THE USE OF ORIPAVINE HYDROCHLORIDE (M-99) IN THE DRUG-IMMOBILIZATION AND MARKING OF WILD AFRICAN ELEPHANT (Loxodonta africana Blumenbach) IN THE KRUGER NATIONAL PARK

By

U. DE V. PIENAAR, Ph.D.
(Biologist, Skukuza, Kruger National Park)

J. W. VAN NIEKERK, B.V.Sc.
(Senior State Veterinarian, Skukuza, Kruger National Park)

E. YOUNG, B.V.Sc.
(State Veterinarian, Skukuza, Kruger National Park)

P. VAN WYK, M.Sc. and N. FAIRALL, B.Sc. (Agric.)
(Assistant Biologists, Skukuza, Kruger National Park)

INTRODUCTION

The steep incline in the growth curve of the elephant population in the Kruger National Park over recent years, has been the cause for some misgiving in conservation circles, and has focussed attention on the fact that reliable data on total number, reproductive potential, food requirements and, particularly, such aspects as migration patterns of elephants were for the most part inadequate or even entirely lacking.

A research programme was launched several years ago aimed at elucidating various facets of the population dynamics of elephants in the Kruger Park, and culminated in an aerial census covering the whole area during July, 1964. The aerial survey revealed that the Park was inhabited during the dry season by a minimum total of 2,374 elephant, and valuable information was also obtained regarding distribution, age structure of the population, productivity, etc. (Pienaar et al. 1965).

With the accumulated data at our disposal, it was now possible to obtain a very fair estimate of the carrying capacity for elephant of the different vegetational zones in the Park, and with the reproductive potential also no longer an unknown factor, the envisaged cropping scheme and control of surplus numbers could be planned on sound ecological principals. (Pienaar et al. 1965).

There remained one aspect however, regarding which very little progress has been made, and which has a very important bearing on the

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calculation of carrying capacities for any particular area, reproductive potential, as well as establishing the allowable kill 'ceiling' for future cropping schemes in such areas — i.e. the range requirements and migration patterns of individual elephants or herds within their chosen habitat, and a clear distinction between resident and immigrant animals.

It is common knowledge that solitary or groups of adult elephants may linger in certain restricted areas within the Park (as elsewhere in Africa), far removed from the breeding herds, for the duration of the dry season. With the coming of spring and the early rains these 'bachelor' bulls disperse and roam over large areas. Their wanderings may take them across our borders into the adjoining Portuguese East Africa and Southern Rhodesia, from whence many possibly enter the Park during the dry season, and others may even join up again with breeding herds during the summer months and partake in breeding activity.

It has long been realized that the only possible method whereby the yearly migration routes of elephant herds, as well as these 'bachelor' bulls may be established with any degree of certainty, thus exposing also the rôle of the latter in breeding activity, would be by marking a sufficient number of individuals in such a way that they may be easily recognised from a distance, for at least a six-month period (but preferably longer) after the date of marking. (Harthoorn, Lock and Luck, 1961).

The practical aspects of effecting the safe handling of wild African elephants by employing the drug-immobilization technique, have received the attention of Harthoorn and his co-workers since 1960, and subsequently also by ourselves, Short and other workers.

Harthoorn et al. (1960) originally experimented with succinylcholine chloride, but it soon became apparent that the dosage rate for elephant was critical, and it was found in practice that with the difficulty in judging the weight of these beasts the estimating of an effective paralysing dose was virtually impossible.

The first wild elephants were successfully immobilized and handled by Harthoorn and his co-workers in 1961, using the muscle relaxant gallamine triethiodide (Flaxedil), at a dosage level of about 1.0-1.4 mgms./lb. body weight. The tolerance of the drug was fair, but reasonably accurate estimating of the body weight was still essential in order to minimise the dangers of fatal overdosage. A reliable antidote in the form of neostigmin (Prostigmin) was a decided advantage.

Harthoorn and Luck (1962) subsequently improved on their technique by employing a system of double injection. The neuromuscular blocking agent (Flaxedil) is injected first, at a lower and safer dosage level (0.8-0.9 mgms./lb.), bringing about a state of locomotory paralysis, but with the animal remaining on its feet. This is followed by a centrally acting drug Sernylan (at 0.05 mgms./lb.), which brings the animal down.

Recovery is facilitated by the double clearance of two drugs and the safety margin is considerably increased. When the action of the Flaxedil was counteracted with neostigmin, the subject seemed able to rise to its feet almost immediately.

Although this technique holds considerable advantage over the use of Flaxedil alone, the disadvantages include the large volume of drug needed to immobilize adult elephant, which minimises the effective range of most projectile syringes, and also the double injection which is essential to success.

Despite the lower dosage level of Flaxedil indicated, it remains a dangerous drug to use and is dependent on reasonably accurate weight estimates, which is exceedingly difficult in the field, particularly in the case of single elephant. In addition, drugs such as scopolamine (Hyoscine hydrobromide) or atropine have to be added to the Flaxedil to guard against pulmonary oedema developing in the immobilized beast, and these drugs may produce toxic symptoms at the required dosage level. (5 mgms./ 100 lbs. body weight in the case of Scopolamine).

The technique of neuroleptic narcosis introduced by Harthoorn in 1961 proved eminently safe and reliable for the capture af square-lipped rhino. (Harthoorn, 1962). The method relies on a drug mixture which combines the use of a neuroleptic (Sernylan) with a narcotic (morphine or synthetic morphines such as diethylthiambutene (Themalon), to induce a catatonic and analgesic state which may be referred to as 'twilight sleep'. (Harthoorn, 1962). Scopolamine (Hyoscine hydrobromide), a parasympatholytic drug is added as a third component to the standard mixture, in view of its inherent properties and synergistic action with morphine compounds. An ataractic, such as chlorpromazine hydrochloride (Largactil) may take the place of the neuroleptic (Sernylan).

This method has a very wide safety margin, is not dependent on accurate weight estimates and the narcotic state can be reliably reversed with morphine-antagonists such as Nalorphine hydrobromide (Lethidrone), resulting in a very high rate of recovery.

Harthoorn (1963) subsequently adapted the technique successfully to elephant, and dosages employed per unit of 1,000 lbs. were: Phencyclidine (Sernylan) 100 mgms., Morphine 500 mgms., and Scopolamine 50 mgms.

The only serious practical drawback remaining was the large dart syringes necessary to contain the total dose necessary to immobilize these huge beasts.

With the advent of the new highly potent morphine analogues of the Oripavine series, this last obstacle in the way of the routine capture and handling of even adult elephants was also eliminated. The modified method was first employed in Natal (during 1962) for the capture of square-lipped rhino, substituting Oripavine hydrochloride (M-99) for morphine or Themalon and the faster-acting, buffered tranquilliser Acetylpromazine maleate for chlorpromazine hydrochloride or phencyclidine.

The M-99 mixture, when first applied in the Kruger National Park during 1962, soon proved to be the most suitable drug-combination for the capture and handling of most large herbivorous species (with the exception of hippopotamus), and in view of the very satisfactory results achieved in the case of most other species (Pienaar, Van Niekerk, et al. 1966 in press), a series of field trials was initiated to ascertain its value also in the case of elephant.

The purpose of this paper then, is to provide an assessment of the merits of Oripavine hydrochloride (M 99) as demonstrated by a series of 31 wild African bull elephants successfully immobilized and handled in the Kruger National Park.

MATERIAL AND METHODS

The basic equipment employed for administering the drug mixture to the selected elephant consisted essentially of the Van Rooyen crossbow, described by us in earlier papers (Van Niekerk & Pienaar 1962, et seq.) and 3 cc. capacity dart syringes fitted with special $3\frac{1}{4}$ inch long needles. Distances between marksman and elephant were estimated by means of a "Wild" hunters' range-finder, which facilitated accurate darting of an animal on a predetermined target-area at ranges up to 120 yards.

The very long range made possible by the light dart syringes proved to be unnecessary, and the majority of beasts were darted from a distance of only 50-80 yards. (See fig. 1.)

It was attempted to hit the animals in the hind-quarters from a position directly behind the beast. This was not essential to success, but made for the recovery of the darts, which are relatively expensive items, and are otherwise easily broken or scraped from the hide when the stricken animal moves through bush or upon collapsing on its side.

A hit scored on the rump to the left or right of the base of the tail (see fig. 4), produced consistent deep intra-muscular injection of the drug mixtures. Subcutaneous injections produce inconsistent results and should be avoided.

For obvious reasons it was contrived to stalk the animals in such a way that they were oblivious of human presence at the moment of firing the crossbow.

The affected animals finally go down on their briskets or flat on their sides, and after it was established that a position of sternal recumbency may be detrimental and often causes fatal respiratory distress, all animals in such a position were assisted into a position of lateral recumbency by means of a rope and truck. This was best and most expediently effected by casting a loop of thick rope or cable around one tusk and applying tension by means of a truck in the direction of the opposite hind leg. (See fig. 6.)

In cases where the body temperature rose excessively in fallen animals (Vide No. 12), attempts were made to lower same by artificial means. Water was sprayed over the body, the ear was folded forwards and an

air current was set up by the waving of branches and the beast was shaded from direct sunlight as far as possible.

The antidote was injected intravenously into any one of the numerous prominent veins on the posterior aspect of the ear. (See fig. 10.)

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In the present series only mature bull elephants were utilised as experimental animals, and the majority were darted in two areas inhabited almost exclusively by single or groups of 'bachelor' bulls during the dry season — i.e. Pafuri, in the far north-eastern corner of the Park, and the Dzombo block, to the south and east of Shingwidzi rest camp.

Immobilized animals were measured, heart and respiratory rates and character were recorded, as well as air and body temperatures. Blood, bone-marrow, saliva, urine and faeces samples were collected whenever possible for pH determination and further qualitative analysis.

The weight estimations presented in the table of results were derived from a few known weights of elephants which have been weighed in toto, and of which accurate body measurements were available. The most useful and constant body measurement to correlate with total weight seems to be the circumference of the fore-feet.

Various marking methods were applied to the immobilized animals before administering the antidote, and time alone will tell which will prove the most durable.

Large, 12 inch high numbers were painted in white (and in serial succession) on the rump, ears and shoulders of the animals. For this purpose a highly durable polyurethane marine plastic paint ("Glatex 8" by Buffalo) was used. (See figs. 8 and 9). The tusks were also numbered close to the upper lip, using a saturated solution of Silver nitrate and staining medium, or by etching with a hot soldering iron. (See figs. 12 and 13.)

Branding with a hot iron number on the body was also attempted, but discontinued after it was found that the upper pigmented layer of the skin peels off over the wound and obliterates the number scar.

Small holes were punched into the ear some 3 inches from the outer rim and a piece of tough white or yellow polyvinyl plastic tubing was securely knotted through these holes to form a streamer of some 12 inches long. (See fig. 5 and 15.)

The drugs employed in the narcotic mixtures and otherwise included the following:—

(i) 6:14 Endoetheno-7-α(2-hydroxy-2-pentyl)-tetrahydro-oripavine hydrochloride, better known as M-99, the principal constituent of the narcotic mixture. (Manufactured by Reckitt & Sons Ltd., England.)

This is a highly potent analgesic with 6,000 times the analgesic activity of morphine and a high therapeutic index.

The powdered drug was dissolved in distilled water (of pH 4) to give

working solutions containing 4 mgms/ml. of M-99. It was also dissolved in the organic solvent dimethyl-sulphoxide (D.M.S.O.) at a rate of 10 mgms./ml.* M-99 is much more soluble in D.M.S.O. than water, and concentrations of even more than 10 mgms/ml. are possible. These solutions are stable except for the fact that the D.M.S.O. crystallises on very cold days and has to be heated slightly to body temperature.

* WARNING: The working solution of M-99 in D.M.S.O. should be handled with the utmost care because of the danger of absorption through the skin.

(ii) 2-Acetyl-10-(3-dimethylaminopropyl) phenothiazine maleate, better known under the trade name of Acetylpromazine maleate. (Manufactured by Boots Pure Drug Co. Ltd. of England). It is an ataractic drug with excellent tranquillising properties and particularly fast induction after parenteral administration. Working solutions containing 40 mgms./ml. of the drug were specially prepared for us by the manufacturers.

(iii) Scopolamine. (Hyoscine hydrobromide). Working solutions were prepared containing 200 mgms./ml. of the drug. The reaction of this drug was primarily tested in elephants because of its parasympatholytic properties, which it has demonstrated in such species as the square-lipped rhinoceros, zebra and giraffe.

(iv) Hyalase. (Hyaluronidase B.P.). Manufactured by Benger Laboratories Ltd., England. 1500 International units were sometimes added to narcotic mixtures to facilitate their more rapid induction.

(v) Prednisolon-trimethylacetate ('Vecortenol', Ciba), Hydrocortisone ('Venocortin', Frederiksberg Chemical Laboratories Ltd.), Heptaminol ('Cortensor', Wander) and Amiphenazole ('Daptazole', Nicholas Laboratories Ltd.), were only used where indicated in cases of respiratory distress, shock, cardiac insufficiency and drug intoxication, and in most instances brought about symptomatic relief.

(vi) The morphine antoganists employed to counteract the effect of M-99 were the related Oripavine derivative M-285 (N-cyclopropyl-methyl-6:4-endoetheno-7-(2-hydroxy-2-propyl)-tetrahydro-nororipavine hydrochloride), manufactured by Reckitt and Sons Ltd., and Nalorphine hydrobromide ('Lethidrone', Burroughs Wellcome & Co.).

Aqueous solutions were prepared in the case of both antidotes at a concentration of 10 mgms./ml. in the case of M-285 and 20 mgms./ml. in the case of Nalorphine hydrobromide.

RESULTS AND DISCUSSION

The original series of field trials with M-99 on elephant, during which 4 animals were successfully immobilized, were conducted as far back as December 1962, when we were also fortunate enough to entertain the presence of that eminent worker in the field of drug-immobilization of game, Dr. A. M. Harthoorn.

The results of these early experiments were rather inconclusive: one animal failed to go down; another recovered only with great difficulty and after the administration of cardiac stimulants and nor-adrenaline to coun-

teract hypotension; a third animal died suddenly from cardiac failure after several attempts to rise from a sternal position; and only one case (the very first) could be described as a satisfactory reaction. (Vide cases A-D of the original series in Table 1.).

It was only after completing the present more extensive series of trials, during which a total of 27 elephant were immobilized, that the merits of the various components of the immobilizing mixture could be assessed with relative clarity.

The results of the 31 cases where M-99 was successfully used to bring about a state of complete restraint in wild elephants are presented in summarized form in Table 1, and will be referred to in the discussion below.

An attempt was made to establish the minimum effective dose on elephant of the drug M-99 alone, without the addition of any synergists.

In this context the minimum effective dose is regarded by us as one which will not only cause a state of locomotory paralysis or 'twilight sleep', with the animal remaining on its feet, but one which will bring about the gentle collapse of the animal either on its brisket or on its side, and the complete suppression of sensory perception.

Contrary to what was initially supposed, elephant retain some control over their trunks, even when otherwise immobilized on their feet, and their sense of hearing and even smell is not entirely suppressed. Elephants which were standing rooted to one spot in a catatonic trance, before finally going down, were on different occasions approached by members of the immobilizing team, and the impression was gained that several animals, although immobile and helpless in other respects, were still aware of their presence. The sense of hearing was the last to be impaired, and the animal sometimes became distressed, and even trumpeted softly, when approached too closely. A few others, when sufficiently aroused, even made a pass at their human tormentors with their partly paralysed trunks.

Despite the obvious difficulty in handling such huge beasts while standing on 'all fours', it is therefore *not* desirable and, in fact, may be decidedly dangerous to approach such animals or to handle them until they are completely narcotized and lying flat on their sides with the eye closed. (See fig. 7).

A total dose of $4\frac{1}{2}$ mgms. of M-99 delivered in separate doses of 4 mgms., $\frac{1}{4}$ mgm. and then again $\frac{1}{4}$ mgm. was sufficient to bring about locomotary paralysis in the case of a 13,000 lbs. adult bull, but failed to prostrate the beast. (Case B. of the original series).

This animal appeared to be in all respects oblivious of human presence and was apparently mentally dissociated from its surroundings. The darts were removed with the animal in a standing position, but the beast was not sufficiently handled to ascertain whether it was in fact completely unresponsive to objects or stimuli normally inciting anger or fear.

The antidote (400 mgms. Nalorphine hydrobromide) was administered intramuscularly, and the animal was left and became ambulatory without ever going down.

Another large bull, of similar size (No. 13 of the present series) received a single dose of 9 mgms. of M-99 dissolved in dimethyl-sulphoxide. It ran and walked for about ½ mile before slowing down and stopping. The first signs of ataxia were noted 15 minutes after darting, with the elephant again on the move. It suddenly threw its head and trunk in the air and collapsed in its stride. The beast fell rather heavily on its side and members of the immobilizing team rushed forward to investigate possible injury. Without warning the animal stirred however, its trunk moved and the tip was directed at the advancing humans. Immediately afterwards, it rose to its feet with surprising alacrity, appeared to be fully conscious once more, and milled around cautiously before walking away. A few minutes later it again collapsed heavily without prior notice, and once more assumed a position of lateral recumbency.

This time ample allowance was made for the beast to lapse into a deeper narcotic state before it was approached and handled. At no time was this particular elephant ever deeply under narcosis. Respiration was strong and regular, the ear flapped occasionally and the eye opened several times, particularly when prodded or handled about the head.

The intravenous injection of 40 mgms. M-285 induced a very rapid recovery, and the animal rose to its feet and walked away almost immediately.

The third elephant bull of similar size (No. 14 of the present series) received an initial dose of 8 mgms. M-99 dissolved in D.M.S.O. The first signs of ataxia occurred at 25 minutes and the animal was standing, unable to walk, 30 minutes after darting.

Although rocking backwards and forwards (with the hind legs remaining rigid and the forequarters sagging) in characteristic manner, it failed to go down, and after 76 minutes had elapsed, it received a further dose of 1 mgm. M-99 and 60 mgms. Acetylpromazine. 10 Minutes after the second dart struck the animal went down and rolled over on its side. (See fig. 4).

While standing, this animal was aware of human presence and could not be handled — the trunk never becoming completely paralysed. Marked salivation was noticed. In its final state of lateral recumbency, the animal was deeply under narcosis and was oblivious to pain.

After receiving 50 mgms. of M-285 intravenously the animal stirred, the eye opened and eye reflexes returned, and respiration became deeper and normal. The beast refused to rise, however, when coaxed, and rested on its side in a state of indifferent somnolence for several hours before finally regaining its feet. It stood yet another while in one spot, heavily sedated, before recovering completely and moving away during the night.

It would appear that the minimum effective dose of M-99 alone is in the region of 8-9 mgms. (total dose) for large adult bulls and 7-8 mgms.

for the smaller class adult bulls. In view of the fact that the affected animal never really becomes completely tractable, and the danger of spontaneous recovery if the beast is sufficiently aroused or molested, there appeared to be no point in continuing with this experiment, and it was abandoned in favour of tests with the promising M-99 — Acetylpromazine mixture.

Elephants varied in their reaction to the immediate impact of the dart. If they had been quietly feeding or just standing, unaware of human presence, they would be startled on feeling the dart, perhaps mill around some or even walk away a few paces. They would soon however, resume their tranquil, somewhat somnolent state, particularly when associated with other bulls also at rest. They will then remain with the rest of the group until the drug exerts its effect, and often go down in the midst of their companions.

This was a most gratifying reaction and, in view of the minimum disturbance which it causes, the technique immediately advocates itself as the method of choice for selective elephant control in breeding herds during any future cropping schme within National Parks. (Pienaar and Van Niekerk, 1963b).

On the other hand, elephant in a state of expectancy or alarm will immediately bolt on feeling the dart strike. The majority made off as fast as they could when aware of human presence, but a few also displayed aggressive tendencies and actively attempted to seek out the source of trouble. For safety reasons such animals should not be darted from a range closer than 70 or 80 yards, but the ideal procedure would be to ignore such beasts and to look for others which can be properly stalked. Elephant on the run after darting have moved as far as $\frac{3}{4}$ mile before slowing down when the drug starts affecting them.

Only in one instance did we notice an animal (which was darted in the shoulder) remove the dart by means of its trunk and cast it away from him. A dart in the rump or hindquarters can not be reached by the trunk.

On two occasions, when one of a herd of 'bachelor' bulls was darted, it was observed how others in the herd assisted their stricken companion when ataxia set in, and actively attempted to keep him upright by means of their tusks and trunks. (See fig. 3.) In one case, a huge bull even attempted to withdraw the dart from the leg of the affected animal, but did not succeed. After going down it happened several times that the other elephants in the group would not leave their fallen comrade — this was particularly true when the darted animal happened to be the largest (and probably leading) bull in a group. The younger bulls will then cluster around it and can only be driven off with difficulty.

The first signs of ataxia were noticed as a rule about 12-17 minutes after darting and the animal became 'fixed' in a state of locomotory paralysis soon afterwards. The animal is now unable to move forwards

and the only movement possible is backwards by shuffling its feet. This is done in an effort to retain its balance. The forequarters sag, often to such a degree that the animal almost rests on its elbows, while the hindlegs are tucked under the belly at an almost 'impossible' angle. (See fig. 2.) When on the verge of sitting back on its haunches the animal pulls itself erect with an effort, the hind legs shuffle backwards and then the rocking motion backwards and forwards (with the front legs as the fulcrum) is recommenced. This process may last for only a few minutes, but can also continue for an hour or more, depending on the dosage rate and rate of absorption.

The animal after 'fighting' the effect of the drug in this manner finally goes down gently on its birsket or, more often, rolls over on its side. The latter is the preferred position, as it is also the natural sleeping position of even the largest elephants, if and when they do not doze while standing on 'all fours'.

It was soon discovered that animals rise from a position of lateral recumbency with much less effort than from one of sternal recumbency — particularly where animals in the latter position often pin down the one hindleg under the body. (See fig. 5.)

The most serious drawback of the sternal position is however, the fact that the recumbent animal very soon develops symptoms of respiratory distress, which, if unaided, may culminate in fatal anoxia and cardiac failure. (Vide Cases D and 17.)

The M-99 Acetylpromazine mixture produces respiratory depression to a greater or lesser degree in all affected elephant, but in animals lying on their sides this is only manifested by a slightly slower respiratory rate and decreased depth of ventilation. Animals lying on their briskets exhibit forced and shallow inhalation which becomes more and more irregular. Dyspnoea leads on to a stage where the animal inhales through the mouth, instead of the trunk, in the form of weak, forced gasps, and ends in apnoea (which is sometimes preceded by acute cardiac collapse as in Case D). (See fig. 5.)

Animals lying on their briskets and displaying even the most severe symptoms of respiratory distress, experience immediate and dramatic relief when rolled over on their sides, and soon recover their normal respiratory rate and depth. (Vide Cases No. 12, 19, 20, 24 and 27).

Elephant No. 17 died in a position of sternal recumbency after developing all the unfavourable symptoms described above. A post-mortem performed immediately after death, with the animal still in a 'sternal' position, revealed the cause of death.

It was clearly evident that with the animal in this position, there was enormous pressure by the intestines and abdominal viscera against the diaphragm, making breathing exceedingly difficult and exhausting. Pressure against the posterior caval vein was also great and may have resulted in stasis, which burdened even further the already depressed cardiac function. When 50 mgms. of M-285 was administered, the blood in the ear veins was

completely cyanotic, and death could be ascribed to anoxia and acute cardiac failure.

In the light of these findings, we regard it as essential that all animals going down in a sternal position should be manually or mechanically assisted into a position of lateral recumbency, failing which, the antidote should be administered immediately.

The assumption that elephants cannot lie on their sides for prolonged periods without incurring damage (Harthoorn, 1962) is not substantiated by the present findings. The anatomy and physiology of the elephant is such that there is, as in the case of equines, no danger of bloating in laterally recumbent animals, and such beasts have been left on their sides for four hours and longer without harmful effect.

The impression was indeed formed that, providing there was no gross respiratory depression, or other contraindications, elephant could be left on their sides to recover from narcosis unaided by an injection of antidote. This is an aspect which merits further investigation.

The majority of elephant immobilized with the M-99-Acetylpromazine mixture exhibited signs of increased salivary flow, but no direct evidence of pulmonary oedema could be found.

When completely narcotized the eye was closed, and the pupil was contracted (pinpoint). Body temperatures varied from 95.6°F-99.5°F, and the highest temperature recorded immediately after going down was 100°F (Case No. 17). The heart rate varied from 42-84 per minute and was usually strong and regular. Only in a few isolated cases was there evidence of tachycardia as was described by King and Klingel (1965) for equines, or of a fall in blood pressure.

The respiration rate varied normally from 6-8 per minute, but dropped to as low as 4 per minute in animals under very deep narcosis. In animals lying on their sides ventilation occurred through the trunk and there was often some degree of rattling in the upper air sinuses or throat (when exhaling), and exhaling was occasionally also partly through the mouth.

Anaesthetized animals usually showed the first signs of recovery some 4-5 minutes after the intravenous injection of the morphine-antagonist, and the sequence of events thereafter followed a set pattern. As a rule the ear was folded forwards over the face to deliver the injection of antidote and then left in this position. The first sign of recovery was usually a sudden holding of the breath followed by a deep and forceful exhalation. Breathing returns to normal and is much deeper and regular. The ear flaps back in position and the eye opens and blinks. (See fig. 11.) The latter is a certain sign that the animal is recovering rapidly and it is soon noticed that the beast focuses on moving objects. The tip of the trunk then shows movement and is directed towards foreign scents. Almost immediately afterwards the animal stirs and makes its first attempts to rise.

The act of rising is commenced by kicking the hind legs high into the air. The momentum of the resultant backlash is utilised by the animal to

pivot itself back into a sternal position (with the stomach acting as fulcrum). As is the case with equines, the forelegs are then extended first with an upward flick of the head and trunk, and the hindlegs are shifted in position to lift the animal back onto its feet. It is indeed a remarkable sight to see such a huge beast regain its feet with such a minimum expenditure of energy and effort. (See figs. 12-14).

Depending on the physical state of the animal, the dosage of ataractic drug in the mixture and also the amount of antidote administered, the recovering elephant either rests in the same spot for a varying length of time (often still heavily sedated), or becomes ambulatory almost immediately on regaining its feet. (See fig. 15.)

The marked animals soon seek out and rejoin their original companions or other groups, and are accepted back without misgiving. (See fig. 16).

The optimum dosage rate of M-99 when combined with Acetylpromazine would appear to be 7-8 mgms. (total dose) in the case of the largest elephant bulls (weighing 12,000-15,000 lbs. +), and 5-6 mgms. for the smaller class adult bulls (of 7,000-12,000 lbs. body weight).

Lower dosage levels for adult cows and younger animals could doubtlessly be calculated on a proportional basis. The therapeutic index of the drug is high however, and there is no need for particularly accurate weight estimates.

Compared with the dosage rate for M-99 in the case of most ruminant species (2.0-4.0 mg. gm./lb.), that for elephants is very much lower (0.47-0.67 mg. gm./lb.).

It seems obvious from the tabulated results that M-99 solutions made up in Dimethylsulphoxide (D.M.S.O.) are more rapidly absorbed than aqueous solutions, probably as a result of the remarkable 'spreading' properties of this organic solvent. D.M.S.O. has the added advantage that much higher concentrations of M-99 (10 mgms./ml. and more) are possible in this solvent than in water (5 mgms./ml. max.), so that the total dose required for even the largest elephant bull, plus the necessary synergists is easily contained in a 3 cc. capacity dart syringe.

The addition of Hyalase to the drug mixture does not appreciably decrease the latent period after darting, and is of no consequence in the case of elephant.

Elephants are equally sensitive to the action of the ataractic drug Acetylpromazine maleate than to that of M-99. The optimum dosage of this synergist appears to be 50-60 mgms. (total dose) in the case of the largest bulls and 40-50 mgms. (total dose) for the smaller class. It was apparent that if more than 60 mgms. Acetylpromazine was administered to adult bulls, its hynotic effect becomes so great that the beasts refuse to rise to their feet after the action of the M-99 is cancelled by the morphine-antagonist. They remain in a state of somnolent lateral recumbency which may last for hours. (Vide cases No. 3, 7, 10, 11, 14, 15 and 17A). The depressant effect of Acetylpromazine was experimentally established in elephant No.

10, where 80 mgms. was deliberately injected intravenously with the antidote. The animal reacted to the antidote in the normal way, and was in the act of rising when it collapsed again, rolled over on its side and rested for almost 3 hours before rising spontaneously.

At the low dosage levels employed there was no evidence of interference by the Acetylpromazine with the heat regulating mechanism of the animals as had been noticed in the case of some ruminants.

It was thought that with the excessive salivary flow exhibited by some elephant affected by the M-99-Acettylpromazine drug mixture, and the possible development of pulmonary oedema, that the addition of Scopolamine (at a low dosage level) to the standard drug mixture may be of advantage. A total dose of 100 mgms. (about 1 mgm./100 lbs.) was added to the immobilizing mixture in the case of three animals of the present series (Nos. 16, 17 and 25).

In the case of elephant No. 16, the effect of the Scopolamine (Hyoscine hydrobromide) was not clear other than an arrest of the flow of saliva and a distinct dilation of the pupil. The animal also remained on its feet longer than was usual after showing the first signs of ataxia.

Elephant No. 17 exhibited the typical reaction of an animal in a state of 'twilight sleep', and wandered about aimlessly for almost an hour in a hypnotic trance-like state before coming to a standstill and going down. The impression was formed that the animal, being blinded by the marked dilation of the pupil, became restless and would not succumb to the depressant effect of the narcotic mixture. A similar effect has been observed in giraffe, zebra and warthog. (Van Niekerk & Pienaar et al., 1965). In the latter instance this reaction may be advantageous and facilitates the handling and crating of these animals while still on their feet. In the case of elephants the wandering effect is of no value and may be detrimental to such a large beast as it might injure itself severely by inadvertently stumbling down a steep slope or stepping into a depression in the ground. When the animal finally goes down, the scopolamine may accentuate the respiratory and cardiac depressant action of M-99.

It is significant that the only two animals which succumbed and died during the course of these experiments both had scopolamine added to their immobilizing mixtures.

Elephant No. 25 went down with its hindquarters lying in a cement drinking hole at a windmill. For fear that the beast might roll over and drown in its helpless state, it received an immediate injection of 50 mgms. M-285. The animal rose to its feet 4 minutes later and stepped out of the drinking hole onto level ground, but soon lapsed again into a heavily sedated, 'trance-like' state. It was even possible to paint a number on the hindleg with the animal completely oblivious of human presence. (See fig. 9.) Ataxia again became evident, and progressively more severe muscular spasms and twitching developed, affecting only the forequarters. Salivary flow was evident. The respiratory rate increased and became more

shallow (up to 14 per minute), and the animal exhausted itself trying to remain erect. It eventually went down again flat on its side, 70 minutes after rising the first time. The pulse was rapid and palpitating (water-hammer), and all symptoms indicated shock.

To obviate the possibility of a narcotic relapse a further 30 mgms. of M-285 was injected intravenously, but there was no response, and the muscular spasms did not subside. The administration of prednisolon and hydrocortisone as well as a respiratory stimulant (Amiphenazole) brought symptomatic relief, and the respiratory rate gradually returned to normal. After resting on its side for 51 minutes, the animal rose to its feet spontaneously and recovered completely some time later.

Although all the unfavourable reactions listed above for case No. 25 may not be ascribed to its action, some of the symptoms at least indicated scopolamine intoxication.

It is our considered opinion that the beneficial prophylactic effect that scopolamine may have in preventing pulmonary oedema, is offset by the other untoward reactions which follow on even such low dosage levels (1 mgm./100 lbs.) which are insufficient to arrest salivary flow completely.

The use of Scopolamine as a synergist in the immobilizing drug mixtures for elephant is therefore not recommended.

We are further of the opinion that for elephant M-285 is much to be preferred as an antidote for reversing the effect of M-99 than Nalorphine hydrobromide.

Not only have such prohibitively large quantities of Nalorphine to be used to revive a single elephant (800 mgms.-4,000 mgms.) that it becomes impractical, but the antagonism by nalorphine may also be followed by a relapse. (King and Klingel, 1965.)

The antagonistic effect of M-285 is prompt and complete, and usually no more than 4-5 minutes elapse after an intravenous injection before the animal regains its feet. The optimum dose of M-285 which reverses completely the effect of 5-8 mgms. of M-99, appears to be in the region of 50-60 mgms.

Lower dosages of M-285 (i.e. 30-40 mgms.) would be more than ample to induce the animal to rise, but apparently do not cancel completely the effect of the M-99, and such animals often remain standing in the same spot for several hours before recovering completely.

One animal (No. 5), which received a total dose of 100 mgms. M-285 intravenously, was the only one which displayed aggressive tendencies immediately on regaining its feet, and charged us twice with murderous intent. There is consequently no advantage in administering more than 60 mgms. of M-285 to a recumbent beast unless its immediate recovery is desired.

It was noticed that in male animals the penis becomes relaxed soon after the injection of M-285 and drops from its sheath when the animal rises to its feet. (See fig. 14).

SUMMARY

The material and methods employed for the drug-immobilization of 31 wild adult elephant bulls are described, as well as procedures adopted for marking them in such a manner that they may be easily recognisable for some time after becoming ambulatory once more.

Previous immobilizing drugs used for the capture of elephants are listed and the disadvantages associated with each are mentioned.

The drug mixtures utilised in the current series of experiments are discussed with particular reference to the merits of Oripavine hydrochloride (M-99), a new highly potent analgesic, in neuroleptic narcotic mixtures.

Optimum dosage levels are provided for M-99 and Acetylpromazine maleate (the main constituents of the drug-immobilizing mixture) and the advantages of dissolving M-99 in Dimethylsulphoxide are propounded. M-99 has a wide therapeutic index and its tolerance by elephant is very good.

The adjuvent effect of Scopolamine to the standard drug mixture was investigated and was found to be negative and even dangerous in the case of elephant.

M-285 is preferred to Nalorphine hydrobromide as the morphine antagonist and has proved to be a highly reliable antidote.

It is considered that neuroleptic narcosis, using a drug combination of M-99 and Acetylpromazine maleate, is a very safe and expedient method of rendering tractable even the largest African elephant, for the purpose of marking, control, etc.

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