

PLAGUE STUDIES *

10. Control and Prevention

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SYNOPSIS

In examining the control and prevention of plague, the author pays particular attention to the control of commensal rodents and their fleas.

The various rat poisons in current use, their efficacy and practical application, and the dangers involved in their manipulation are described in great detail. The author also discusses other anti-rodent measures such as fumigation, rat-proofing, sanitation, protection of food, etc.

The second part of the study deals with : vector control—the outstanding value of DDT application in rodent-flea control is emphasized—the direct control of bubonic and pneumonic plague, and the control of the spread of plague at a distance.

ANTI-RODENT MEASURES

Control of Commensal Rodents

Killing by mechanical means

The method of killing rats with the aid of sticks or clubs may be advantageous under special circumstances, for instance in order to deal with animals met with when digging out burrows, or when otherwise carrying out harbourage demolition. However, since numerous rats are sometimes met with in the course of such operations, some of the animals are bound to escape unless many helpers are available, or unless—as was sometimes successfully carried out in China in the case of smaller structures—the buildings in question are temporarily surrounded by a fence made of corrugated iron sheets.

* This is the last of a series of studies which will be published as a manual on plague in separate editions in English and in French.—Ed.

paign in Lyons, France, wrapped their baits, which contained 3.5 % of the poison, in quantities of 4-5 g in newspaper. Though they distributed 20-60 of these packets per building, each packet containing 140-175 mg of ANTU, they did not encounter any untoward incident.

Besides being used in the usual form of baits, ANTU (in a concentration of 20 % in pyrophyllite or some other inert material) has been distributed in the form of copious patches on rat-runs, in rat-burrows, or in other harbours in order to kill the rodents which, after having walked through these patches, consume the poison by licking it off from their paws and fur. One must, however, agree with the handbook on rat-borne disease²¹⁷ that the use of this rather expensive procedure should be restricted to localities where it would be inadvisable to distribute ANTU in ordinary baits.

A modification of this method was to utilize a mixture containing 8 % DDT as well as 20 % ANTU and 72 % of an inert powder, so as to kill the rat-fleas as well as the rats coming in contact with the patches. However, Wiley²³¹ found that in buildings so treated only 41 % of the Norway rats were killed. Deaths among the commensal mice amounted to 70 % but there can be little doubt that this better result was due to the action of the DDT rather than to that of the ANTU.

So far, no antidote to ANTU poisoning in man has been found. However, as pointed out by Richter,¹⁷⁷ the marked insolubility of this compound makes prompt voiding of the stomach, preferably by lavage, an effective counter measure. Cathartics and alkalis should not be used in cases of ANTU poisoning. Should oedema of the lungs develop, one should stop the intake of fluids and administer oxygen.¹⁷⁷

Sodium fluoroacetate

Often called "1080" according to the catalogue number of the originally tested sample, sodium fluoroacetate was singled out as a most effective rodenticide in the course of large-scale screening tests carried out in 1943 and 1944 in the USA (Kalmbach, 1945,¹⁰⁰ 1948¹⁰¹). Most interestingly, it was afterwards learnt that monofluoroacetic acid was the toxic principle of a plant (*Chailletia toxicaria*) used to poison rats in Sierra Leone (Klingensmith¹⁰⁷) and also of *Dichapetalum (Chailletia) cymosum*, commonly called "gifblaar", feared as a stock poison in South Africa (Marais¹²⁶).

Sodium fluoroacetate is a light, white, crystalline compound, which is tasteless and possesses no, or at least no marked, odour. It is easily soluble in water, but practically insoluble in oils. As shown by the figures quoted below, this poison is a most effective rodenticide but, unfortunately, is at the same time also most dangerous for other animal species and for man.

As can be seen in table IV dogs, cats, pigs, and goats are particularly susceptible to 1080. As pointed out in this connexion in the handbook on rat-borne disease,²¹⁷ a dose of 2.5 mg, capable of killing 50 % of Norway

rats weighing about one pound (0.45 kg), would also kill a dog weighing 25 pounds (11 kg) or a cat weighing 10 pounds (4.5 kg). As far as it is permissible to judge from the experiment made in monkeys, a 15-pound (7.5-kg) child might be killed by consuming 35 mg of 1080, i.e., less than the amount (50 mg) contained in a 1/2-ounce (14 g) cup-full of 1080 solution as used to poison rats.

TABLE IV. LD₅₀ OF SODIUM FLUOROACETATE EXPRESSED IN MG PER KG BODY-WEIGHT *

Animal	LD ₅₀ (mg/kg)	Animal	LD ₅₀ (mg/kg)
Norway rat	3-7 (or less ^a)	Horse	1.0
<i>R. rattus</i>	1-4	Pig	0.3
Albino rat	2.5-7	Chicken	6-30
Commensal mouse	8-10 ^b	Mourning dove (<i>Zenaidura macroura</i>)	? 10 ^{b, c}
Cat	0.35-0.50	Sparrow (<i>Passer domesticus</i>)	2.7 ^{b, d}
Dog	0.07-0.20	Rhesus monkey	5-7.5
Goat	0.3-0.7	Man (estimated)	2.0

* Data obtained from *Rat-borne disease: prevention and control*.⁶⁷

^a The LD₅₀ in 55 starving Norway rats poisoned by Dieke & Richter⁴⁸ with the aid of a stomach-tube was 0.22 ± 0.01 .

^b According to Hughes.⁶⁸

^c Only 33% of these birds were killed.

^d LD₁₀₀.

Symptoms in rats poisoned with sodium fluoroacetate begin to appear after 20 minutes, and the animals succumb after 1-8 hours or even sooner (according to Dieke & Richter⁴⁸ after 45-240 minutes as compared to 12-90 minutes in the case of strychnine sulfate). The rats, obviously because they are rapidly overcome by the action of the poison, usually die in the open, quite frequently near the places where the poison baits or cups have been exhibited. Hence, unless stringent precautions are taken, instances of secondary poisoning in cats, dogs, or pigs, which devour or even merely gnaw the carcasses of 1080-poisoned rodents or birds, are bound to occur, the more so because the carcasses of the poisoned animals remain dangerous even if they have decayed or have become dry. The death-toll recorded by Gilcreas⁶⁸ in an instance where 1080-baits had been placed deep in the rat-burrows of a village dump was about 20 dogs and cats.

It is important to note in this connexion that, as proved by Gratch et al.,⁷¹ (a) sodium fluoroacetate does not reach the liver and spleen of rats killed by this poison in sufficient amounts to cause secondary poisoning in guinea-pigs inoculated with such tissues for diagnostic purposes, and

(b) 1080 in the concentration used for rat-poisoning does not exert a bacteriostatic action on *Pasteurella pestis*.

As shown by studies of Chenoweth & Gilman,²⁵ the causes of death in animals poisoned with methyl fluoroacetate were different in different species. In the case of rabbits, goats, horses, and spider-monkeys, the heart became primarily affected and death was due to ventricular fibrillations. In the case of the dog and guinea-pig, the central nervous system was primarily affected and death was caused by cessation of the respiratory activity. In cats, pigs, and rhesus monkeys both the heart and the central nervous system became involved. Rats as well as hamsters developed changes in which depression and delayed bradycardia were prominent, but did not usually exhibit ventricular fibrillation. Death in these two species, if occurring early (4-6 hours after), appeared to be due entirely to respiratory depression.

As stated in the handbook on rat-borne disease,²¹⁷ rats surviving the administration of sublethal doses of the poison "show neither aversion to nor serious tolerance of 1080". However, Barnett & Spencer¹² found that, in five out of six field tests made by them, "populations of *R. norvegicus* which had survived baiting with 1080 showed shyness [refusal] of the poison when it was given in a new bait base". The general conclusion reached by these two workers was that "although 1080 is probably more effective in direct poisoning than other poisons used in the past, it does not give as consistent results as the standard poisons do after prebaiting".

Though 1080 may be easily admixed with all sorts of solid bait materials, the workers in the USA urged with great reason that this poison should be distributed preferably in fluid form. It must be kept in mind, in this connexion, that the rodents, instead of immediately consuming solid poison-baits, may carry them away to places where they cannot be recovered.

As has been shown by Nicholson et al.,¹⁵⁰ a concentration of 12 g of sodium fluoroacetate per gallon of water is fully effective in killing Norway rats. Addition of 7 g of 1080 per gallon of water suffices to kill *R. rattus* and mice.

Though sometimes advantage has been taken of watering-fountains as used in chicken yards to make 1080 solutions available to the rodents, as a rule, shallow cups, able to contain no more than 3/4 of an ounce (21 g), and filled to only half their capacity, are utilized for this purpose.

Wiley²²² recommended the use of cups made of waxed paper, on which were stamped, by means of red waterproof ink, the word "Poison" and suitable symbols (e.g., a skull and cross-bones). He also advocated that the cups should be dyed a light-brown colour so as to make them less conspicuous to children.

As a further precaution it was recommended that a solution of nigrosine be added to the 1080-containing fluids so as to give them a warning black colour.

The acceptance of the solutions by the rats seemed not to be materially reduced by the addition of this dye.²¹⁷

Concentrations of 1080 varying from 0.25% to 1% have been used by different workers for the preparation of solid baits. The standard recommendation of Ward²²⁰ was to mix one gram of the poison with each pound (0.45 kg) of the bait material, thus using 1 ounce (28 g) for 28 pounds (12.7 kg) of bait.

Rubber gloves must be worn by the staff members preparing 1080 solutions or baits. The latter must not be touched with bare hands but must be distributed and collected with suitable instruments. Unused baits as well as poisoned rodents, which must be collected as soon as possible, should be disposed of by thorough incineration or by burial at a depth of at least 2 feet (0.75 m). The latter method should also be used when it is impossible or inadvisable to dispose of unused 1080-poisoned water by flushing it down a sewer. Preferably, the cups used for the distribution of the solutions should not be utilized again but should be burnt or deeply buried as soon as they have been collected.

Large-scale use of sodium fluoroacetate has been made by some workers with success and, as has been shown by Macchiavello¹¹⁹ and Macchiavello et al.,¹²² the community-wide distribution of this poison in combination with DDT application is an effective means of cutting-short plague outbreaks. Nevertheless, in the opinion of most workers, 1080 should not be utilized for general anti-rat campaigns but should be employed only if possibilities for the primary or secondary poisoning of domestic animals, as well as danger for human beings, can be fully excluded. Certainly, however, one should not hesitate to utilize this most effective poison in locations where it is safe to do so, for instance, during weekends in factories, godowns, schools, and offices, or in other buildings which are not frequented at the time. In emergencies, possibilities for the temporary evacuation and locking-up of the premises to be dealt with ought to be given consideration.

It deserves great attention that, as shown by the work of Hughes,^{90, 91} quite satisfactory results may be obtained when using 1080 in place of fumigation procedures to free ships from rats. As this worker summarized in 1950,⁹¹ the ratio of rats killed by 1080 to that of rats estimated to be aboard was 85.5% in the case of the 96 vessels baited in 1946 and 1947, and 91.8% in the case of 283 vessels baited afterwards. The value of this procedure, which could be applied easily in the case of vessels of even smaller size plying on inland waterways as well as in seaports, is certainly considerable.

So far no specific antidote for treating 1080 poisoning in man is known. The symptomatic treatment to be used in such cases is outlined by Hughes⁹⁰ thus :

"Ten-eighty is absorbed readily by the gastrointestinal tract and must, therefore, be removed immediately if harmful effects are to be prevented. The patient should be

made to vomit at once by sticking a finger in the throat or [the stomach should be voided] by other means. Give a dose of magnesium sulfate (Epsom salt) or other cathartic as a purge.

In the event of nervous system excitation the careful use of barbiturates of medium duration of action, such as sodium amytal, intravenously if necessary, is suggested. Other than complete rest and adequate sedation, little can be done to prevent progression of cardiac symptoms. Should ventricular fibrillation occur, intracardiac injection of 5 cc. of 1-percent solution of procaine hydrochloride might be attempted to restore an organized heartbeat. Although symptoms of 1080 intoxication will usually subside within 1 day, the patient should be kept quiet for a period of 3 days if there is any sign of action on the heart."

It is interesting to note that, as shown by Tourtelotte & Coon,²¹⁶ dogs poisoned orally with approximately $2 \times LD_{50}$ of 1080 were invariably saved when barbiturate treatment was started half an hour or 3 hours after poisoning. 80% of dogs which had received $4 \times LD_{50}$ of 1080 were saved when such treatment was started half an hour after poisoning, only 17% of those poisoned with the same dose were saved when the treatment was commenced after 3 hours. In the case of dogs poisoned with $6 \times LD_{50}$ of 1080, barbiturate treatment was ineffective even if started half an hour after poisoning. Sodium acetate and ethanol had some antidotal effect when given to dogs immediately after they had been poisoned with 1080, but these agents were of no value as adjuncts to barbiturate treatment when given half an hour after poisoning.

Anti-coagulants

The mode of action of the anti-coagulants used for the purposes of rodent control is fundamentally different from that of the above-described rodenticides. The efficacy of the latter depends upon their administration in single doses adequate to kill the animals. Single doses of the anti-coagulants, unless excessively large, are incapable of exerting a lethal action. However, if repeatedly ingested in smaller or even quite small doses, the anti-coagulants, because they inhibit the formation of prothrombin, are apt eventually to prove fatal to the poisoned animals by producing haemorrhages in the tissues of the body, and occasionally also external bleeding. It is clear that this peculiar "residual" action of the anti-coagulants can take place only if their admixture with the bait material is not recognized by the rodents, because otherwise the animals would cease to consume the poison-baits for sufficiently long periods.

O'Connor,¹⁶² who seems to have been the first worker to use anti-coagulants for rat-extermination, as well as Diagne et al.,⁴⁰ is stated to have obtained satisfactory results with dicoumarol (3 : 3'-methylene-bis-4-hydroxycoumarin), but, as shown by Armour & Barnett,⁵ the consumption of this compound is apt to produce acquired bait refusal (bait shyness) in the rats. However, general agreement has been reached that 3-(α -acetylbenzyl)-4-hydroxycoumarin, recommended as a potential rodenticide by