Restraint of Undomesticated Animals

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Summary

The capture, by means of chemical immobilization, of about 100 large African animals of 17 different species was accomplished by use of compound M.99, an oripavine with morphine-like activity, but with approximately 1,000 times the activity of morphine. Usually, the compound was used in conjunction with a tranquilizer and scopolamine. The small dose required enabled M.99 to be administered by a projectile syringe of 2-ml. capacity.

The effect of the immobilizing compound can be reversed with nalorphine or with compound M.285.

A NUMBER of different compounds have been used over the years for aid in capture of wild animals.[6] Successful and safe restraint of animals such as the rhinoceros was achieved in 1960 with the development of a synthetic morphine (diethyl thiambutene)*-tranquilizer-scopolamine mixture.[5] Some of the problems associated with the use of this mixture, such as that of large bulk, were solved with the use of M.99,** a compound with morphine-like activity but with an analgesic activity 6,000 times that of morphine.[1] The effective strength of M.99 for immobilization is approximately 1,000 times that of morphine.

Compound M.99 has been used successfully on at least 100 African animals, representing 17 different species, including the elephant [weighing up to 12,000 lb. (5,448 kg.)], white rhinoceros [5,000 lb. (2,270 kg.)], black rhinoceros, hippopotamus, giraffe, buffalo, zebra, and a number of kinds of antelope such as the wildebeest, kudu, eland, and nyala.

Compound M.99

Compound M.99 is an oripavine derived synthetically from thebaine, a naturally occurring alkaloid in opium and in itself a therapeutically useless by-product of morphine and codeine manufacture. Though thebaine has some action on the central nervous system, it is devoid of analgesic activity.[10] Dienophil derivatives of thebaine have been described as having high analgesic potency, and a number of the ketonic adjuncts were found to have actions similar to that of morphine.[3] Primary and secondary alcohols, produced by the reaction of Grignard reagents on these dienophil derivatives of thebaine, were found to possess greater analgesic activity. Compound M.99 is an alcohol of this type. The formula for M.99 is 6,14-endoetheno-7-α(-2-hydroxy-2-pentyl)-tetrahydro-oripavine. However, the compound is supplied in the form of the water-soluble hydrochloride.

The bases obtained have analgesic activities up to 10,000 times greater than that of

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*Themalon, Burroughs Wellcome & Co., London, England.

**Reckitt Pharmaceutical Research and Development Laboratories, Hull, England.

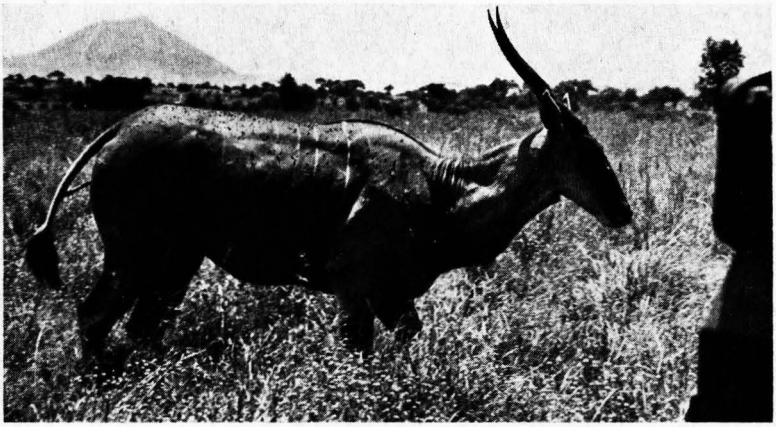

Fig. 1—A cow eland, exemplifying how animals under the influence of M.99 tend to approach a motor vehicle. The projectile syringe can be seen under the tail. The objects on the back are seedheads.

morphine when determined by the subcutaneous route in rats (tail-pressure method); high activities have been confirmed in other animals.[3]

In doses higher than that needed to produce analgesia, a tranquilizing effect is apparent. Further increases in doses produce a state of "total analgesia" or areflexia without apparent loss of consciousness. Unlike morphine, these analgesics do not liberate histamine even in doses many times higher than that required to produce analgesia.[10]

Compound M.99 has a pharmacologic profile similar to that of morphine. In laboratory animals, M.99 produces analgesia, depression of respiratory and cough centers, and lowering of the body temperature. In the hoofed animals, the injection of M.99 in immobilizing doses produces minor depression of respiration, cessation of ruminal movements, a stiffness of the musculature of the neck and limbs, tachycardia in some animals such as the sheep and donkey, and a rise in the blood pressure in the sheep.

At low doses, the animals will remain on their feet but may walk with a high-stepping or "hackney" gait, which gives way at high dose levels to a stiff stance with all 4 limbs straight. During this stage, the animal may lean against a tree or log. At slightly higher doses, the animal will go down but will usually retain upright recumbency, with the head held off the ground.

One of the central effects of M.99 is the alleviation of the feeling of fear, so that animals are often drawn to bodies that excite their curiosity even if these are normally avoidance objects (Fig. 1).

Dose.—For M.99, the dose rate for most animals is about 1 to 2 mg. total dose (e.g., the zebra requires about 1.5 mg.; the rhinoceros, 1.0 to 1.5 mg.), so that only small amounts need be used. For wild animal capture, M.99 is dissolved in water at a concentration of 5 mg./ml., so that only a fraction of 1 ml. need be injected to effect capture. In practice, a tranquilizer and scopolamine are usually added, making up the bulk of solution for injection to 2 ml. It is thus possible to standardize on 2-ml.-capacity syringes. The small quantity injected results in expeditious absorption and overcomes one of the principal disadvantages of the thiambutene mixture used previously. The quantity of thiambutene mixture needed for rhinoceros caused ballistic problems associated with the need for 20-ml.-capacity projectile syringes, and there was slow absorption of the large bulk of injected solution.

The species differences for M.99 doses are small, and generally animals of the same size need very similar amounts for capture. An optimum dose rate may be established for grown animals of a particular species, and the rate need not be computed per unit of body weight. Variations in the amount injected are used principally in relation to the required pattern of immobili-

zation; for example, 1.0 mg. is sufficient to enable a zebra to be restrained after an indefinite time lapse. With an injection of 1.5 mg., the zebra will become immobilized in approximately 8 minutes and usually will go down. With 2.0 mg., it will be down in 3 to 4 minutes.

Dose rates for a series of African animals have been given elsewhere.[9]

Safety.—The variation in dose is large. This variation is sufficiently great to obviate the need of weight estimation in the medium-sized ungulates and greatly facilitates assessing the dose for the large animals such as the giraffe and elephant.

The full extent of the safety margin for wild animals has not been computed; neither has the minimum lethal dose for domestic stock. A considerable variety of doses has been administered to domestic stock without fatality. Five hundred times the "knock-down" dose given intravenously permits spontaneous recovery in the goat. Ten times the immobilizing dose was given safely to steers and donkeys, although use of an antidote was required.[7]

Mortality.—Approximately 100 wild animals have been captured with M.99, the rhinoceros composing half of these. Actual mortality directly attributable to the drug

Fig. 2—A bull elephant, under the influence of M.99, is tested for reaction before an approach is made from the front. With the elephant standing in this position, circulatory experiments may be performed. Access to ear veins is gained by use of a ladder placed against the back. The object in the right ear is an aberrant syringe fired at the shoulder but intercepted by the ear. This shot was ineffective because the ear was completely pierced by the needle.

Fig. 3—A bull rhinoceros, body weight about 4,500 lb. (2,025 kg.), waits quietly under the influence of M. 99, prior to shipment. Entry into the shipping crate can be induced by a gentle push or the injection of antidote.

has been observed only in 2 elephants that died during the recovery phase about 1 to 2 hours after capture. One white and 1 black rhinoceros died some hours after apparent recovery while in a crate during transport. One giraffe died after regurgitating and then inhaling ruminal ingesta, subsequent to inexpert casting after being immobilized in a standing position.

The deaths in elephants occurred in an early series, and the procedure has been since modified, particularly with regard to the length of time these large animals are left lying on the ground if they go down on their brisket. The black rhinoceros had chronic endocarditis and had in fact been caught and transported a year previously under the effect of phencyclidine.* The giraffe should not be cast with the head held on the ground, except under the most exceptional circumstances and with special precautions.

Posture.—At medium dose rates, the animals tend to remain on their feet (Fig. 2 and 3). If they go down, they will, in most cases, remain in sternal recumbency. This retention of the righting reflexes is of considerable advantage when dealing with animals in the field, particularly as these animals may be temporarily lost from view and therefore remain without the benefit of resuscitation for some time.

When the animals are on their feet, or have been brought to their feet after a small dose of antagonist to the immobilizing drug, they may be walked to a weighing platform or led into a crate for transport. Giraffes have been led several miles to a holding enclosure under drug influence, and the rhinoceros to an area accessible to the truck carrying the crate.[8]

The upright position greatly facilitates the taking of accurate measurements and the general examination of the animal.

Behavior.—The demeanor of animals under the influence of M.99 is tranquil and sedated, and this attitude will, in most cases, remain after the antidote to the com-

*Sernylan, Parke, Davis and Co., Detroit, Mich.

pound has been administered. It is usually not possible to tranquilize wild animals with tranquilizing compounds alone in the short time available in the field. If a tranquilizer is mixed with an immobilizing narcotic compound and the latter is reversed, then the animal will remain in a tranquil state. More tranquilizer may be given later, or it may actually be mixed with the narcotic antagonist. The partial or residual effect of the M.99, together with the effect of the tranquilizing agent, renders most animals completely docile. While in this state, the animals may be handled for physiologic investigation with little or no physical restraint.

Antidotes.—Most of the animals given injections of M.99 were given nalorphine* to counteract the effects of the M.99.

In medium- and small-sized animals, the effect of nalorphine is almost immediate awakening. Animals that are down will jump to their feet in 30 to 90 seconds and usually canter off.

The large animals such as the elephant and rhinoceros are somewhat slower to respond. The elephant is the only species that has on occasion failed to respond to nalorphine alone, necessitating the use of stimulants.

For full effect, nalorphine must be given in quantities relating to the animal's body weight rather than to the dose of M.99. Thus, the reversing dose of nalorphine for a 500-lb. (225-kg.) zebra captured with 1.5 mg. of M.99 would be 40.0 to 80.0 mg.; for a 5,000-lb. (2,250-kg.) rhinoceros, the comparable dose would be 0.5 to 1.0 Gm., and for elephants, a larger dose is needed. Nalorphine itself, in large quantities, has a depressant effect, and large doses are expensive and tend to be deleterious.

More recently, for large wild animals, nalorphine has been replaced as an antidote to M.99 by M.285. A resuscitating dose of M.285 for an elephant is about 40 mg. Compound M.285 counteracts the analgesic action of morphine in the rat and is approximately 35 times as effective as nalorphine.[2] This compound has been found effective in counteracting the depression caused by M.99 in wild animals and much more effective than nalorphine in reversing the immobilizing effect of M.99 in elephants.

The reversal reaction of the animal with the use of nalorphine or M.285 in counteracting the effects of M.99 is very different from the reaction with the use of neostigmine methylsufate* in counteracting the effects of curare. In amounts which are insufficient to effect complete recovery, neostigmine injected intravenously will induce almost immediate reversal of the paralysis so that the recipient animal may turn on his captors or break away. The reaction of the animal to nalorphine or M.285 used to counteract the effects of M.99 is much more gradual and can, in fact, be graduated. In this way, the narcotic effect may be replaced by using additional tranquilizer, or the animal may be led into a crate while still sedated.

Discussion

Like morphine, whose action it resembles, M.99 tends to cause a certain amount of excitement. This excitement stage may militate against its use on animals in close confinement.

Undue excitement may, however, be prevented in several ways. A tranquilizer may be given routinely at the same time as the injection of M.99. In captivity, the tranquilizer might with advantage be given prior to administration of the immobilizing agent.

The excitement stage is prolonged as a result of a very light dose and may be undetectable when a heavy dose is given. Doses therefore should be adjusted accordingly.

The degree of excitement engendered by M.99 differs among the various species, and the various hoofed animals may be divided into 3 or 4 different groups according to whether they need no, little, or much tranquilizer. Elephants fall into the first group, zebra and wildebeest into the 2nd, and eland, nyala, oryx, and kudu into the

*Lethidrone, Burroughs Wellcome and Co., London, England.

*Prostigmin, Roche Products, Welwyn Garden City, Herts, England.

3rd. The giraffe is regarded as being in a group by itself.

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Cerebrospinal Nematodiasis of Moose Infected with *Pneumostrongylus tenuis*

The histopathologic lesions in the central nervous systems of 17 moose with signs of neurologic disease were represented by changes in the parenchyma in the form of microcavitations, gliosis, and perivascular cuffing. There were verminous granulomas and nonsuppurative inflammation in the meninges. Ocular lesions were also present.

The finding of adult nematodes, ova, and larvae in the central nervous system confirmed the presence of *Pneumostrongylus tenuis* in Minnesota moose. The lesions described substantiate the hypothesis that *P. tenuis* is a pathogen of moose and causes neurologic disease during natural infection.—*H. J. Kurtz, K. Loken, and J. C. Schlotthauer. Am. J. Vet. Res., 27, (March, 1966): 548.*