Report V..44.....

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M-SERIES

VETERINARY APPLICATIONS REPORT

2684

by

R. D. JONES

on

RHINOCEROS, BLACK

date submitted 4/11/66

Report V..44...

TELEPHONE 55641

DEPARTMENT OF VETERINARY CLINICAL STUDIES
SCHOOL OF VETERINARY MEDICINE
MADINGLEY ROAD
CAMBRIDGE

4th November, 1966.

G.Colman Green Esq.,
Manager,
Pharmaceutical Research & Development Laboratories,
Reckitt & Sons Ltd.,
Hull.

Dear Mr. Colman Green,

I would be very grateful if you would examine the enclosed paper to see if there is anything that you or Reckitt's might object to. It is virtually the final draft - I just have some grammatical errors to sort out, but it is essentially as I would like to have it published.

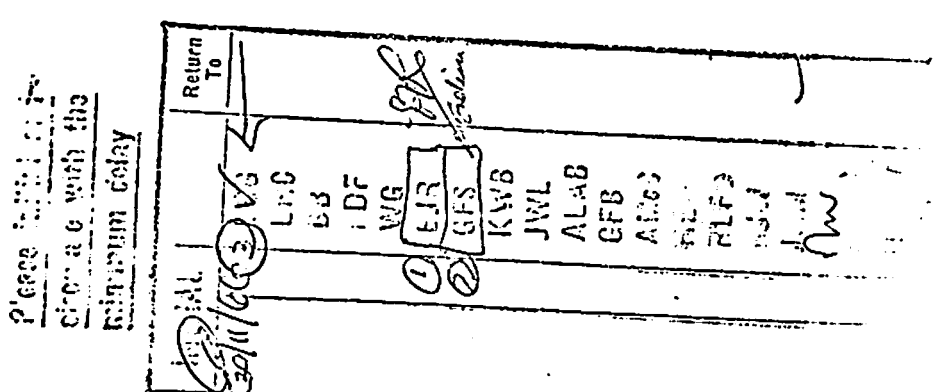
One point that I wonder if you can help me on, and that is whether there is any literature proving that potentiation between M99 and the phenothiazine derivatives does occur (see page 10). If there is I would be grateful for the reference.

I would like to thank you very much for a very pleasant evening at Newmarket, and am sorry that I could not spend more time with you, Dr. Somers, and Dr. Short the next day. Roth never managed his proposed visit as he was ill, so I don't know when he might be over here. I have written to Robinson in Rhodesia following hearing that he has been in touch with you.

I look forward to hearing your comments on the rhino paper.

Yours sincerely,

R.D.Jones.



A Comparison between Morphine and M99 as Narcotics for the Immobilisation of the Black Rhinoceros (Diceros bicornis)

R.D. Jones — covering letter 4/11/66 Cambridge.

Introduction

Due to the pressure of expanding human habitation on the southern border of Lake Kariba, it became necessary to translocate the resident black rhinoceros population. This was carried out by the Rhodesian Department of National Parks and Wild Life Management during the months of July to September, 1964 and 1965.

A total of 36 rhinoceros were captured and this offered an excellent opportunity to compare two narcotic immobilising mixtures. During 1964 a mixture of Morphine, hyoscine and chlorpromazine (M/H/C) was used exclusively, but in 1965 a mixture of M99 and hyoscine was used as well.

The rhinoceros live in a habitat of jesse bush (thickets consisting mainly of Combretum species) interspersed with mopane woodland (Colophospermum mopane) and therefore have to be darted from close range. This gave an opportunity to compare the relative merits of the projectors and projectiles used.

Materials and Methods

1). Drugs

a) Immobilising mixtures

i) Morphine-hyoscine-chlorpromazine (M/H/C) mixture.

The M/H/C mixture used was based on the principle described by Harthoorn, 1962, 1966. For an adult rhinoceros the dose given was 900 mg. morphine sulphate[+], 450 mg. chlorpromazine hydrochloride[++], and 90 mg. hyoscine hydrobromide[+++] in 10 ml.

ii) M99 - hyoscine mixture.

A dose of 1.0 to 1.5 mg. M99[++++] for an adult black rhinoceros was mixed with 100 mg. hyoscine hydrobromide and the solution made up to 3 ml. with 5% w/v dextrose in saline solution (pH 4.0 to 4.5)

b) Antidotes

i) Nalorphine hydrobromide[o] at a total dose of approximately 0.5 mg./Kgm.

ii) M285[oo] - an experimental antagonist.

\+ morphine sulphate B.P.
++ Largactil. May & Baker, Ltd.,
+++ hyoscine hydrobromide B.P.
++++ M99 6:14 endoethno-7 (-2-hydroxy-2-pentyl) tetrahydro-oripavine HCl. Reckitt & Sons, Ltd.
o Lethidrone. Burroughs Wellcome & Co., Ltd.
oo M285 N-cyclopropylmethyl - 6:14 endoetheno-7 (2-hydroxy-2-propyl) tetrahydro nororipavine HCl Reckitt & Sons, Ltd.

c) Therapeutics

i) Procaine penicillin was given routinely before the antidote at a dose of 10 million units for an adult rhinoceros.

ii) Berenil* or Ethidium** was given prior to translocation because of the probable high incidence of trypanosomiasis in the rhinoceros of the Zambezi valley.

2) Equipment

a) Cap-Chur gun, and 10 ml. or 3 ml. Cap-Chur darts+

b) Yeoman cross-bow++ with Cap-Chur darts specially adapted in order to be fired from the cross-bow.

c) Drug ejection was effected either by the bi-carbonate acid or the detonator system+.

3) Methods

The rhinoceros were darted from on foot. Due to the thickness of the habitat it was impossible to use any form of mechanical transport and, further, it was usually necessary to fire the dart from very close range (7 - 25 yards) in order to prevent the dart being deflected by twigs.

* Berenil: Hoechst Farbwerke A.G.
** Ethidium: Boots Pure Drug Co., Ltd.
\+ Palmer Chemical & Equipment Co., Inc.
++ Jack the Yeoman Ltd.

After being hit the animal would run off and then had to be tracked until located. The difficulty of some of the tracking is reflected by some "location times" in the tables. After locating the narcotised rhinoceros a road would be cut to it, and it would be transported to the holding pens. (Savidge, 1965).

The rhinoceros were held at the catching camp for about a month in order that they might settle down, before being transported to Wankie National Park and released.

Effect

1) Drugs

a) The M/H/C mixture

Nineteen cases are recorded in which this mixture was used and the results are tabulated in Table 1.

After being darted the rhinoceros travelled an average estimated distance of just over one mile, while it took an average of 85 minutes to locate them (this figure ignores No. 6 as this animal was darted at night and not tracked until dawn).

The only mortalities following M/H/C administration were in two animals debilitated through injuries received in the wild before capture. These mortalities

occurred some time after capture, and the cause of death was not determined.

b) The M99-hyoscine mixture.

This mixture was used in 17 cases. In the first animal (No.19) darted with the mixture, acepromazine+ was included, but this was subsequently left out for two reasons. Firstly, the effect of the ataractic appeared to mask the antagonistic effect of nalorphine, and secondly there was some reason to believe that M99 would immobilise black rhinoceros satisfactorily without the inclusion of an ataractic. (Colman Green, personal communication). The latter point was born out by the rest of the series.

The results are summarised in Table 2. After being darted, the animals travelled an average estimated distance of ¾ mile, while it took an average of 48 minutes to locate them. One animal was located down in 4 minutes while six were located in less than twenty minutes.

Little is known of the physiological norms of black rhinoceros, while no accurate records were made of their behaviour under the influence of the M/H/C mixture in this operation. However after darting with the M99-hyoscine mixture the animals were usually found in lateral recumbency.

+ Acetylpromazine: Boots Pure Drug Co., Ltd.

There appeared to be tachycardia, a depressed respiratory rate, "tight breathing" and a depressed corneal reflex. The pupillary reaction was difficult to evaluate but was probably dilated with the hyoscine, while the rhino often sweated and salivated slightly.

Shortly after being located the rhinoceros were given a small dose of antidote (Nalorphine or M285) to reduce the heart rate and to relieve the dyspnoea.

Three mortalities occurred after receiving the M99-hyoscine mixture. The first, No 19, died twenty four days after capture, having been transported to Wankie National Park. The post-mortem, which was not done by a veterinarian or a pathologist, showed excess pericardial fluid, ascites, and anasarca in the abdominal region. It had been listless for some days and it is quite possible that its heart was damaged, therefore one cannot exclude the possibility that M99 or Berenil was involved. In addition, the animal was caught when still with its mother and pining due to the separation may have been relevant. Nos. 29 and 35 were both old animals that were debilitated. However, the rapidity with which they were immobilised (6 minutes in each case) may be significant.

c) Nalorphine

Nalorphine was the sole antidote used against the M/H/C mixture and was used in 9/17 cases immobilised with M99 and hyoscine. Small doses were given shortly after location of the drugged rhinoceros to lighten the narcosis while the final injection, given in the holding pens, would enable animals to rise after an average of 10 minutes. This injection was usually not given until just over 6 hours after the animal had been darted due to the problems of transportation. The total dose given was approximately 0.5 mg./Kgm. - all injections were intra-muscular.

d) M285

Intra-muscular injections of M285 were given in 7 cases immobilised with the M99-hyoscine mixture. One of these, No. 29, died before rising. In the other six, the animals got to their feet after an average of 11 minutes - again approximately six hours after being darted.

The small doses used in the field had a similar effect to nalorphine in lightening narcosis and easing the dyspnoea and tachycardia. However, the individual response to the final injection did vary considerably (King and Carter, 1965). Total doses ranged between 4.0 and 6.0 mg. except in case No.22 which was injected

with a further 2.5 mg. when already on its feet. The difficulties experienced with M285 were most marked with case No. 22 in that it developed a panting respiration which lasted for a period of five hours after which the rhinoceros recovered and was quite well. (see Fig.1). It was felt that nalorphine was more reliable to use than M285, although, with further study, the latter may prove equally effective.

2). Equipment

a) Cap-Chur gun

Although the Cap-Chur gun was used with 10 ml. darts exclusively in the 1964 operation, it certainly had its deficiencies as can be seen from the following figures. In a series of 40 shots the needle failed to penetrate in 12 instances. Of the 28 successful penetrations, only 20 animals were immobilised (50% of shots).

The reason for failure to penetrate was lack of power, either due to CO_2 leakage or excess range. Of the eight cases in which the needle penetrated the skin but the rhinoceros was not immobilised, half were due to the needle breaking at the base before the drug was injected. This was because the rhinoceros would turn on feeling the impact and knock

the large (10 ml.) dart against some bush. In three cases it is not known why the drug was not injected, - this may have been due to a core of skin blocking the needle - while in the last the spoor was lost during tracking (Table III).

Unfortunately such a record was not kept for the 3 ml. darts or for the cross bow. However, there is little doubt that the gun is a much more desirable weapon in such thick habitat because it is less cumbersome and, if efficient, is the weapon of choice.

b) Yeoman cross-bow (Short and King, 1964)

The cross-bow proved to be more powerful and easier to maintain than the Cap-Chur gun. Its chief limitation was in its width, being difficult to handle in Combretum thickets during a stalk.

3 ml. Cap-Chur darts were used, but adapted to fit a 6" arrow shaft into the base.

c) The two types of drug injection used both have their advantages and disadvantages. Compared with the detonator system the bicarbonate-acid system is slower in ejecting the drug but requires less impact. It therefore ensures less tissue damage and is more reliable. However its very slowness does result in a risk of the needle breaking or the dart

coming out before total drug ejection, especially with a 10 ml. dart. This risk is virtually nullified by a 3 ml. dart as its volume, weight and length are so much less.

Discussion

This operation offered a useful opportunity to compare the efficacy of the narcotics morphine and M99 for the immobilisation of the black rhinoceros. Furthermore, previously M99 had been used in conjunction with phencyclidine (King and Carter, 1965) or acetylpromazine (Harthoorn and Bligh, 1965) and it was felt that M99 might prove a satisfactory immobilising drug on its own. Its potency has been indicated by Lister, 1964, as well as in field work (Harthoorn and Bligh, 1965; King and Carter, 1965). In this operation it was used successfully with hyoscine, but whether hyoscine is also necessary is open to question. There is evidence that M99 is potentiated by the phenothiazine derivatives ( ) and one can therefore reduce the dose of M99 by adding acepromazine.

However the differences between the M/H/C mixture and the M99-hyoscine mixture were clear. The M99-hyoscine mixture immobilised the rhinoceros much more

rapidly thereby enabling the capture team to locate it and transport it to the pens more quickly. On the other hand, from casual observation, it did appear to stress the animal more by increasing the dyspnoea and tachycardia compared to the M/H/C mixture (Thompson report to Dept. National Parks, Rhodesia, 1965).

The real advantage was in the smaller volume of dart necessary. This meant a higher proportion of immobilised rhinoceros per shots fired because a flatter trajectory, a better penetration, and a greater range were achieved whilst maintaining accuracy, and finally the drug was more certain of being injected before the needle broke or the dart fell out.

The mortality rate suffered during this operation compares favourably with that encountered during the Kariba rescue (Roth & Child, 1963). Then, with Flaxedil^{+}, seven out of twenty-five rhinoceros were lost, and with the M/H/C mixture three out of twenty-two were lost. In this operation two out of nineteen were lost with the M/H/C mixture and three out of seventeen with the M99-hyoscine mixture.

No problems were encountered with radial paralysis although no special measures were taken against this and despite the fact that the rhinoceros were often immobilised for at least six hours (cf. King and Carter, 1965).

The results obtained by King and Carter with M285 are difficult to explain in relation to these findings. It seems possible that their use of phencyclidine confused the issue, resulting in doses of M285 being given that were sufficiently high to produce sedation (Bentley et.al., 1965). In this operation, although M285 did prove reliable on several occasions, it was mistrusted after the experience with case No.22. The dose used was in relation to that successfully used in other species (Jones - unpublished data) and it is felt that this was near the correct dose range.

In conclusion one may say that M99 is an advance for black rhinoceros immobilisation work because it enables much smaller volumes to be used, thereby decreasing the difficulties of satisfactorily projecting the immobilising mixture. At the moment nalorphine is more reliable than M285 but further research may show that M285 is an equally useful antidote.

Summary

The results of the immobilisation of 36 black rhinoceros are recorded. Morphine and M99 were the basic constituents of the cocktails used and the latter was found to have distinct advantages in case of administration with its greater potency.

Both Nalorphine and the experimental antagonist M285 were used as antidotes; nalorphine seemed more reliable.

Some of the problems encountered with the capture equipment are discussed.

Acknowledgements

Rupert Fothergill and Ron Thomson darted all these rhinoceros and without their help and xxxxxxx records this investigation would not have been possible. I am very grateful to them and many other members of the Department of National Parks & Wild Life Management, Rhodesia, for their encouragement and assistance. I wish to thank the Director of the Department for permission to conduct this research, for technical assistance, and for the use of Departmental records. I am particularly grateful to Dr. H.H.Roth, Assistant Director (Research), for stimulus and guidance at all stages of this work, and to Dr. R.V.Short, School of Veterinary Medicine, Cambridge, for much support and advice.

The supplies of M99 and M285 were very kindly xxxxxx made available for this trial by Reckitt & Sons Ltd., Hull. Thanks are particularly due to Mr. G.Colman Green, Manager of the Pharmaceutical Research Division.

Finally I would like to thank the following for financial assistance: Cambridge University Arts Study Group; Mary Euphrasia Mosely Memorial Fund; and Queens' College, Cambridge.

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Table III

Cap-Chur gun — Fired 40 times using 10 ml. darts

Needle penetrated - 28 times

Failed to penetrate - 12 times

Of the 28 penetrations:-

20	-	rhinoceros successfully immobilised
4	-	needles broke before drug injection occurred
3	-	no injection (possibly core of skin in needle)
1	-	lost rhinoceros spoor

Table 1.

IMMOBILISING WITH THE M/E/C MIXTURE.

Mr. P.D. Jones — Cambridge See his 4/4/66.

EFFECT (after darting)				REMARKS
Time to locate coun (mins.)	Distance travelled (yards)	Time to antidote injection (mins.)	Time to get on feet (mins.)	
145	?	405	430	Uneventful
55	900	320	333	"
45	900	329	347	"
80	1800	360	378	"
123	2700	534	538	"
475+	400	682	686	"
20*	1800	20 369	– 371	"
25	1300	305	310	"
170	400	521	528	"
20*	200	236	243	"
70	1800	205	213	"
120	5400	360	364	"
200	3600	518	525	"
135	4500	400	403	"
20	600	265	272	"
45	2700	340	353	"
50	1800	? 217	– 233	"

Table 1.

IMMOBILISATION OF BLACK RHINOCEROS WITH THE M/H/C MIXTURE.

ANIMAL			DOSE (mgms)				EFFECT (after darting)		
	Sex	Est. Wt. (Kgms)	NARCOTIC MIXTURE			ANTIDOTE	Time to locate down (mins.)	Distance travelled (yards)	Time to inject
			M	H	C	NAl			
-	?	850	1000	100	500	400	145	?	4
2	?	550	1000	100	500	300	55	900	3
3	?	950	1000	100	500	300	45	900	3
4	M	1050	1000	100	500	400	80	1800	3
5	F	1050	1000	100	500	400	123	2700	5
6	F	820	1000	100	500	400	475+	400	6
7	F	230	550	50	275	200 100	20*	1800	3
8	F	720	1000	100	500	500	25	1300	3
9	M	850	1000	100	500	300	170	400	5
10	F	850	1000	100	500	500	20*	200	
11	M	1000	1000	100	500	400	70	1800	3
12	F	1050	1000	100	500	600	120	5400	3
13	F	820	1000	100	500	400	200	3600	3
14	F	1000	1000	100	500	600	135	4500	4
15	F	950	1000	100	500	400	20	600	3
16	M	820	1000	100	500	400	45	2700	
17	M	820	2000	200	1000	200 900	50	1800	

Table 1 (cont.)

ANIMAL			DOSE (mgms)				EFFECT (after d		
			NARCOTIC MIXTURE			ANTIDOTE	Time to locate down (mins.)	Distance travelled (yards)	Time injec
No.	Sex	Est. Wt. (Kgms)	M	H	C	Nal			
33	M	910	1000	100	500	400	165	2700	37
36	M	820	1000	100	500	100 200	46	1300	25 35

+ = darted at night, located next morning.
* = time of actually going down.
M = morphine sulphate B.P.
H = hyoscine hydrobromide B.P.
C = chlorpromazine hydrochloride (Largactil, May & Baker Ltd.).
Nal = nalorphine hydrobromide (Lethidrone, Burroughs Wellcome Ltd.).

Table 1 (cont.)

EFFECT (after darting)				REMARKS
Time to locate down (mins.)	Distance travelled (yards)	Time to antidote injection (mins.)	Time to get on feet (mins.)	
165	2700	370	380	Uneventful
46	1300	259 355	259	"

aker Ltd.).
s Wellcome Ltd.).

Table II.

[illegible] OF BLACK RHINOCEROS WITH M99 + HYOSCINE.

EFFECT (after darting)				REMARKS
Time to locate down (mins.)	Distance travelled (yards)	Time to antidote injection (mins.)	Time to get on feet (mins.)	
22	400	40	–	Died 25 days later ?heart failure?
		334	+	
		349		
		454		
93	3600	113	–	Uneventful
		148	–	
		383	398	
16	250	71	–	Uneventful
		127	–	
		291	310	
12	300	44	–	See text
		230	241	
		289		
33	600	51	–	Uneventful
		60	–	
		290	291	
25	900	76	–	Uneventful
		335	345	
46	1800	51	–	Uneventful
		106	–	
		241	246	
110	4400	360	363	Hit low in leg – ? slower absorption?
4	300	10	–	Uneventful
		254	–	
		328	333	

Table II.

IMMOBILISATION OF BLACK RHINOCEROS WITH M99 + HYCO

ANIMAL			DOSE (mgms)					EFFECT (after darting)		
No.	Sex	Est. Wt. (Kgms)	NARCOTIC MIXTURE			ANTIDOTE		Time to locate dorm (mins.)	Distance travelled (yards)	Time inje
			M99	H	A/P	Nal	M285			
19	F	400	1.5	75	30	300	–	22	400	
						200	–			
						200	–			
						200	–			
20	F	1000	1.5	100	–	200	–	93	3600	
						100	–			
						400	–			
21	M	820	1.25	100	–	–	1.0	16	250	
						–	0.5			
						–	3.5			
22	M	1000	1.25	100	–	–	1.5	12	300	
						–	4.5			
						–	2.5			
3	M	820	1.25	100	–	100	–	33?	600	
						100	–			
						400	–			
	F	730	1.25	100	–	–	1.0	25	900	
						–	3.0			
	F	910	1.25	100	–	–	0.5	46	1800	
						–	1.0			
						–	2.5			
	F	950	1.25	100	–	?	–	110	4400	
		350	1.0	100	–	300	–	4	300	
						200	–			
						400	–			

Table II.

: ON BLACK RHINOCEROS WITH M99 + HYOSCINE.

EFFECT (after darting)				REMARKS
Time to locate down (mins.)	Distance travelled (yards)	Time to antidote injection (mins.)	Time to get on feet (mins.)	
22	400	40 334 349 454	– +	Died 25 days later ?heart failure?
93	3600	113 148 383	– – 398	Uneventful
16	250	71 127 291	– – 310	Uneventful
12	300	44 230 289	– 241	See text
33	600	51 60 290	– – 291	Uneventful
25	900	76 335	– 345	Uneventful
46	1800	51 105 241	– – 246	Uneventful
110	4400	360	363	Hit low in leg – ? slower absorption?
4	300	10 254 323	– – 333	Uneventful

Table II.

IMMOBILISATION OF BLACK RHINOCEROS WITH M99 + ETORPI

ANIMAL			DOSE (mgms)					EFFECT (after darting)		
No.	Sex	Est. Wt. (Kgms)	NARCOTIC MIXTURE			ANTIDOTE		Time to locate down (mins.)	Distance travelled (yards)	Time inje
			M99	H	A/P	Nal	M285			
3	F	400	1.5	75	30	300 200 200 200	- - - -	22	400	
0	F	1000	1.5	100	-	200 100 400	- - -	93	3600	
1	M	820	1.25	100	-	- - -	1.0 0.5 3.5	16	250	
2	M	1000	1.25	100	-	- - -	1.5 4.5 2.5	12	300	
3	M	820	1.25	100	-	100 100 400	- - -	33	600	
4	F	730	1.25	100	-	- -	1.0 3.0	25	900	
5	F	910	1.25	100	-	- - -	0.5 1.0 2.5	46	1800	
	F	950	1.25	100	-	?	-	110	4400	
		360	1.0	100	-	300 200 400	- - -	4	300	

277	2600	462	481	2 mg M285 given at 646 mins.
6	400	50	-	Died at 390 mins.
9	400	21 116	- 421	Uneventful
38	2600	45 90 130 225	- - - 235	Uneventful
65	1800	72 184	- 191	Uneventful
45	2600	55 275	?	After antidote at 55 mins. rhino was given 0.25 mg M99 to calm i
23	400	40 500 545	- - 553	Uneventful
6	50	15 400 435 455	- - -	Very old animal. Died.

Co. Ltd.).
Wellcome Ltd.).

Table II (cont.)

28	M	775	1.5	100	-	-	4.0	277	2600
29	F	850	1.25	100	-	-	1.0	6	400
	F	250	0.75	100	-	- -	1.0 3.0	9	400
	F	820	1.0	100	-	200 - 200 - 200 - 400 -		38	2600
32	F	860	1.0	100	-	200 - 300 -		65	1800
33	M	910	1.0	100	-	200 - 600 -		45	2600
	M	720	1.0	100	-	200 - 600 - 200 -		23	400
	M	775	1.0	100	-	200 - 600 - 400 - 300 -		6	50

\+ = on feet before injection of antidote.
* = time of actually going down.
H = hyoscine hydrobromide B.P.
A/P = acetylpromazine (Acepromazine, Boots Pure Drug Co. Ltd.).
Nal = nalorphine hydrobromide (Lethidrone, Burroughs Wellcome Ltd.).