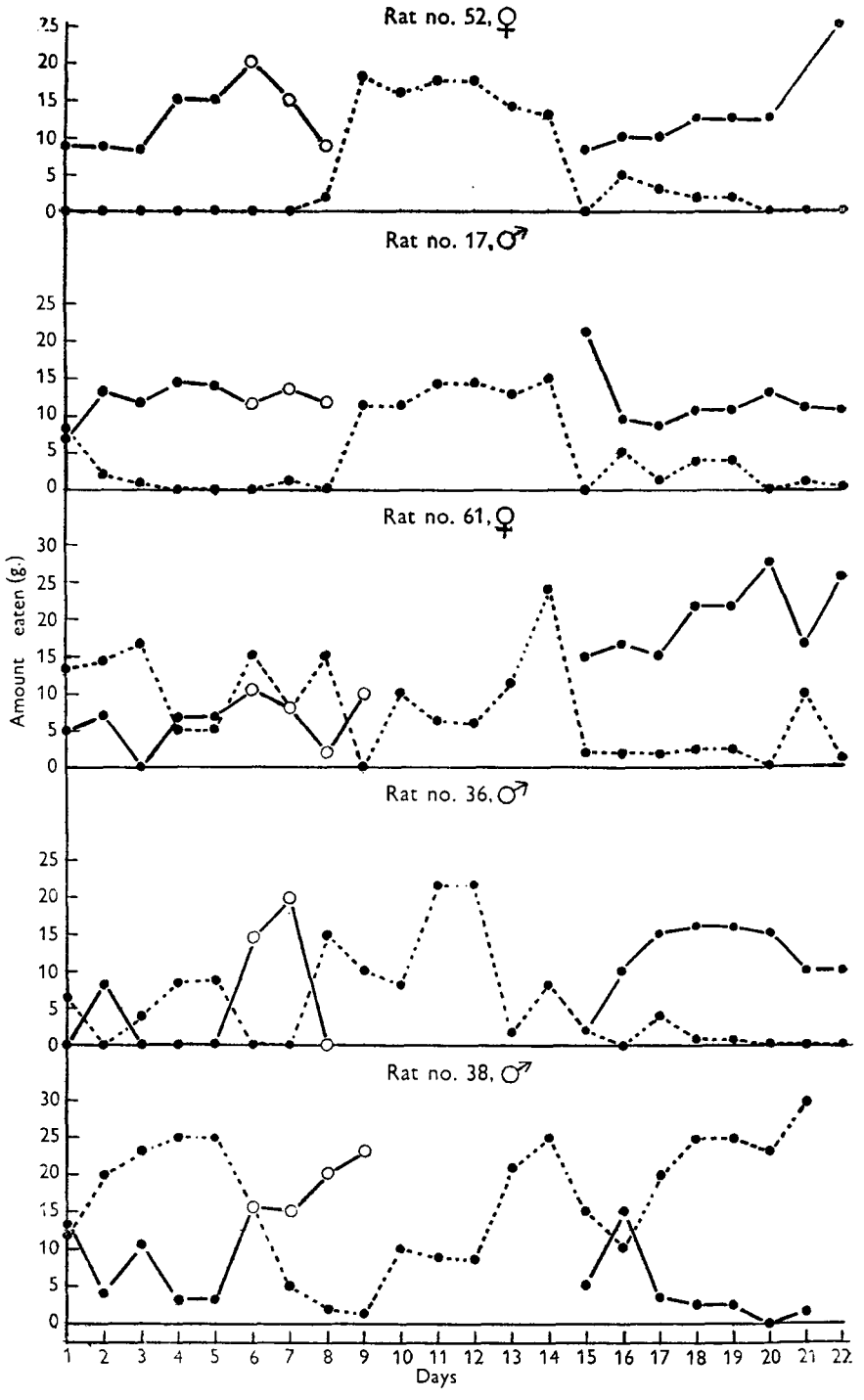

Text-fig. 5c.

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the laboratory tests (series (i) and (ii)), in which a marked preference for the plain bait was general from the first.

A possible explanation is that chronic dicoumarol poisoning caused bait-shyness, i.e. the refusal of a food which has caused illness. While, in the field tests, the initially low weekly consumption of dicoumarol bait compared with the daily consumption of wheat suggested distastefulness, the decline in consumption, which appeared greater than could be accounted for by the reduction in numbers, suggested the possibility of shyness. It was this that led to the changes of bait base in the experiments, and the rise in weekly bait consumption which followed the change fitted the hypothesis of shyness. The experiments on wild rats in the laboratory (series (iv)) go some way to confirm it. The claim by O'Connor (1948) that dicoumarol is neither distasteful nor liable to cause shyness is therefore not supported.

The appearance of bait-shyness in rats poisoned by a substance with a slow and unobtrusive action was unexpected, and is of some general interest. The shyness studied by Rzoska (1950), Chitty (1950) and others was induced by poisons which have a conspicuous effect within a few hours of ingestion, and it is a sufficiently remarkable phenomenon itself. With dicoumarol in the field shyness is probably developed quite slowly, with less intensity and with more individual variation than with strong poisons. It may perhaps be compared with the reported selection by laboratory rats of mixtures of high nutritional value, in preference to others of less value (Richter, 1942; Young, 1946; Scott & Verney, 1947). 'Shyness' may in fact be one aspect of a behavioural phenomenon of which 'dietary self-selection' is another part. Whether this is true or not we have no physiological explanation of shyness, and the extension of the scope of shyness suggested by our results merely enlarges the problem of dietary selection.

The two major defects of dicoumarol, its distastefulness to rats and its apparent capacity to cause shyness, suggest that it is unlikely to solve the problem of efficient chronic baiting. If it is used it should preferably be mixed with a dry bait, possibly an oily one. To mitigate the effects of shyness it might be useful to alternate two bait bases, but further experiment in the field is needed to determine whether this would be effective. A further question which is left open is the optimum concentration of dicoumarol in the bait. Further experiments would have been undertaken to solve these problems, but it now seems possible that other anti-coagulants may be more effective (Krieger, 1949).

The deficiencies of dicoumarol do not signify that chronic baiting is impracticable. For this general question the important fact is that, despite its imperfections, dicoumarol in our three main tests reduced the rat populations by about 70 % or more in 6–9 weeks with only weekly baitings. Successful chronic baiting is therefore still a possibility. The problems are: (i) to find a better poison, which may or may not be an anti-coagulant; (ii) to devise at least one bait mixture which remains effective for, preferably, several weeks; (iii) to design a bait container which will continue to deliver bait for several weeks without attention. Such containers could be left in place for long periods, and shifted only occasionally in response to changes in the distribution of the rat population or in the routes of reinvasion.

The first of these problems is likely to prove the most difficult, but there is no reason to think that they cannot all be solved.

We are grateful to Miss M. M. Spencer for help with the field tests, and to L. E. Hammond, Mrs A. Hill and R. I. Spearman for assistance in the laboratory.

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EXPLANATION OF PLATES

PLATE 1

Figs. 1, 2. White rats which had died after being fed on a dicoumarol mixture for 12–13 days. There were skin lesions, and in one there is bleeding from the nostrils and round the eyes.

PLATE 2

Fig. 1. A wild rat which died after being given dicoumarol (0·064 %) in wholemeal for 15 days. Bleeding has taken place in the neck, thorax and abdomen.

Fig. 2. Drainpipes on site no. 372, showing the method of laying bait and the typical scattering of dicoumarol mixtures.

(*MS. received for publication* 3. III. 50.)

After this paper had gone to press we received a copy of a paper (Schein, M. W., *Rep. U.S. Publ. Hlth*, **65** (1950), 368) reporting field tests on the anti-coagulant 'Compound 42'. The results of these tests resemble, on the whole, those we obtained with dicoumarol.

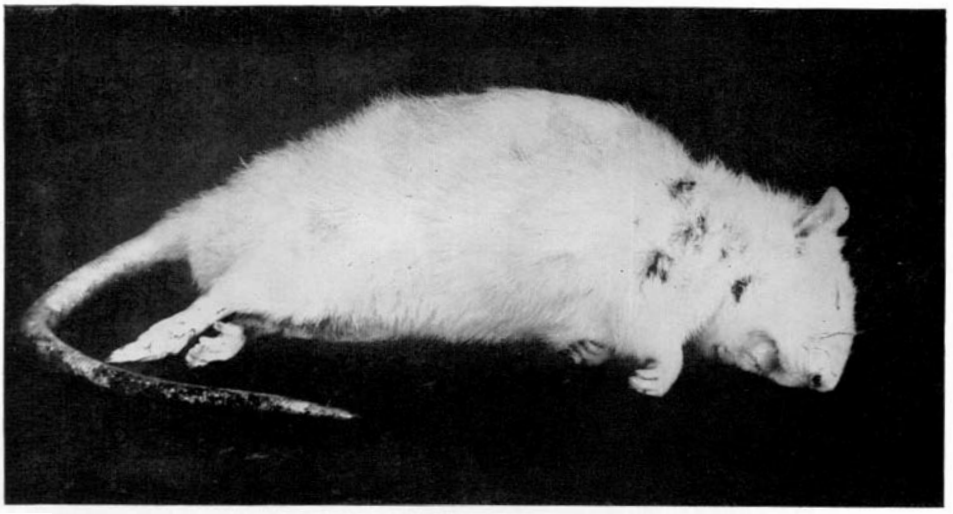

Fig. 1

Fig. 2

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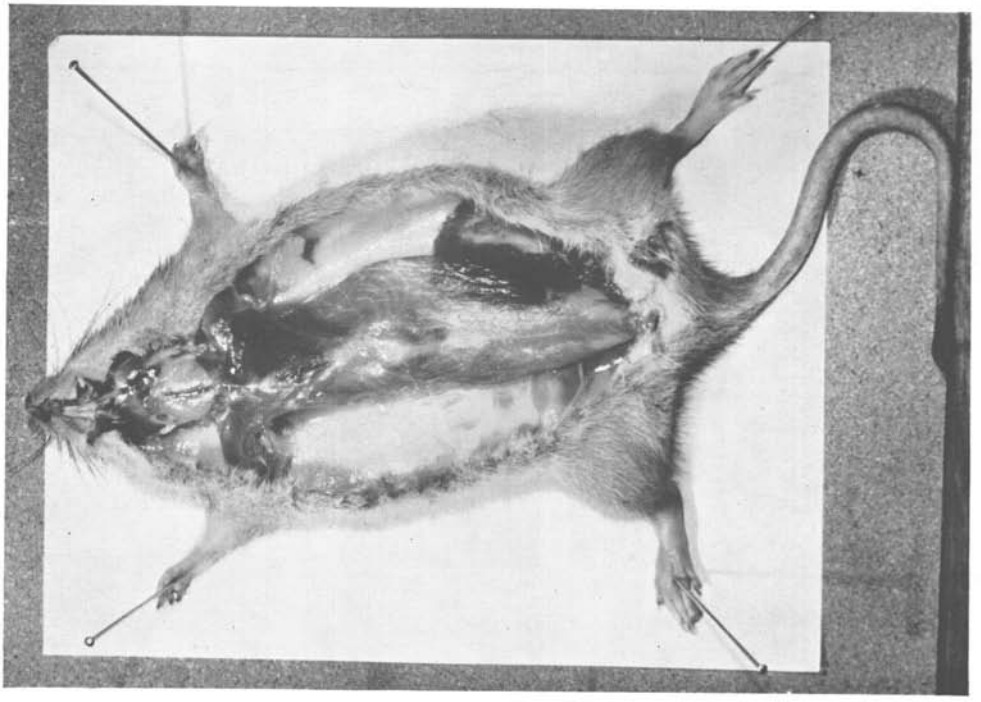

Fig. 1

Fig. 2

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