INJECTION OF DRUGS
Barbiturates

Where a veterinarian is available and the numbers of dogs to be killed are not high, the intravenous injection of sodium pentobarbital is the technique which comes nearest to the ideal of euthanasia. Skilled persons working under the supervision of a veterinarian may also carry out this procedure successfully. A competent assistant is necessary to help with restraint of the animal.

Barbiturates depress the central nervous system and their first major effect is to produce unconsciousness. This is followed by arrest of breathing which leads to a rapid cessation of the heart action. The drug of choice is sodium pentobarbitone (pentobarbital sodium) and this is available in three forms vis:

—Sterile solution for anaesthesia at about 65 mg/ml.
—Non-sterile, triple-strength solution for euthanasia at about 200 mg/ml.
—Powder form, often in containers of 1 kg.

The anesthetic solution is too expensive for routine use and even the stabilized commercial euthanasia solution is considered too costly for mass euthanasia in many countries. Where it can be obtained, the powder is the most economic form to employ.

When using the powder, care must be observed that it is kept dry in an airtight container. The powder is readily dissolved at the rate of 200 mg per ml in distilled water, or water which has been boiled and allowed to cool. It is advisable to use the solution within one week during which time it should be kept in an airtight bottle in a cool dark place. A solution which has a deposit or has become cloudy should be discarded.

Although dosage rate of 50 mg per kg is sometimes used, it is generally recommended to employ 100 mg per kg as a routine minimum dose.

Apart from the intravenous injection other routes are employed. Intracardiac injection can give good results with a skilled operator and a reliable assistant. But the humaneness of intracardiac injection is to be questioned. When this method fails and intra-pulmonary injection occurs, the action is delayed and obvious or apparent distress is often caused. Intraperitoneal[4] injection is also used and although the full effects may not be seen for 15 minutes or longer, at least there is less discomfort than when the operator fails to inject into the heart.

One of the practical disadvantages of barbiturates is their price. In many countries the commercial solutions are too expensive for routine use while the powder form may not be marketed. In the industrial countries, especially, control over the use and distribution of barbiturates is likely to become progressively stricter and their availability to pounds may be greatly reduced: the social implications of handling dangerous and addictive drugs must always be stressed.

For regulations and sanctions governing the use of barbiturates for animal euthanasia in the U.S.A., see Appendix.

[4]The intra-hepatic (liver) route is also claimed to be effective causing little discomfort and rapid uptake.

T61*

The use of this commercial product for killing dogs and cats was first reported by Eikmeir (1961) in West Germany and he concluded from experience in killing 350 dogs and cats that the material was very suitable for euthanasia in practice. Its use in private practice has spread in some countries and a major attraction has been that it is sometimes cheaper than commercial solutions of barbiturate (except when barbiturates are bought in bulk). In Italy, under the trade name "Tanax" this material is being widely used to kill unwanted animals in municipal animal pounds.

T61 consists principally of an agent (N [2- (m-methoxyphenyl) - 2 ethylbutyl - (1)] 2-hydroxybutyramide) which has a strong narcotic action as well as a paralytic effect on the respiratory center, combined with a curariform-like drug (4.4-methylene-bis cyclohexyl-trimethyl-ammonium iodide) which exerts a paralytic action on striated muscle and rapidly induces circulatory collapse.

With paralytic drugs of this nature, doubt naturally arises as to whether unconsciousness occurs before the paralyzing effects. There appears to be no reported work resulting from electroencephalograms (EEG) on test cases although an unpublished experiment in Canada (Roswell, 1974) determined that in a rat given T61, the EEG became isoelectric within 4 seconds.

The manufacturers recommend that in dogs the injection should preferably be given intravenously or into the heart, otherwise by the intrapulmonary route. With intrapulmonary injection, care should be taken not to displace the lung tissue and inject into the pleural cavity. This is avoided by using a sharp needle long enough to allow rapid, deep penetration. In cats the intrapulmonary route is considered by the manufacturers to be the most practicable method.

Dosage rates are as follows:

Dogs — intravenously: 0.3 mg/kg, given at medium pace with interruption. Similarly for intracardiac injection.

— intrapulmonary: up to 10 kg give 7-10 ml, above 10 kg give 10 ml, and after falling give additional 3-10 ml

Cats — kittens up to 6 months, give 1-3 ml by intrapulmonary injection

— cats up to 5 kg, give 5 ml

— cats over 5 kg, give 10 ml

When there is greater confidence that T61 is a painless way of causing death, it is likely to become more generally used. Its advantages include its relative cheapness, and the fact that it will not be controlled so strictly as barbiturates. In practice, its use intravenously seems far preferable to the slower and less certain intrapulmonary route.

In animals that are weak, emaciated or have some circulatory abnormality, absorption of the compound may be delayed, euthanasia protracted with distressing convulsions and possibly premature respiratory paralysis before narcotic unconsciousness.

In animals that are moribund, in extremely poor condition or have some circulatory abnormality, the uptake of the compound may be delayed,

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euthanasia protracted with distressing convulsions, and possibly premature respiratory paralysis before narcotic unconsciousness.

The curare-like drug is included to control seizures which may be triggered by the narcotic component. Cerebral excitation will occur if this drug is not administered intravenously according to the manufacturer's instructions (give the first two-thirds at a smooth rate of 1 ml per 5 seconds and then the rest rapidly). The curare-like drug also has a second purpose according to one company veterinary representative: it insures that "if the animal were to regain consciousness, it would die anyway from respiratory arrest" (i.e. suffocation).

Pain reactions, as when a little of the compound is injected subcutaneously by accident, may cause considerable distress even though a local anesthetic ingredient (tetracaine hydrochloride) has been added by the manufacturers.

The manufacturers are not stringent enough in their recommendations. This compound, because of the excitation effects, must be administered by an experienced person. T61 should never be given intraperitoneally or to a sick animal since its uptake will be slow and over-excitation would be unavoidable. There is also the possibility that the curariform effects may then begin to act before the animal is unconscious — a situation analogous to the use of siccinylcholine which is clearly contraindicted as a method of euthanasia. The recommended intrathoracic (lung) route should also be questioned since fluid in the lungs in some animals may cause significant distress prior to unconsciousness. For the same reason T61 should never be given via the intracardiac route unless the administrator is experienced and is 100% confident of entering the heart every time. This intracardiac route for the administration of any material for euthanasia should also be questioned since it may be extremely painful to the animal unless performed by an experienced person.

Other Agents

Chloral hydrate in a 100% aqueous solution and at a dosage of about 2 ml/kg has been used by the intravenous route to kill dogs.

Magnesium sulphate in a saturated aqueous solution approximately 1 g/ml) is also in use and effective when a dose of 2.5 to 4.0 mg/kg is given intravenously.

Chloral hydrate has a slower effect on the cerebrum than the barbiturates so that induction of unconsciousness is preceded by more tendency to struggle. Death may occur only after unpleasant manifestations such as gasping, muscle spasms and whining. There is also the reported problem of wide individual differences in response. Since chloral hydrate is a dissociative anesthetic, the corneal blink reflex may not be acceptable as an indicator of unconsciousness. Since it depresses the brain slowly, restraint is usually necessary.

In the case of magnesium sulphate the medullary and cerebral cortex depression occurs simultaneously so that there is loss of sensation before the respiratory paralysis, which causes death, occurs. It quite often happens that muscular spasms with gasping and whining are produced prior to death, especially when the lethal dose can be given only slowly as in the case with larger dogs (Aramez et al., 1958).

Lucke (1975) has drawn attention to experience with magnesium sulphate in humans in which muscle paralysis preceded loss of consciousness.

Small amounts have a neuromuscular blocking effect and in no way depress the nervous system.

Heavner and Rudolph (1973) in their study of magnesium sulphate in cats found that 50-75 mg/kg intravenously caused muscle paralysis and respiratory depression. There were no EEG signs of sedation or narcosis. Magnesium sulphate, to be effective, should be given at a higher dosage and rapidly, the immediate physiological consequence being cardiac arrest. This would probably not be painful and would be similar to fainting syncopy in man. Similarly, a high dose and rapid intravenous injection of potassium chloride may produce immediate cardiac arrest. The use of these relatively cheap chemicals warrants further evaluation, since they may be valid substitutes for more costly (and dangerous/addictive) drugs.

The attraction of these three drugs is that they are cheaper and more rapidly obtained than the barbiturates, but they have the limitation of being effective only through intravenous or intracardiac injection. While the use of either following a barbiturate injection sufficient to cause unconsciousness will effect a saving in cost, neither drug may have potential for the painless killing of dogs and cats in the future, except in those countries where costs are prohibitive for anything but the most inexpensive solutions.

Air Embolism

Air embolism is an extremely effective and rapid way of producing death in rats. H.C. Rowsell (personal communication) states, "Following 2 ml of air intravenously, the blinking reflex was present for 15 seconds and after 10 seconds, the electroencephalogram became abnormal and flat in 45 seconds. There was vocalization and gasping when 5 ml of air intravenously was given; it did not change the time for the blinking reflex to disappear. It disappeared in 15 seconds; however, the electrocephalogram became abnormal within 4 seconds and became flat within 29 seconds. I appreciate the fact that air is not included because of the variability of the amount required and the rapidity with which it can be injected in larger dogs. Again, however, if a standard method could be developed which would present the amount of air required for various sizes and weights of dogs, it may be less traumatic and faster than the exposure of animals to anoxic methods such as nitrogen, CO_2, decompression, etc. Of course there is a requirement for a considerable degree of technical competence in administering air emboli." However, it is comparable to the target effect of potassium chloride and magnesium sulphate in causing cardiac arrest and thus, in cutting off the blood supply to the brain, will render the animal unconscious quickly and efficiently. Dr. Rowsell concludes that air emboli works the best in any animal already anaesthetized.

Sanford (1976) has pointed out that ketamine and the mixture of steroids known as Saffan may find a use in euthanasia as they allow anaesthesia to be produced rapidly following intramuscular injection. Death could then be caused by injection of the previously mentioned drugs or by some other inexpensive means. Sanford (1976) states that, "The advantage of these compounds is that they act rapidly following intramuscular administration. This may be important where it is impossible to make an intravenous injection. The steroid mixture is not suitable for use in dogs, since, in this species, one of the ingredients of the solution causes histamine release with

an anaphylactoid response. Ketamine induces a state described as "dissociative anaesthesia" with some muscular rigidity in which the animal may respond to external stimuli. It follows that neither of these anaesthetic agents can be regarded as a drug for first choice for euthanasia." (See also chemical capture/restraint).

There is a general agreement that strychnine, curariform drugs and hydrocyanic acid cannot be recommended for humane killing of any animal and so it is sufficient only to mention them. Their use can only be justified under extreme circumstances, such as with a savage or rabid animal. (see also poison baits, page 40)

Addendum

Professor H.C. Rowsell has made the following additional observations concerning the use of potassium chloride and magnesium sulphate for euthanasia.

> "With respect to intravenous potassium chloride, this does cause rapid cardiac arrest. Our studies using the rats have demonstrated that as little as .125 ml. of a saturated solution of potassium chloride intravenously will produce a loss of the blinking reflex in 15 seconds. At the same time a flattening of the electroencephalogram occurs.
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> "Respirations ceased in three seconds following loss of the blinking reflex and the flattening of the EEG. In potassium chloride intravenously, the electroencephalogram and the blinking reflex both disappeared simultaneously in an average time of 14 seconds. There was however a variation in the degree of struggling after the electroencephalogram became flat. The muscular activity in the rats injected with potassium chloride was not visually as disturbing as that seen following the intravenous injection of a saturated solution of magnesium sulphate. With the magnesium sulphate the disappearance of the blinking reflex and the flattening of the EEG were comparable, however with magnesium sulphate the flattening of the EEG occurred on the average of three to five seconds after the blinking reflex disappeared.
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> "The Canadian Council on Animal Care has had some concern about the use of both potassium chloride and magnesium sulphate because of their neuromuscular activity. Both potassium chloride and magnesium sulphate, the EEG become flat and the blinking reflex disappears at a much earlier time period than in any of the anoxic methods for euthanasia. In the latter unconsciousness usually occurs around the 50-90 second period of time. Nevertheless we do not know whether or not the potassium or the magnesium in which affects muscle physiology, may also produce a period of pain albeit for a very short period of time. Therefore, I believe we must be cautious in our acceptance of both magnesium sulphate and potassium chloride."

Recommendations for Research

There does not appear to be need for further research into the use of barbiturates for killing small animals.

For the product T61, it seems essential to demonstrate that unconsciousness occurs before the effects of the paralyzing agent. It will be necessary to study EEG data obtained during trials following the procedures advised by the manufacturers. Only when evidence from such recordings can be examined and found to be acceptable could T61 be considered a satisfactory euthanasia agent. This could be termed Project 2.

Additional information on the efficacy and economics of using certain of the other agents mentioned, either alone or in conjunction with barbiturates, could prove useful. Further research on inexpensive chemicals such as magnesium sulphate and potassium chloride are warranted where economic restraints limit the choice of euthanasia methods.

Further research is needed on these euthanasia agents. Heavner and Rudolph (1973) reported that in cats, "Any anesthetic or analgesic action of magnesium is overshadowed by its neuromuscular blocking effect." Lucke (1975) similarly concludes that, "The use of magnesium salts for euthanasia does present a problem because, as far as I am aware, it is not known at what stage the animal becomes unconscious, if indeed unconsciousness does occur before respiratory paralysis and cardiac arrest."

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