ASSESSMENT OF HUMANENESS OF VERTEBRATE PESTICIDES

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ABSTRACT

Vertebrate pesticides used in Ontario were studied in order to establish whether or not they produced a humane death.

Using pentobarbital sodium anesthesia, bipolar electrodes were implanted into the brains of male Sprague-Dawley rats weighing an average of 250 grams.

A polygraph designed for the purpose recorded the electroencephalograms (EEG). Behavioral characteristics were assessed prior to and during the experiment. Detailed post mortem examinations were conducted and coagulation studies and clinical pathology test carried out as required. The time from exposure to the pesticide to the time of unconsciousness or death was designated the "lag phase".

The rats were either fed the vertebrate pesticide or its active principle, or the latter given by gavage. Pesticides studied included: Red Squill; those containing anticoagulants - Difenacoum, Brodifacoum, Chlorophacinone and Warfarin, zinc phosphide and 2% N-3 – pyridylmenthil-N-p-Nitrophemyl urea (vacor). Avitrol, 4 aminopyridine, a repellent for birds was studied using White Carneaux pigeons and a comparison made between their electroencephalographic patterns and those produced by the dissociative anaesthetics chloral hydrate and ketamine hydrochloride.

On the basis of this study it is concluded that:

1) If without signs of pain or distress, lag phases of several days may be acceptable.
2) All vertebrate pesticides containing anticoagulants must be considered capable of producing a humane death.
3) Additional research is required before other vertebrate pesticides studied can be considered humane.
4) Avitrol appears to be humane based on scientific evidence. However, clinical signs of convulsive seizures will affect public acceptance of this chemical repellant. Both depressive and dissociative anaesthetic electroencephalographic changes occur during its course of action.
5) It is possible to assess vertebrate pesticides for humaneness using techniques designed to study methods for euthanasia. Behavioral, clinical and electroencephalographic observations are important in such assessments. The time for the loss of blinking reflex and a flat EEG are valuable in assessing humaneness.

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INTRODUCTION

In 1975 the Honorable William Newman when Minister of the Environment for Ontario, stated that only humane vertebrate pesticides were to be used in that province. As our laboratory had been studying methods used for euthanasia, we had developed techniques to establish whether or not methods for killing animals were humane, that is, producing rapid unconsciousness without distress. The Ministry's Pesticide Advisory Committee therefore requested that our laboratory undertake a study of vertebrate pesticides used in Ontario, to establish whether or not they produced a humane death.

The concerns of today's society regarding Man's attitude toward animals are constantly before us. Discussion continues on the use of animals in research and our ethics concerned with animal experimentation (1, 2, 3, 4). Questions are raised concerning the trapping of animals for the fur trade. Protests and publicity have been generated concerning the seal hunt off the east coast of Canada. However a note of inconsistency is evident in that those authors animal welfare organizations clamoring for animal liberation or animal rights and attacking "speciesism" (1, 3, 5, 6) have never raised the issue of how man rids himself of the pest or predator animal. In the United Kingdom before and during the last general election, there was a movement to "put animals into politics" (7, 8). The entire country was surveyed and ridings categorized on the basis of sensitivity to animal welfare issues. However, even this animal welfare conscious movement did not list as a concern how pest animals are killed.

Numerous publications are available concerned with pesticides and the destruction of pest animals (9, 10, 11). Some of these describe the toxicity and pathology produced. However, no mention is made of whether or not the pesticide produces pain or distress in the animal before death. It is obvious that to most individuals pest animals are considered as second or third class animals. It is not likely that a protest on their behalf will be mounted on Parliament Hill. There will be no "Save the Rat" campaign. Nevertheless, we should, as concerned human beings, demand that these pests, when killed be killed humanely.

The vertebrate pesticide in order to produce a humane death, must have as in any method for euthanasia the ability to produce an initial depressive action on the central

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nervous system. Therefore, in listing requirements for vertebrate pesticides, we can refer to publications concerned with methods for euthanasia (12, 13). Vertebrate pesticides should not be only painless but safe, reliable and simple to use. Their impact on the environment is also important. Additionally, similar to the requirements in the search for humane traps, vertebrate pesticides should be specific for the target animal.

Some of the vertebrate pesticides that are in use in Canada did not require testing using our laboratory methods for assessment of pain or distress, for sufficient evidence establishing their inhumaneness was available (14). Such agents as nicotine sulfate and strychnine are unacceptable as vertebrate pesticides because they do not depress the central nervous system, but instead affect neuromuscular activity. In spite of this knowledge they are being used. Nicotine sulfate is the common agent used for immobilization in capture guns. Although the use of these two agents for wolf and coyote control is decreasing in most of the provinces, strychnine remains a common poison for predator control in Canada and the United States. Only in the Province of Ontario have commercially available rodent baits containing strychnine been banned.

In the laboratory we ask the scientist using animals: Is the pain always justified? (4). Are they using " the right animal for the right reason" (15) or are they following the principles of "reduction, replacement or refinement" (16)? Despite these genuine concerns, the general public is exposed to claims by antivivisectionists and Animal Rights proponents (1, 2, 3, 6,) that scientists are cruel. The media both press and television, are willing vehicles to promote such claims. Even here, the dog and cat receive greater attention and concern than most other animals. This attitude was obvious in Ontario in the late '60s when the debate concerning the Animals for research act (17) was at its height. The Ontario Government received more mail on the subject of the use of dogs and cats in research than on any other issue that had ever come before parliament. That record response still stands today, despite numerous important human concerns such as Medicare, housing and unemployment.

This clamor was concerned with the use of dogs and cats in research. However the plight of the unwanted companion animal is largely ignored, with the exception of pleas from animal welfare agencies, kennel clubs, and veterinary associations (18, 19) for responsible pet ownership. The result is the euthanasation of thousands of dogs and cats whose only error was to be born.

The general public cares even less for the fate of the pest animal. Instead the criterion of the successful and useful vertebrate pesticide has been that it produces a dead animal. Little concern is shown, for example, for the "lowly" groundhog when a sulfur dioxide bomb (one of the approved, commonly-used pesticides) is sprayed into its burrow. When this gas hits the mucous membranes of the eyes, mouth, nose, and the respiratory tract, it is converted to sulphuric acid, thus causing intense degree of pain before the animal dies of asphyxiation. Similarly, the rat that eats a strychnine bait must endure a period of painful muscular rigidity before dying if asphyxiation.

We, as veterinarians and as members of the Canadian Association for Laboratory Animal Science, should demand for pest animals the same standards and requirements for a humane death (euthanasia) that we consider mandatory for the experimental animal. Furthermore we should make governments, pesticide manufacturers and the general public aware of our concerns and demands for a humane death for animals classified as pests or vermin.

MATERIALS AND METHODS

Using pentobarbital sodium anesthesia, bipolar electrodes were implanted into the brains of male Sprague-Dawley rats weighing an average of 250 grams. Each rat was implanted with a unilateral bipolar electrode in the dorsal nucleus of the hippocampus and one in either the contra lateral, intra – laminar nucleus of the thalamus or reticular formation. The electrodes were anchored to the skull using stainless steel bone screws and dental acrylic.

A polygraph designed for the purpose recorded the electroencephlograms (EEG). Initially, the normal brain tracings were recorded. A pinch of the skin of the rat with a towel clamp was used as a painful stimulus to demonstrate the electroencephalographic changes.

The rats were then exposed to the vertebrate pesticide. The product was either fed in the commercially available form or, in some cases; the active principle was fed or given in solution by stomach tube.

Behavioral characteristics of the rat were assessed prior to and during the entire period of the test.

The period from the time of administration of the pesticide to the time of unconsciousness or death was designated the "lag phase".

When the clinical signs were present, electroencephalograms were recorded at regular intervals and the time of abnormal patterns recorded. The time of unconsciousness was recorded when the blinking reflex (cornea] or palpebral reflex) disappeared and the electroencephlogram became isoelectric or flat.

Detailed post mortem examinations were conducted including histological sections of liver, spleen, kidney, lungs, heart and brain as well as gastrointestinal tract. In the case of pesticides containing anticoagulants, coagulation studies were carried out using standard laboratory techniques. Similarly, when clinical pathology tests were required, standard acceptable methods were used.

The following vertebrate pesticides were studied: Red Squill; those containing anticoagulants - Difenacoum, Brodifacoum, Chlorophacinone and warfarin; zinc phosphide, and 2% N-3 pyridylmenthil-N-p=Nitrophemyl urea (vacor).

Avitrol, 4 aminopyridine, a repellant for birds was studied using White Carneaux pigeons. As the impregnated corn chips bait was refused the active ingredient was administered by stomach tube. A single bipolar electrode was inserted in the reticular formation under chloral hydrate anesthesia and using standard techniques similar to those in rats.

A comparison was made between the electroencephalographic patterns produced by Avitrol and those produced by the dissociative anesthetics chloral hydrate and ketamine hydrochloride which also were administered to White Carneaux pigeons. A single bipolar electrode was implanted in the same location as in those exposed to Avitrol.

RESULTS

The results in this paper are those which are important in assessing the humaneness of individual or groups of vertebrate pesticides. Details concerning the results of specific vertebrate pesticides will be published elsewhere.

The changes in the electroencephalograms when the central nervous system is excited or depressed by the action of the vertebrate pesticide are demonstrated in Figures 1 and 2. All vertebrate pesticides under study produced similar EEG changes. However, in those vertebrate pesticides which were considered to fulfill the requirements for a humane death, the lag phase was short.

Although all vertebrate pesticides produced changes in the appearance and condition of the rats, the animals did not show clinical evidence of pain or distress such as vocalization, shivering, escape reactions or aggressive behavior on touching.

Zinc phosphide compounds are odoriferous. When fed this compound the rats initially ate vigorously but soon appeared to shun the food container, eating only small amounts. Within three to six hours after feeding most animals had a phosphorous or onion smell about their mouths. A small percentage kicked at their abdomens with the hind feet. Generally death occurred within eight hours.

On post mortem examination, a catarrhal enteritis was found in the first 6-8 centimeters of the duodenum; the remainder of the intestine showed no gross or histological changes.

Red Squill, a glycoside, initially produced a posterior weakness and flaccid paralysis. The difficulty in movement about the cages gave the appearance that the rats were uncomfortable. However, again, there were no overt signs of pain or distress. Unfortunately, this posterior paralysis remained until death which took over 24 hours from the onset of signs; thus the lag phase was long.

With the anticoagulant-type agents the lag phase varied from 24 to 72 hours. The animals' electroencephalograms checked during this period showed normal patterns, until signs of imminent death were evident as demonstrated by prostration and rapid breathing. During this latter period a slowing in the response of the blinking reflex was noted and the EEG was depressed. Following the disappearance of the blinking reflex the EEG became flat.

The newer anticoagulant pesticides produced death within 24 hours of exposure; thus the shorter lag phase resulted in fewer changes in the gross appearance of the rat.

Post mortem examination of the rats on anticoagulants showed bleeding, characteristically in the abdominal or thoracic cavity. Almost every rat had some bilateral hemorrhage in the epididymus. Rarely was there any hematoma production. There was no evidence of a hemarthroses (bleeding into joints) or hemorrhage into the brain. No gross or microscopic changes were observed in the liver. The prothrombin times were double normal values and whole blood clotting times were almost triple normal values.

DISCUSSION

All vertebrate pesticides studied produced death in the test animals; however, the length of time required to cause death varied from compound to compound. In general, the lag phase varied from 24 hours to 72 hours. A lag phase of this duration would be unacceptable in other methods used for euthanasia.

There is concern now that the hypoxic methods for euthanasia such as carbon monoxide, carbon dioxide, nitrogen flushing or argon flushing create too long a lag phase, during which time the animal may be able to feel pain. In some cases it has been observed that while the blinking reflex was present that the animal vocalized. Although we do not know precisely whether or not the vocalization is the result of pain, it may be. The CVMA Humane Practices Committee has indicated (17) that until the hypoxic methods for euthanasia can be accepted as humane, additional research is required.

As a euthanasia method cyanide fulfills the requirements of rapid depression of the CNS through immediate paralysis of the respiratory center in the brain. However, there are great risks associated with its use because of its irreversibility and rapidity of action.

With the exception of cyanide, any oral vertebrate pesticide presently available or likely to be developed in the future will continue to have variables but a longer "lag phase" than is acceptable for other methods of euthanasia due to inherent dangers associated with the use of vertebrate pesticides: accidental poisoning of human beings or non –target animals.

One of the requirements of a vertebrate pesticide is that the compound have an antidote which will reverse its action or correct the defect it has caused; thus, we speak of "safety" in acceptable vertebrate pesticides. In this regard, probably the safest of the vertebrate pesticides are the anticoagulant group. In case of poisoning by these, administration of natural Vitamin K will correct the defect in the synthesis of prothrombin by the liver.

Although "safety" for the vertebrate pesticide is an important concern, the industry should be encouraged in the production of pesticides with a more rapid lag phase.

With the exception of zinc phosphide and Red Squill, the lag phase of other vertebrate pesticides produced a change in condition in the animal which was visually aesthetically disturbing. However, using the tests available to us, pain or distress could not be demonstrated. Although it is a truism that we cannot "get inside of the brain of the animal" to know truly what it is experiencing, decreased amplitude and frequency of the EEG tells us the animal is in a depressed state. Scrambling of the brain waves due to convulsions or the action of dissociative anesthetics is accepted as an indication that the animal cannot feel pain because it cannot remember the experience. The latter observation at least is true for human beings.

The flattening of the EEG tells us that if it continues we have an animal with brain death. Also, the blinking reflex (cornea] reflex, palpebral reflex) disappears at the last plane of anesthesia with the exception of administration of dissociative anesthetics such as chloral hydrate and ketamine. Thus we may measure clinically the loss of this important reflex as a indication that the animal is insensitive to pain. With all vertebrate pesticides this occurs as a terminal event. Therefore, we must continue to examine animals exposed to vertebrate pesticides basing judgement on clinical signs of pain, shivering, escape reactions, defensive aggression, painful kicking or muscular rigidity or spasms, and vocalizing.

Both Red Squill and zinc phosphide produced distress of varying degree. Additionally baits impregnated with these compounds were not as readily consumed by the test animals as the anticoagulant baits. This may or may not apply to the field situation. Also one may not, in the feral rodent, see the clinical signs of kicking at the abdomen (as noted in zinc phosphide poisoning) which may be interpreted as a sign of gastrointestinal pain. The feral animal through evolution and environment may have a more resistant gastrointestinal tract. Nonetheless it would be sensitive to the action of the zinc phosphide which converts in the stomach to phosgene gas which is absorbed, hemolyzing the red cells and producing anemia and hypoxia with eventual anoxia and depression of the CNS. This, in theory, should produce an acceptable, humane death. Red Squill a potent glycoside similar in activity to digitalis, should cause cardiac arrest with immediate unconsciousness; however, it did not do this in our test animals.

Anticoagulants work (through a loss of red cells and thus oxygen) by causing hemorrhage. They appear to fulfill the requirements of an acceptable humane death, although again the lag phase may be long and the animals appear in poor condition. In this case there is evidence of depression of the CNS activity as hypoxia and cerebral anoxia develop. Additionally, these agents do not produce joint hemorrhage which would be painful, as evidenced in human beings and animals with hemophilia, blood coagulation or platelet disorders. Again, although hemarthroses did not develop in test animals, we cannot say equivocally that joint bleeding would not occur in the wild rodent exposed to a different environment.

Vacor, a cellular respiratory enzyme, in theory appears to be a valuable vertebrate pesticide; however, the observations for this agent are not complete. The agent acts in relatively short period with posterior paralysis ascending anteriorly. However, the rat appears to be in distress. Thus, additional study is essential.

Avitrol, 4 aminopyridine, is designed for use as a bird repellant. It is to be used principally in areas where bird accumulation can be considered as a hazard such as around airports, or a public health problem around hospitals, food factories or mills, where bird droppings pose a source of contamination or media for growth of pathogenic bacteria or fungi. Avitrol has been used widely as a repellant for blackbirds predating crops such as corn.

Upon eating the active ingredient of Avitrol in a corncob base, the birds then begin to flap wings, vocalize and convulse. Other birds seeing this activity in their colleagues become alarmed and fly away to another area. Critics of the use of bird repellants such as Avitrol claim that their use merely shifts birds from one area to another where they may again become pests.

Avitrol is not intended to kill birds; however, some do die although the numbers are minimal in comparison to the hundreds that make up the flock.

Our studies with Avitrol were intended to study the bird before, during and following exposure to the active ingredient, 4-aminopyridine. Although the result of ingestion of this product is visually repugnant, our studies suggest that the chemical does not cause pathological changes in the organs or tissues capable of causing pain or distress. Before the onset of convulsions electroencephalographic changes are similar to those produced by dissociative anesthetics; during this phase it is considered the bird cannot feel pain.

Studies of convulsions in Man (20) indicate that during the convulsion the individual is not in a painful state. However, the muscular spasms and rigidity during the convulsion can result in tenderness and pain following recovery. Although the convulsion is aesthetically unpleasant to observe, the individual suffering the seizure is not aware of the events during the convulsion. Although it is not possible to determine whether or not birds suffer from muscle pain or weakness following the convulsion, behaviorally they did

not appear to: they sat clucked and walked around normally, with a normal EEG. However, it should be emphasized that immediately following the convulsion, the EEG of the pigeon is decreased in amplitude and frequency, indicating a depressed state (Fig. 3).

Although in man muscle weakness and pain may be an aftermath of convulsive seizures, clinical evidence of this in pigeons following recovery from exposure to Avitrol did not exist.

There is a need to control birds for safety, health and economic reasons. On the basis of our studies in the laboratory Avitrol appears to effectively repel birds within acceptable humane boundaries, based on clinical and electroencephalographic observations. Nevertheless it would be difficult if not impossible to use this agent in built-up, urban areas where birds would be seen during the resultant seizures, as the general public would consider such hyperactivity and seizures painful. All of the evidence in the laboratory relating to clinical and electroencephalographic observations, no matter how scientifically convincing, would not change the opinion of those observing the effects of Avitrol. Therefore, it appears this agent may be of most value around airports and in rural areas. Unfortunately, there are a few good bird control pesticides available. The one most employed is strychnine, and its use should not be condoned by society.

CONCLUSIONS

It is important that when animals are to be killed that they be rendered unconscious and insensitive to pain as rapidly as possible. Unfortunately, vertebrate pesticides must incorporate a certain lag phase because of the risk of accidental exposure. Although the lag phase is important, it is often without signs of pain or distress and lag phases of several days may have to be accepted. Once clinical signs of impending death develop, the length of time for unconsciousness to occur and the electroencephalogram to become isoelectric or flat are important values in assessing humaneness.

On the basis of this study all vertebrate pesticides containing anticoagulants must be considered capable of producing a humane death.

As zinc phosphide causes gastrointestinal irritation in some rats, caution must be expressed concerning the humaneness of this pesticide.

Additional research is required before the other vertebrate pesticides studied can be considered humane.

Avitrol, a repellant for birds, appears to be humane based on scientific evidence. Although clinical signs of convulsive seizures will affect public acceptance of this chemical

repellant, our studies indicated that both depressive and dissociative anesthetic electroencephalographic changes occur during its course of action.

It is possible to assess vertebrate pesticides for humaneness using techniques designed to study methods for euthanasia. Behavioral, clinical an electroencephalographic observations are important in such assessments. The period of time for the loss of blinking reflex and a flat EEG are valuable in assessing humaneness.

Figure 1. A depression of the EEG with excitation (higher amplitude) followed by depression.

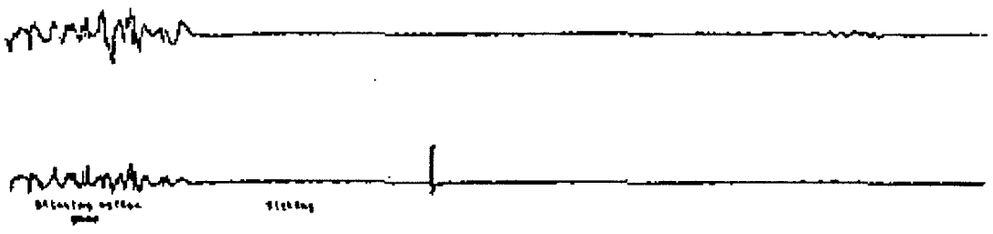

Figure 2. Terminal EEG pattern; blinking reflex absent with Concurrent reflex movement but brain death; flat EEG.

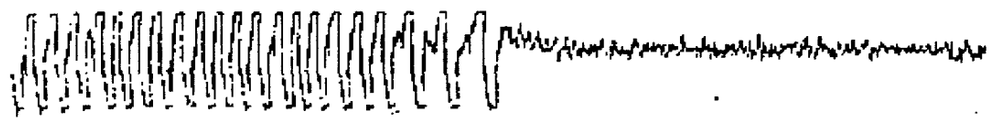

Figure 3. Pigeon - 8 minutes after administration of 1 ml
Avitrol - Irritation - To Depression Tracing
- EEG Flat at 12 minutes
- 4 minutes after this tracing

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