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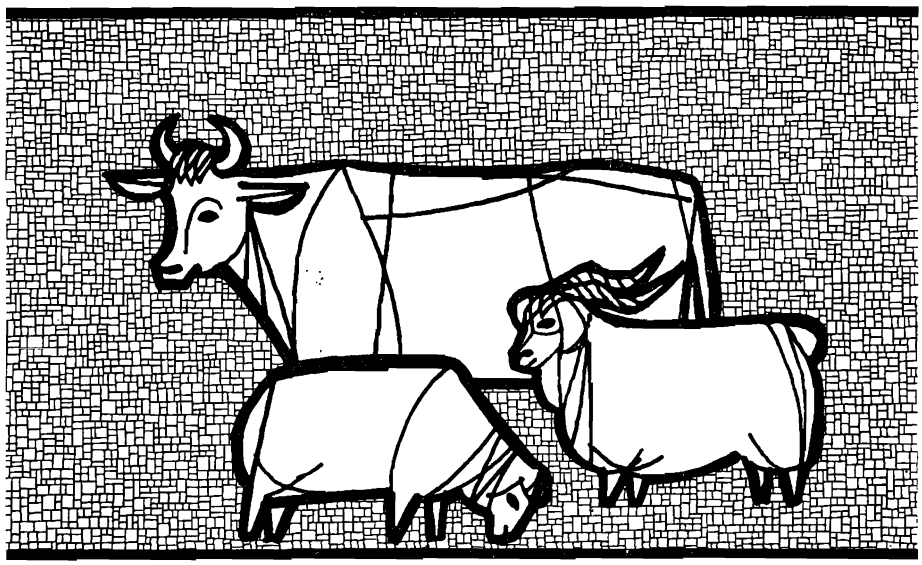

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THE ISOLATION OF *TOXOPLASMA GONDII* FROM FERRETS IN SOUTH AFRICA

R. D. BIGALKE*, R. C. TUSTIN*, J. L. DU PLESSIS*, P. A. BASSON* AND R. M. MCCULLY**.

SUMMARY

The isolation of *Toxoplasma gondii* (Nicolle & Manceaux, 1908) in laboratory mice from naturally infected ferrets is reported. This is apparently the first published report on the isolation of *T. gondii* in South Africa.

Cysts of *T. gondii* were found in the brains of mice inoculated six weeks previously with suspensions of brain, and brain pooled with other tissues, from ferrets. Proliferative forms were found in the peritoneal exudate of both cortisone-treated and untreated mice inoculated with mouse-brain suspensions containing cysts of the newly isolated strains. Six weeks after infection, cysts were again demonstrated in the brains of the survivors. A strain has been taken through four serial passages in mice by subinoculation of cyst-containing brain material.

Five out of six ferrets were found to be infected, which suggested a high incidence of infection in the ferret colony. There were no indications, however, that *T. gondii* was a cause of ill health in the animals examined.

INTRODUCTION

Investigations in numerous countries all over the world have shown how successfully *T. gondii* has established itself as a parasite of warm-blooded animals and man[1 2]. Surveys based on serological tests have revealed a high incidence of infection. This has been amply substantiated by microscopical demonstration in, and isolation of the parasite from diseased and apparently healthy subjects.

Perusal of the available literature indicates that toxoplasmosis has not received much attention in South Africa. A small number of cases of congenital and acquired toxoplasmosis has been recorded in man. In two reports the diagnosis was based on the histopathological demonstration of the organisms[3 4]. Clinical, as well as serological evidence of infection was presented in a number of instances[5 6 7 8]. Fairly extensive evidence of human toxoplasmosis based on serological[9 10 11 12 13 14 15] and dermal hypersensitivity[16] tests has also been forthcoming, but attempts to isolate *T. gondii* have given negative or inconclusive results[11 12 15].

Toxoplasma-antibodies have also been found in cattle, pigs, horses, donkeys[11] and dogs[9] in South Africa. Parasites have been seen histologically in sections of the liver, spleen, lungs and lymph nodes of dogs[17]. They have been demonstrated in spleen smears of a black-backed jackal (*Canis mesomelas* (Schreber))[18 19], and in an unspecified site in a Cape hunting dog (*Lycaon pictus* (Temminck))[20 21]. There is also an unpublished record of the isolation of *T. gondii* from gerbilles and serial passage of the parasite in these animals[22].

Cysts which were morphologically indistinguishable from those of *T. gondii* were observed by three of us (J.L. du P., 1963; P.A.B. and R.M. McC., 1964) in the cerebellum and cerebrum of two ferrets. When further mortality occurred in the ferret colony it was decided, in addition to pathological studies, to attempt the isolation of *T. gondii* from the dead animals. Experimental evidence that *T. gondii* was present in two ferrets that had died, in one that was moribund, and in two apparently healthy animals selected at random, is presented in this report.

MATERIALS AND METHODS

Ferrets.

Six adult ferrets were examined. Necropsies were performed on three that had died (Nos. 1, 2 and 4) and one that was killed *in extremis* (No. 3). Portions of brain, liver, lung and spleen were collected from the first three, and brain and spleen from the fourth animal for inoculation into mice. Brain material was collected for the same purpose from two apparently healthy ferrets which were destroyed with chloroform.

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Mouse inoculation.

Laboratory mice approximately six weeks of age were obtained from a closed colony bred at the Veterinary Research Institute, Onderstepoort.

A mechanical homogenizer or a pestle and mortar was used to prepare suspensions of the ferrets' tissues in Hanks' solution containing 0.5% lactalbumin hydrolysate, and 200 units penicillin, 200 micrograms streptomycin and 2 micrograms fungizone per ml. The suspensions were strained through two layers of gauze and a group of six to eight mice was inoculated with the filtrate of each suspension, individual mice receiving 0.5 ml by the intraperitoneal route (see Table). Each group of mice was housed together in a cage, and several uninoculated mice were usually placed in each cage as controls.

Approximately six weeks after infection the survivors were killed with chloroform. Their brains were removed and examined for the presence of cysts of *T. gondii* by means of the technique, described by Beverley and Watson[2,3] which was slightly modified. This involved crushing half of the brain in 1.0 ml of phosphate-buffered saline and placing 0.02 ml of the resultant suspension onto a slide, which was covered with a cover glass and examined microscopically for cysts under the 10x objective (total magnification being 100x). The total number of cysts present was calculated for subinoculation purposes. Mice that died before six weeks had elapsed were not examined.

The brains of 33 uninoculated mice obtained directly from the mouse colony were examined by the same method.

Passage of strains in mice.

Seven mice were infected with the strain isolated from ferret No. 3 by intraperitoneal inoculation of a mouse-brain suspension, each mouse receiving approximately 25 cysts. Three of the mice were injected with 10 mg cortisone acetate* by the same route the following day. Peritoneal fluid was aspirated from each mouse seven days after infection, a drop of which was dried on a slide, stained with Giemsa and examined for proliferative forms of *T. gondii*. Similar preparations were stained by Gram's method.

Five mice were each similarly inoculated with approximately 68 cysts of the strain isolated from ferret No. 2. Peritoneal fluid was examined from one of these. Six weeks after infection the survivors were killed and their brains examined for cysts. The strain was further passaged in mice.

Histopathological studies.

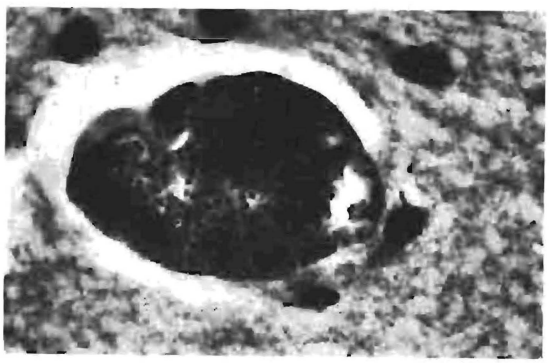
Representative tissue specimens were collected for histopathological examination from ferrets Nos. 1, 2, 3 and 4 at necropsy. Brain specimens were obtained from ferrets Nos. 5 and 6 and from the mice inoculated with ferret tissues. Haematoxylin-eosin stained sections were prepared from these tissues by standard methods. A few sections from heavily infected mice were stained by the Periodic Acid Schiff and by Gram's methods.

RESULTS

Ferrets.

No macroscopic lesions suggestive of toxoplasmosis were seen. The cause of death in ferret No. 4 was septicaemia as a result of acute purulent endometritis, that of ferret No. 2 was not established; neither was the cause of illness in ferret No. 3, which was killed *in extremis*, determined. Cysts indistinguishable from those of *T. gondii* were found in histological sections of the cerebrum of ferret No. 4 and in the cerebellum of ferret No. 6 (Plate 1). There was no evidence of an inflammatory response in the brain sections of ferret No. 4, but a lymphocytic meningo-encephalitis was noticed in the vicinity of the one cyst observed in ferret No. 6. No lesions suggestive of distemper were seen.

Plate 1.



T. gondii cyst in the cerebellum of ferret No. 6 — stained haematoxylin-eosin. X 1200.

Inoculated mice.

With the exception of the group inoculated with material from ferret No. 1, some or all of the mice constituting the survivors in the various groups inoculated with suspensions containing

* Vecortol-Scanpharm

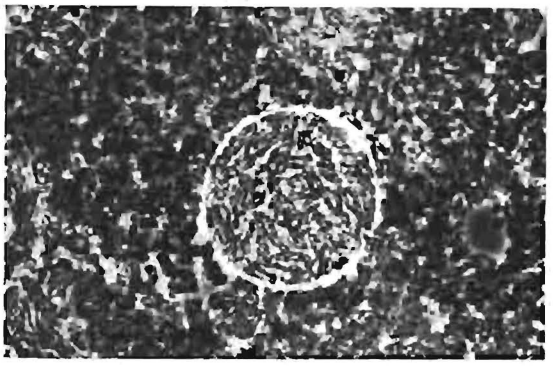
TABLE.—THE PRESENCE OF *T. gondii* CYSTS IN THE BRAINS OF MICE SURVIVING IN EACH GROUP SIX WEEKS AFTER INOCULATION.

Ferrets		Mice	
Ferret No.	Tissues subinoculated	Inoculated	Controls
1	Brain, spleen, liver, lung	0/3	0/1
2	"	3/5	1/1
3	"	3/6	0
4	Brain	6/6	0/3
	Spleen	0/2	0/3
5	Brain	8/8	0/2
6	"	7/7	0/2

A higher percentage of positive cases was detected by the brain suspension technique than by histopathological examination, which was to be expected as only a limited number of sections was examined from each brain. The cysts in brain suspensions were usually spherical (Plate 2), rarely subspherical or elliptical in shape. There was considerable variation in the size of the cysts. In some cysts individual organisms could be clearly seen but in others they were so tightly packed that it was difficult to trace their outlines. The thin cyst wall was discernable and found to be extremely resilient. The cyst illustrated in Plate 2 had been compressed under a cover slide with considerable force. Although a number of organisms were expressed from the cyst in the process, it retained its original shape and showed no evidence of collapse. The calculated total number of cysts per mouse-brain varied from approximately 100 to 4,400.

In haematoxylin-eosin stained sections the cysts were spherical or subspherical in shape (Plate 3),

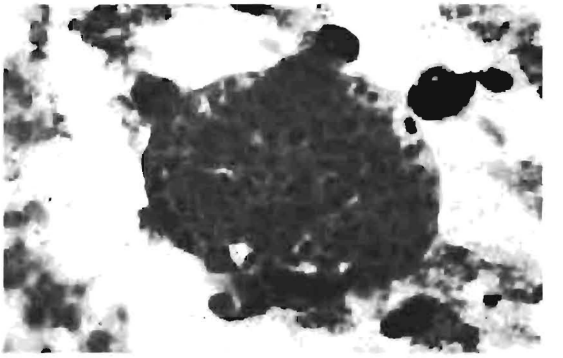
Plate 2.



T. gondii cyst in mouse-brain suspension (fresh preparation — phase contrast). X 615.

and the thin cyst wall was clearly visible. Nuclei of the numerous cyst organisms stained well, but individual parasites were not recognizable. There was no evidence of residual material within the cysts. The organisms were PAS-positive and Gram-negative, which is characteristic for *T. gondii*, and rules out *Nosema cuniculi* (Levaditi, Nicolau and Schoen, 1923)[23].

Plate 3.



T. gondii cyst in the cerebrum of a mouse — stained haematoxylin-eosin. X 1920.

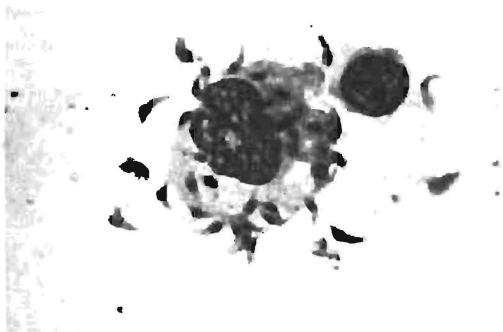
The brains of the uninoculated control mice were histologically negative for *Toxoplasma* cysts. They were also negative when examined by means of the brain suspension technique, with the exception of one mouse in which two cysts were found in 0.02 ml of the suspension. This was apparently an oversight and was considered to have occurred due to the accidental use of the same mortar and pestle previously employed on the same day to prepare suspensions of infected brains. No cysts could be found in brain suspensions of 33 mice which were examined immediately after having been obtained from the mouse colony. Hence it is assumed that the mouse colony is free from naturally acquired toxoplasmosis.

Passage in mice.

Seven days after infection proliferative forms of *T. gondii* were relatively plentiful in the peritoneal fluid of cortisone-treated mice. The crescentic, extracellular organisms were present in considerable numbers and parasitized macrophages were also seen (Plate 4). A fairly profuse peritoneal exudate developed in some of the mice. Organisms were also found in the peritoneal fluid of an untreated mouse, but they were rare. Six weeks after infection cysts could be demonstrated in the brains of survivors by both the suspension technique and histological examination. The four controls were negative.

ferret brain were found to have *Toxoplasma* cysts in their brains (see Table). The two surviving mice injected with spleen material from ferret No. 4 were negative for toxoplasmosis.

Plate 4.



Proliferative forms of **T. gondii** in the peritoneal exudate of a mouse — stained Giemsa. X 1200.

The strain isolated from ferret No. 2 was subjected to four serial passages in mice. Despite the use of small numbers of cysts in the inoculum the mortality rate was high (an average of 60%) and the survivors were often noticeably smaller in size than the uninfected controls.

Discussion

The identification of *T. gondii* on purely morphological grounds is not regarded as being very reliable[2,24]. Proliferative organisms are very similar in appearance to a number of other parasites such as *Besnoitia, Sarcocytis,* merozoites and sporozoites of various members of the order Coccidia, *Nosema* (=*Encephalitozoon*), *Leishmania, Histoplasma* and *Cryptococcus. Toxoplasma* cysts are more distinctive, but schizonts of Coccidia, cysts of *Sarcocystis* and *Besnoitia,* and accumulations of *Nosema* may confuse the issue[2,24].

In order to make a specific diagnosis it has been recommended by Levine[2], Lainson[24] and others that the parasite should be isolated in laboratory animals from tissues which harbour suspected *T. gondii.* Mice are preferred not only because they rarely become infected naturally, but also because they are highly susceptible to artificial infection. After intraperitoneal inoculation, particularly when augmented by cortisone, they usually develop a peritonitis with a profuse peritoneal exudate in which proliferative organisms abound. If the mice survive, cysts of *T. gondii* can generally be found for long periods in brain preparations where they are particularly amenable to manipulations such as differential staining reactions. Cross-immunity or serological tests can also be performed to substantiate the diagnosis.

With the exception of immunological examinations, the foregoing requirements have been met in this investigation, and it is, therefore, considered that a diagnosis of *T. gondii* infection in ferrets is justified. This is apparently the first published report on the isolation of *T. gondii* in South Africa. It is not, however, the first report of the isolation of the parasite from ferrets, Lainson[25] having done so in England in 1957.

Since no proliferative organisms were seen histologically in the tissues of the ferrets, it is assumed that cysts in the brain were the source of infection for the mice used in the experiments. Five of the six ferrets tested were infected and it, therefore, appears that the incidence of toxoplasmosis is very high in the ferret colony under discussion. With the exception of one of the healthy ferrets which was killed for examination and in which a localized lymphocytic meningoencephalitis was observed in the vicinity of a cyst, there were no histological indications in the other four cases that the parasites exerted any deleterious effects on their hosts. The occurrence of the *T. gondii* cysts was apparently an incidental finding, but this does not necessarily mean that the parasite is never responsible for ill-health in the colony. This, as yet, remains to be determined.

An interesting question arising from this investigation is that of the epizootiology of toxoplasmosis in the ferret colony. The ferrets were originally obtained from the United Kingdom and no new introductions have been made since October, 1955. The animals are housed in wire-mesh cages under a galvanized iron roof. Conditions exist that are conducive to spread of toxoplasmosis by a variety of theoretical methods, viz., by close contact, via the food, by some arthropod vector and congenital transmission. A thorough investigation of the epizootiology of toxoplasmosis in this colony might well serve to elucidate the problem of the mode of transmission of acquired toxoplasmosis.

ACKNOWLEDGEMENTS

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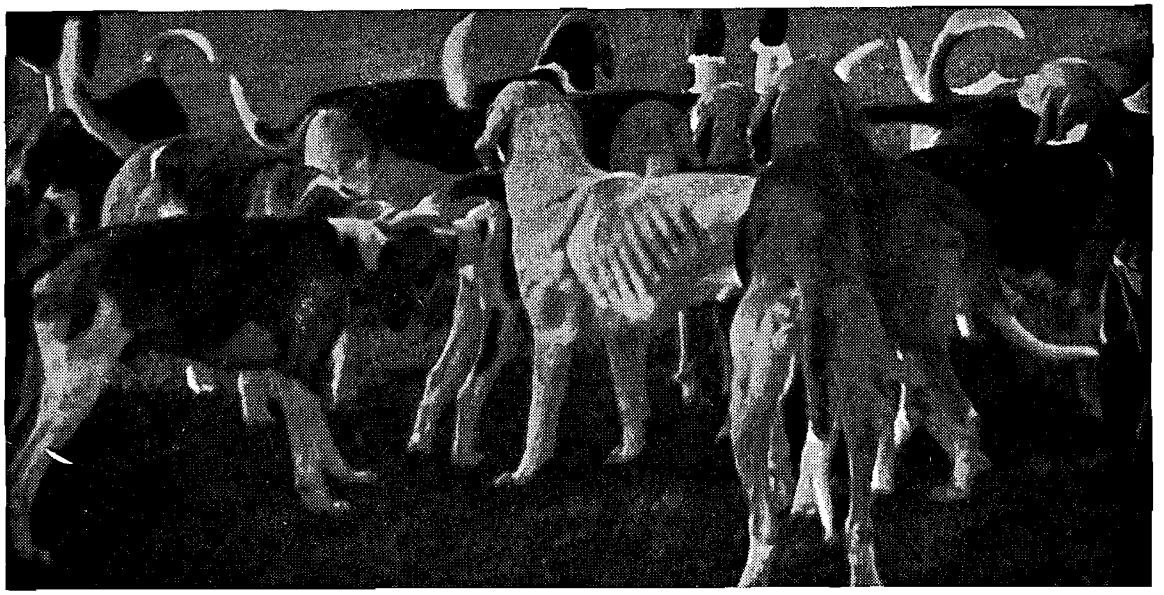
— K. v.d. W.



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MENINGEAL SETARIOSIS: REPORT ON TWO CASES IN ANTELOPES.

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SUMMARY

Meningeal setariosis of two species of antelopes in Southern Africa is reported.

1) Waterbuck (*Kobus ellipsiprymnus* (Ogilby, 1833)). *Artionema labiato-papillosa* (Perroncito, 1882) Yeh, 1959 was found in the subdural cavity in association with eosinophilic cerebrospinal pachymeningitis.

2) Gemsbuck (*Oryx gazella* (Linnaeus, 1758)). One specimen of *Artionema hornbyi* (Boulenger, 1921) Yeh, 1959 was recovered from the subdural cavity without any related lesions.

INTRODUCTION

Setariosis in goats, sheep and horses has been known in the Far East for many years. It was initially described by Emoto[1] as 'lumbar paralysis' and thought to be caused by *Streptococci.* The actual causal parasite, however, eventually proved to be a filarid worm identified as *Setaria digitata*[2] and later suggested to be *Artionema* spp. by Yeh[3]. This parasite was regarded to have cattle and water buffalo as natural hosts[2 4 5] and the adults were found to reside in the abdominal cavity without causing damage. Adults or juveniles were also recovered from a foetus and the eyes, intermuscular connective tissue and intestines of various animals[3]. Mosquitoes were found to be responsible for transmitting the larvae[2 6]. The migratory pattern of the developing parasite has not been fully elucidated, but evidence of tissue migration rather than bloodvascular migration has been presented by Innes and Shoho[7]. In their course the worms pass through the nervous system where lesions are caused in unnatural hosts[2 8]. Innes and Shoho[7] further suggested that the disease in sheep, goats and horses might be an example of an action of a parasite in an abnormal host. Further records of other nematodes invading the central nervous system are fully dealt with by Sprent[9].

The cases that are presently reported were incidental findings in a survey of antelopes for *Gedoelstia* spp[10]. The antelopes showed no paralysis or evidence of migratory routes through the neural substance. The parasites concerned in these cases were *A. labiato-papillosa* and *A. hornbyi.* These antelopes and other Bovidae as well as individual cases in giraffes and baboons known to occur in South Africa are listed in Table 1 together with the *Artionema* spp. reported in them from various parts of Africa[3 11-16].

MATERIALS AND METHODS

During a study of oculo-vascular myiasis in the Kalahari area of South West Africa[17] two gemsbuck were shot and examined for the presence of *Gedoelstia* larvae. This study required very careful examination of the cardiovascular system, brain and its membranes and resulted directly in the detection of another parasite in the subdural cavity of one of these antelopes. The animal concerned was an emaciated, aged bull. The spinal cord was not examined and no tissues were preserved for microscopical study.

In another survey of antelopes in the Kruger National Park for besnoitiosis[18 19], the carcasses were again additionally examined for the presence of *Gedoelstia* larvae. Attention to the brain, spinal cord and craniovertebral canal led to the observations reported below. These and various other tissues and parasites were collected in 10% buffered formalin for histopathological studies and identification purposes. Paraffin blocks were prepared from the tissues, sections cut at 3-4μ thickness and stained with haematoxylin and eosin. The Pandy test[20] was applied to the subdural fluid. Smears were prepared from the lepto- and pachymeninx and stained with Giemsa.

Results

Macroscopic findings.

1. *Gemsbuck.*

Only one parasite was found free on the pachymeninx just below the medulla oblongata. This helminth was subsequently identified by Ortlepp[11] as a female of *A. hornbyi*. No lesions were noticed in the brain or meninges. Specimens of the same parasite were also obtained from the abdominal cavity.

2. *Waterbuck.*

This animal which was shot at random showed no signs of paralysis. One immature parasite was recovered from exactly the same area as in the gemsbuck and identified as a female of *A. labiato-papillosa*. The volume of fluid in the subdural cavity was increased and gave a mildly positive reaction with the Pandy test. Small, raised, opaque greenish- or greyish-white foci, the size of which varied from almost pinpoint to about 2 mm in diameter, were found disseminated throughout the dura mater. These lesions were more prominent in the spinal canal (fig. 1B, C) and in the area just below the medulla oblongata. The leptomeninx covering the occipital lobes of the cerebral hemispheres also showed mildly thickened, opaque foci. (fig. 1A). *Artionema* sp. were also obtained from the abdominal cavity and a similar coiled parasite, which was not specifically identified, occurred in the liver just beneath the capsule of Glisson.

Microscopic findings.

Waterbuck.

Only the histopathological findings of the relevant tissues are given, viz.:

Brain. The arachnoid meningothelium was more cellular in some areas, particularly over the occipital lobes. In certain areas within and adjacent to the longitudinal fissure the collagenous elements were increased. A very mild mixed cell infiltration surrounded a few vessels in this area. Bilaterally symmetrical areas of swollen axis-cylinders occurred in the medulla oblongata. Few apparently necrotic neurones which stained homogeneously purple and scattered swollen axis cylinders were noticed in the midbrain.

Spinal cord. No specific changes other than a suspected mild, focal proliferation of the arachnoid were present.

Dura mater. The most significant lesions were confined to the pachymeninx of both brain and spinal cord (fig. 1C-F). The inner layers and some perivascular zones were infiltrated with eosinophils, round cells or both, with eosinophils predominating more frequently. This was more marked in certain areas. A small number of plasma cells and patchy necrosis of the inner layers were also present. A few foci showed a mild proliferation of the meningothelium and aggregates of syncytial groups of fairly large cells with mildly basophilic cytoplasm. The nature of these could not be determined definitely. The possibility that they were derived from the meningothelium was considered. No microfilaria or other parasites could be found anywhere in the inflammatory foci.

Spinal nerves. Some of the nerves showed the presence of an eosinophilic substance between the fibres and underneath the peri- and endoneurium (fig. 1G, H). Occasionally foci of leucocytic infiltrations were adjacent to certain segments of the nerves (fig. 1I).

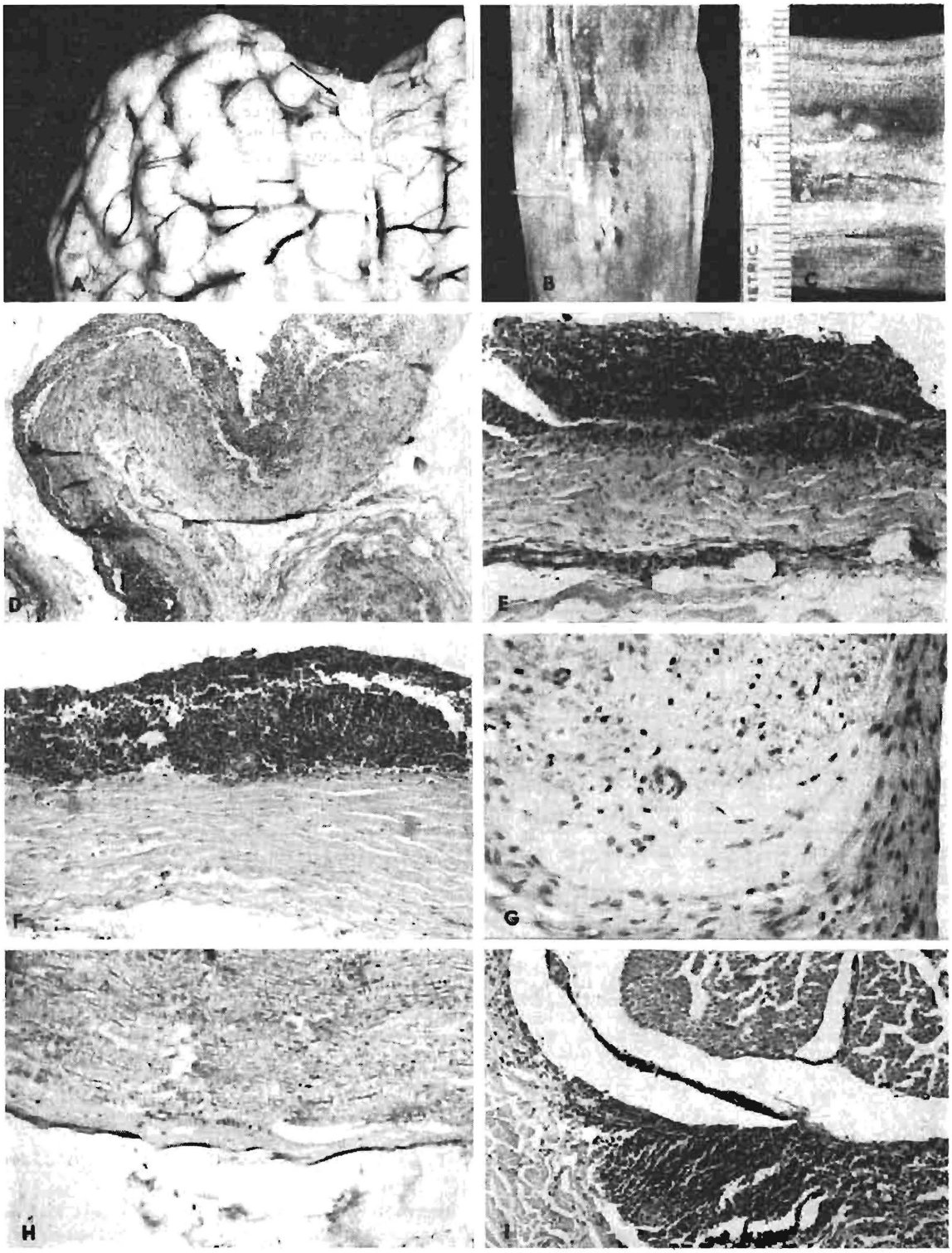
Liver. The coiled parasite underneath Glisson's capsule was dead and surrounded by granulation tissue.

The smears prepared from the pachymeninx revealed many eosinophils. No microfilaria, other parasites or organisms were noticed.

Discussion

In the absence of other possible aetiological agents, more specifically of helminths and dipterous larvae, *A. labiato-papillosa* is considered the most likely explanation for the patchy, eosinophilic pachymeningitis in the waterbuck. With the absence of malacic lesions or cavitation, the foci of swollen axis-cylinders, on the other hand, have a somewhat doubtful relation to the parasite. The eosinophilic substance underneath the peri- and endoneurium of certain nerves was regarded as proteinaceous, oedematous changes and directly as a result of the increased volume of subdural fluid.

In considering the present findings in the light of previous observations that 'lumbar paralysis' has been encountered only in abnormal hosts of *Setaria digitata*[2 7 8] (*Artionema* spp.)[3], certain interesting aspects like host-specificity merit further clarification. Except for *A. labiato-papillosa* and *A. africana*, which are fairly regularly encountered in cattle and Tragelaphinae respectively, the evidence available to date is inadequate to draw any conclusions as to which animals are the natural hosts of the other species. A good example of this is the case with *A. hornbyi* which has been reported from the abdominal cavity of a wide range of hosts (Table 1). In the present two cases the parasites were also encountered in the abdominal



cavities. Their presence in this location, which is considered the usual habitat, is some evidence for their probably being in natural hosts. Should these antelopes therefore prove to be natural hosts of the two *Artionema* spp. under discussion, it is evident that they are not completely harmless in their migratory behaviour and that some of the parasites could show an aberrant tendency by residing in the craniovertebral canal. Furthermore, one can only surmise that the eventual outcome would be of similar nature, should these parasites infest abnormal hosts like sheep or even man. Whether some sporadic cases of paralysis in South Africa and more specifically of spinal or epidural abscessation can be explained in this way, will still have to be determined.

TABLE I.—SOUTH AFRICAN HOST-RANGE OF *Artionema* SPP. FROM AFRICA.

Parasite	Host	References	Locality	Habitat
A. yorkei (Twaite, 1927) Yeh, 1959.	Baboon	OP Collection	Unknown	P.C.
do	Impala (*Aepyceros melampus*)	Twaite, 1927	Zambia	do
do	Bushbuck (*Tragelaphus scriptus*)	Twaite, 1927; OP collection.	Zambia, Mocambique	do
A. labiato-papillosa[*1] (Perroncito, 1882) Yeh, 1959.	Cattle (*Bos*) spp.	OP collection	R.S.A. Lowveld areas.	do
do	Waterbuck (*Kobus ellipsiprymnus*)	do	R.S.A.	*. S.D.&P.C.
do	Giraffe (*Giraffa camelopardalis*)	do	do (lowveld)	P.C.
do	Buffalo (*Syncerus caffer*)	Ortlepp, 1961	Unknown	Unknown
A. scalprum (von Linstow, 1908) Yeh, 1959.	Steenbuck (*Raphicerus campestris*)	Yeh, 1959	Kalahari, R.S.A.	P.C.
do	Impala (*Aepyceros melampus*)	Yeh, 1959	Zambia	do
do	Oribi (*Ourebia ourebi*)	Yeh, 1959	Uganda	do
A. caelum (von Linstow, 1904) Yeh, 1959.	Duiker (*Sylvicapra grimmia*)	Yeh, 1959	West Africa	do
A. poultoni (Twaite, 1927) Yeh, 1959.	Red Hartebeest (*Alcelaphus buselaphus*)	Twaite, 1927	Uganda	do
do	Waterbuck (*Kobus ellipsiprymnus*)	do	Uganda	do
A. hornbyi (Boulenger, 1921) Yeh, 1959.	Roan antelope (*Hippotragus equinus*)	Vevers, 1923	London Zoo	do
do	Gemsbuck, (*Oryx gazella*)	OP collection	South West	*2 S.D.
do	do	do	Africa	do
do	Sable antelope (*Hippotragus niger*)	Boulenger, 1921	Zambia	P.C.
do	Waterbuck (*Kobus ellipsiprymnus*)	Mönnig, 1933	Transvaal, R.S.A.	do
do	Klipspringer (*Oreatragus oreatragus*)	Ortlepp, 1961	Unknown	Unknown
A. boulengeri (Twaite, 1927) Yeh, 1959.	Reedbuck (*Redunca arundinum*)	Yeh, 1959	Zambia	P.C.
do	Rooi Ribbok (*Redunca fulvorufula*)	Twaite, 1927	Transvaal, R.S.A.	do
do	Lechwe (*Kobus ledhe*)	Yeh, 1959	Zambia	do
A. bicoronata (von Linstow, 1901) Yeh, 1959.	do	do	Mocambique, Zambia, Malawi	do
do	Reedbuck (*Redunca arundinum*)	do	do	do
A. africana Yeh, 1959.	Nyala (*Tragelaphus angassii*)	Yeh, 1959	Zululand, R.S.A.	do
do	Cattle (*Bos* spp.)	do	do	do
do	Bushbuck (*Tragelaphus scriptus*)	Ortlepp, 1961	Unknown	Unknown
do	Kudu (*Tragelaphus strepsiceros*)	O P collection	Lake Kariba,	P.C.
A. dipetalonematoides (Chabaud and Rousselet, 1956) Yeh, 1959.	Blue duiker (*Cephalophus monticola*)	Yeh, 1959	Brazzaville, Congo	P.C.&I.M.
Artionema sp.	do	O. P collection	Zululand, R.S.A.	P.C.
do	Sheep (*Ovis aries*)	do	Kuruman, R.S.A.	do

*1 The validity of the species is dealt with in detail by Yeh, 1959 *2 The cases presented in this report.
A = Artionem O P = Onderstepoort P V = Peritoneal cavity. S D = Subdural cavity. IM = Intermuscular tissue.
R.S.A. = Rep. of South Africa.

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NEWSOM'S SHEEP DISEASES

Hadleigh Marsh. Bailliére Tindall and Cox, London. Third edition, 1965. Pages xiv + 456. Numerous illustrations.

Veterinarians all over the world, dealing with diseases of sheep will be grateful to Dr. Hadleigh Marsh for again revising this classical publication on sheep diseases.

There are no major changes in the general organization of the material as compared to the second edition, but in bringing this edition up to date some of the sections have been rewritten extensively.

Although the diseases and toxic plants described are more commonly encountered in the United States, the author's wide experience also in countries like Australia and Britain, and the inclusion of material from the world literature, help to maintain the position of Newsom's as the definitive reference work on sheep diseases.

Like the previous edition, descriptions of diseases are concise and to the point. The bibliographies are not claimed to be comprehensive but include the more important publications on a particular condition which enable research workers, practitioners and students to read more extensively if they so wish.

Many veterinarians already possess and cherish the second edition of Newsom's Sheep Diseases. They would be well advised to aquire the third edition and it only remains to recommend this book to all veterinary students and to those who are newcomers in sheep practice.

— K. v.d. W.

MANHANDLING THE BABY CHICK. II. EFFECT OF DRUGS AND FOOD ADDITIVES.

V. R. KASCHULA. U.N.D.P. BAGHCAD. IRAQ.

SUMMARY

Since there has been an enormous increase in the use of drugs and other food additives in the poultry industry in the past few years, it is questioned whether this trend is justified. The literature, which is scanty as relating to poultry, is reviewed. Since antibiotics, sulpha drugs and others are no doubt capable of side-effects in the human, it is reasoned that this may be an important factor in the chicken also. It is felt that to a large extent drugs are used unnecessarily, and that side-effects and other adverse influences may be occuring yet unnoticed. However there is insufficient information to prove whether the widespread use of drugs has harmful effects but it is hoped that this article will stimulate interest in this aspect of poultry nutrition.

V. R. Kaschula.

INTRODUCTION

In a previous article the author[1] discussed the effects of vaccines and modern methods of husbandry on the baby chick and the diseases to which it is subject. Since drugs are widely used, a discussion of the effect of drugs on the chicken, and especially the baby chick, is relevant. The object of this article is to review some of the literature on the toxicity and side-effects of some of the drugs used in the poultry industry, but as the literature is scanty, reference has been made to some of these drugs in other animals.

In his book "Drugs, doctors and disease" Brian Inglis[2] has recorded some of his findings about the drug industry as it affects human medicine. He reveals some disturbing facts with regard to the side-effects, development of resistance of strains of organisms and social hazards resulting from the over-use of drugs. He also claims that the use of drugs in human medicine is dominated by high-pressure salesmanship by the drug houses whose main interests are economic rather than the promotion of health.

While the medical press has interested itself in these matters there is very little attention paid to them in veterinary literature, which is especially scanty about poultry in spite of the fact that there has been an increase in the use of drugs.

Poultry owners place far too much reliance on the value of drugs. For every disorder it is generally assumed that there is some appropriate remedy. When chickens become sick it is customary to think in terms of a diagnosis and the drugs to be used. Sometimes expert advice is sought but on many occasions experienced farmers will make their own diagnosis, sometimes correctly but on other occasions incorrectly. The general attitude is to resort to drugs when in many cases the basic problems are connected with faults in husbandry, hygiene, nutrition or some other factor.

Modern methods of highly intensive production have created many new problems connected with overcrowding. While drugs are effective in controlling some of the diseases there is generally too little attention paid to the basic faults which caused the trouble. Furthermore there is generally very little if any consideration given to the possible harm that drugs may cause.

Often drugs are used too late in the course of a disease to be of any value and on other occasions the wrong drugs are used due to lack of a proper diagnosis. In still other instances the drugs would have no effect when diseases are viral or nutritional in nature. It is also felt that vast quantities of drugs are used prophylactically when in fact they are unnecessary. This is particularly true of coccidiostats in rations for baby chicks. In many cases they may even be used because it is considered fashionable to do so. An indication of the desire to appear to be up to date is that there is always a marked preference for new drugs over old ones.

HISTORY AND PRESENT POSITION

Twenty years ago very few drugs were used in the poultry industry. Only those common household remedies such as sulphur, permanganate of potash, copper sulphate, magnesium sulphate, garlic and others were generally used. Sometimes these had excellent response, e.g. when perosis was developing and potassium permanganate was given

in the drinking water. In other cases drugs used did more harm than good. Flowers of sulphur was often used to treat coccidiosis. Unfortunately this upset mineral metabolism possibly through adverse influences on the parathyroid and Vitamin D3 so that rickets frequently followed its use. A rather similar situation arises even today where cod liver oil is added to poultry mashes in order to correct either Vitamin A or D3 deficiencies. If the cod liver oil-containing mash is allowed to become rancid — which happens quickly in the tropics — destruction of Vitamin E may result in outbreaks of encephalomalacia when the chicks reach two or three weeks of age. In the tropics the high environmental temperatures adversely effect mineral metabolism with the result that there is an inclination to add large quantities of oyster shell and other mineral compounds. These may play a role in the destruction of vitamins in the food[3]. Even such commonly used food ingredients as soya-bean meal, if not correctly processed before being mixed in the food, can be responsible for destruction of Vitamin A in the mash[4]. Some of the sulpha drugs and other coccidiostats may also help to destroy vitamins or prevent proper metabolism of food ingredients.

There is even a hint that certain batches of cod liver oil high in stearine fraction may influence the incidence of lymphocytomatosis in chickens[5].

There have been significant advances in the formulation of poultry mashes in the past 50 years not only in the knowledge of vitamin and mineral requirements but of proteins and other factors. Norris (1958)[6] has reviewed the most important developments up to that date. Since then, there has been a greater emphasis on the incorporation of drugs, vitamins, and other additives. There is no doubt that feeds are more efficient which has enabled farmers to change methods of husbandry from free range to highly intensive ones, also with greatly increased production. These highly intensive systems are conducive to disease as overcrowding is the usual result. Yet these medicated mashes are largely responsible for the success of these methods, and have made mass production in poultry possible.

The purpose of this article however is not to discuss the merits of these rations but rather to draw attention to some disadvantages, to some of the demerits and indeed to some of the dangers in the trends in the use of medicines in the poultry industry. In the following paragraphs some of the toxic effects, side-effects and the development of drug resistance in organs will be discussed with special reference to the baby chick.

Evidence of toxicities.

The occasional harmful effects of cod-liver oil, causing encephalomalacia, of calcium, oyster shell and other minerals in producing vitamin deficiencies and of moulds in foodstuffs causing aflatoxin and other poisonings have already been discussed. These are mainly of an accidental nature.

It is however mainly with the deliberate incorporation of drugs in foods that this article is concerned, particularly in the food of the baby chick. It is felt that too often drugs are used as food-stuffs and that their possible harmful effects are overlooked or ignored.

All forms of poisoning or other harmful effects may be produced by drugs. Almost without exception, the baby chick is more sensitive than older birds. The chick embryo is even more sensitive and many drugs and ingredients which would be relatively harmless to chickens are highly toxic to the embryo. Thus vitamins A and D[7], antibiotics and furazolidone[8], and metallic solutions[9] even in minute quantities are likely to cause death of embryos. With the new techniques of dipping eggs in antibiotic solutions and other drugs these factors should be borne in mind, not only because of the actual mortality caused but perhaps less obvious defects and retardation of growth, that may occur. It must also be borne in mind that these same materials may be toxic to the day old chick, although probably relatively less so.

The use of drugs in breeding hens producing eggs for the hatchery may affect hatchability and cause death of the embryos. Thus amprolium fed to hens may result in a thiamine deficiency of the yolk of the eggs resulting in chick embryo mortality (Polin[10] et al. and Ott et al[11]). Phenothiazine and carbon tetrachloride can also cause embryo mortality when they are used in laying hens (Szopa, 1963)[12].

Studies on the toxicity of commonly-used drugs in young chicks indicates that they are generally much more sensitive than older chicks. It has been shown that chlordane[13], carbon monoxide[14 15], nicarbazin[16 17], sulphaquinoaline[18 19 20], megasul (nitrophenide)[21], nitrofurazone[2 3], furazolidone [4], (nitrophenide) [1], nitrofurazone[22 3], furazolidone [4], (nitrophenide) [1], nitrofurazone [23], furazolidone[24], sulphonilamide[25], sulphamerazine[26], amprolium[9 10], zoalene[27], and pyrimethamine[28 29], copper[30] and barium[31], were all considerably more toxic for the baby chick than slightly older chicks or even less so for those several months of age.

Antibiotics in feedstuffs.

Antibiotics have more than one mode of action in promoting growth but all workers agree that they affect the microflora of the gut. Jukes and Williams[32] postulated that the antibiotic may inhibit or destroy organisms which produce subclinical infection or facilitate an increase in numbers and activity of organisms which synthesize known and unknown vitamins and other growth factors. Much has been written in recent years on this subject.

It appears well-established that the presence of an antibiotic reduces the requirements for many dietary factors such as pantothenic acid, cyanocobalamin, niacin and manganese. Possible reasons for this are the reduced requirements of a lowered bacterial population or more efficient absorption through the intestinal wall. The exact role of the intestinal tract in this mechanism has not been fully elucidated but it apparently plays an important part in the promotion of growth.

Although antibiotics formerly were regarded as relatively safe drugs with very little danger of side-effects even in humans, evidence collected over the years has accumulated to show that they have been responsible for many different kinds of side-effects such as aplastic anaemias, allergies, etc. (Inglis)[2]. Very little is known about this in animals but it is feasible that some side-effects do occur, yet are unnoticed. The effects on chick embryos have already been discussed. There is considerable support for the theory that antibiotics and sulpha drugs upset the normal bacterial flora in the chicken and they have been suspected of being indirectly if not directly involved in the causation of haemorrhagic disease[33 34 35].

There is considerable evidence that the use of antibiotics in feedstuffs may depress certain organisms and encourage others thus upsetting an equilibrium. Work done in other animals has been reviewed by Owen[36] who has discussed the findings about tetracyclines (TC). He quotes the experiences of Roine *et al*[37] in which heavy doses of 100 mgms CTC per kilo caused illness and death in guinea-pigs and that later some of these guinea-pigs which had received CTC died of listeria infection. They suspected that CTC permitted the infection to become established. He also quotes Cossar and Kilsky who showed that CTC and TC in heavy doses of 50 mgms per kilo killed hamsters in three days. These workers drew the conclusion that these drugs induced the growth of a pathogenic intestinal flora since the use of sulphaguanidine reduced the mortality considerably. Chinchillas which were fed pellets containing 0.2 mgms CTC per ounce for 12-18 months suffered a 10 per cent mortality from an entero-colitis possibly due to *Staphylococcus aureus*. Most rabbits given TC, OTC and CTC in daily doses of 5-50 mgms/kilo died within two weeks shewing severe enteritis probably due to Bacillus proteus. Owen[38] also discusses the effects of tetracyclines on the intestinal flora and Campbel *et al*[39] express the opinion that TC acts on the bacterial flora in such a way as to make available unidentified growth factors for *C. albicans*. Van der Gulden and Zuur[40] attribute deaths in three horses from fungal infections to treatment with P and S for acute septic processes. In the author's experience in Nigeria there was a high rate of *Aspergillus fumigatus* infection in chickens suffering from respiratory disease which had received heavy dosages of antibiotics. It was thought that the use of the antibiotics in some way promoted the development of clinical aspergillosis as an after-effect of the respiratory disease. The organisms were ubiquitous in all poultry houses and chicks that were otherwise healthy and not treated seldom showed any signs of this disease.

Another consideration in the indiscriminate use of antibiotics is the production of drug resistant microbes. Williams Smith and Crabb[41] found a much higher proportion of TC resistant *E. coli* in faeces of chickens which had received a diet containing low levels of tetracyclines. Similar observations have been made by Harry[42] and Garside *et al*[43]. In another observation Williams Smith and Crabb[44] discuss the transmission of CTC and OTC resistant strains of staphylococci to the attendants of poultry flocks receiving medicated rations. Huey and Edwards[45] presented evidence that the widespread use of TC in poultry foods in America resulted in more frequent occurrence of TC resistant *S. typhi-murium*. Elliot and Barnes[46] found that CTC sensitive streptococci originally present in the intestinal tract of chickens were suppressed by the antibiotic but resistant strains then took their place.

A further factor which should be noted is that Tejerina[47] has reported that the antibacterial activity of kanamycin was inhibited by serum of rabbits that had i.m. injections of antibiotic for 1 month. Specific anti-kanamycin antibodies were detected by the complement-fixation test. While it is not yet known how this finding affects the efficiency of prolonged treatment, it would seem that in addition to drug resistance developing in the microbes, there may also be a resistance developed by the animal.

Discussion and conclusions.

Today the use of drugs in the poultry industry has assumed astronomical proportions. Various antibiotics, coccidiostats and sulpha drugs are added to mashes routinely and vast tonnages of these drugs are manufactured for the poultry industries of the world. Most of these are mixed in feedstuffs but in addition similar drugs are made available to the poultry farmer in convenient forms so that he can administer them easily. Since drugs are so widely used in the industry it is an important matter to consider whether this is always justified and if perhaps there is an abuse in the use of drugs.

There is no doubt that the improvement and availability of these drugs and their efficiency have helped to make possible the mass production of poultry which the competition in the industry demands. But it is also felt that they are frequently misused, for reasons already stated. Apart from the misuse of drugs, there are many other aspects that need consideration such as side-effects, development of drug resistance and the economics of medication to the poultry farmer.

Inglis[2] claims that in the medical profession, information and knowledge and uses of drugs are disseminated mainly by the drug companies who naturally only give the merits of the drugs and seldom if ever warn of the dangers. If this is true for the medical profession it is equally true of the veterinary profession, and particularly as it concerns the poultry industry. This is not a satisfactory state of affairs. If the veterinary profession depends on their instruction about these drugs on the trade only, they cannot be expected to influence the use of drugs in the industry. It is urged that the veterinary profession considers this aspect seriously.

Inglis has drawn attention to the effect of high pressure salesmanship on the use of drugs in the medical profession where most of the sales are only through the profession. In the veterinary field and particularly in the poultry industry, salesmen sell many of their drugs direct to the poultry farmer or the mash producer who often knows little about the drugs and of the diseases which they are intended to prevent or cure. It is felt that large quantities of drugs are used unnecessarily by the poultry industry through this. In many cases the drugs are not needed and in other cases the wrong drug may be used. It is particularly in the case of the baby chick that drugs are often used pointlessly and often with harmful effects.

Since baby chicks are generally put down on clean floors and are in good health from the start they are not exposed to heavy infections at this stage of their life. The need for coccidiostats at least is unnecessary for several weeks. However, the calculated use of vitamins and antibiotics in certain instances may be needed in the baby chick especially to reduce losses from omphalitis, enteritis and pneumonias especially during periods of extreme stress. If drugs are discovered that control viral infections such as the leukosis complex and avian encephalomyelitis, their use in the baby chick may be indicated, but such drugs are not yet available.

The use of coccidiostats and other harsh drugs in chicks under two weeks of age is to be discouraged for reasons given above. Much more reliance should be placed on good hygiene, housing, nutrition and other sanitary measures. Particular attention should be given to these matters when the chicks are first put down on the floor. Teaching the baby chick to feed and drink is usually done by traditional yet unsatisfactory methods and as a result they are exposed to unnecessary infection at this early age. It is basically wrong for chicks to walk in their food and water which is what usually happens. It is felt that the design of feeders and waterers should be improved to minimise this error. Mashes produced for baby chicks are usually the same for the age of one day to one month of age. It is felt that there should be different mashes for chicks under two weeks of age. Such mashes should not contain coccidiostats or harmful drugs but they may contain specially needed proteins, vitamins, minerals and antibiotics as their needs must be different from chicks that are a little older.

In conclusion there is no doubt that various drugs have their value and place in the poultry industry especially in the control and treatment of infectious diseases. A factor which is not sufficiently emphasised however is the importance that environmental factors play in the spectrum of diseases, whether infectious or not, to which flocks are subject. Kaschula[48] has pointed out that there was a marked difference in the diseases appearing in village flocks as compared with those under modern commercial conditions. It is an interesting fact that there is a difference in importance of various diseases from decade to decade and these are obviously associated with changes in nutrition, husbandry, and housing practices. The use of different vaccines and medications also play a role. It is therefore obvious that when these diseases appear their cause should be sought with environmental predisposition in mind.

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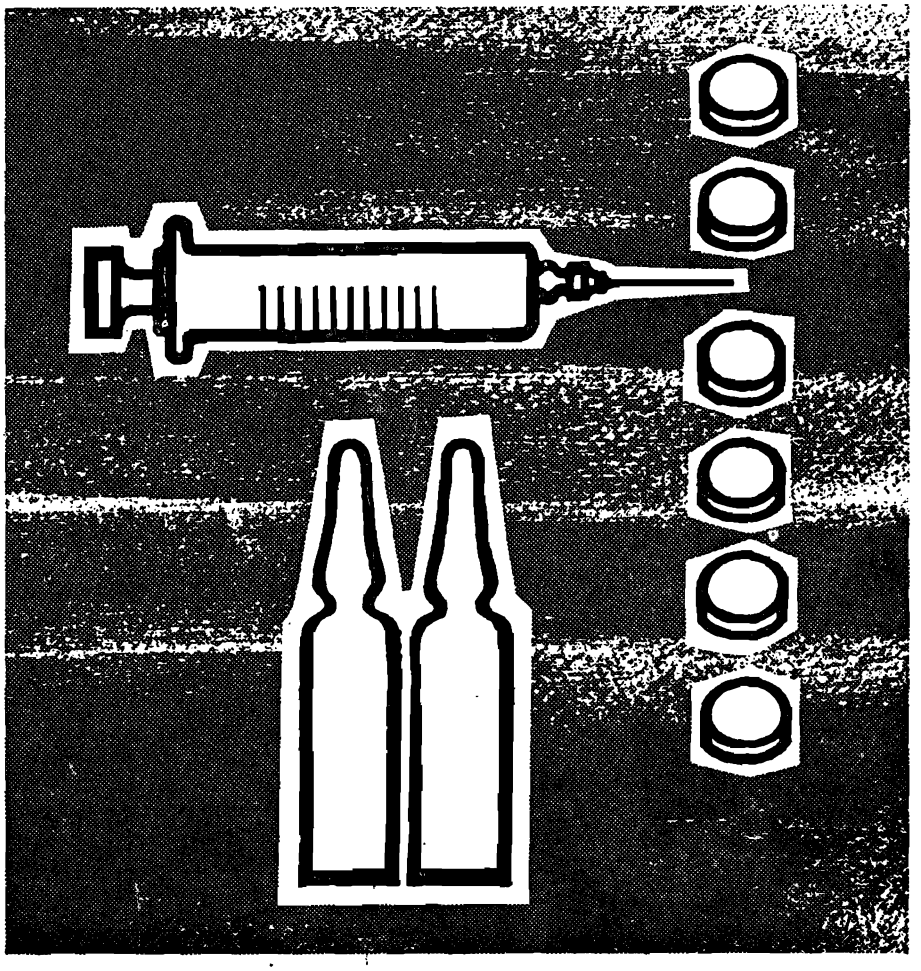

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CLINICO-PATHOLOGICAL STUDIES OF *BABESIA CANIS* INFECTION IN DOGS. V. THE INFLUENCE OF THE INFECTION ON KIDNEY FUNCTION

W. D. MALHERBE, Section of Clinical Pathology, Veterinary Research Institute, Onderstepoort.

SUMMARY

The effect of *Babesia canis* infection on the kidneys was studied by means of the estimation of blood urea nitrogen (B.U.N.) in three categories of dogs representing three degrees of severity of the disease.

In early acute cases, in spite of early nephritic changes found on urine analysis, evidence of nitrogen retention was seldom present. More advanced cases with well developed anaemia showed a decided tendency to elevated urea nitrogen levels, while nearly all cases with any degree of icterus gave levels mostly much in excess of the normal range.

The pathogenesis of the effects on the kidney is discussed and compared with that in human malaria. There is a close similarity and in both cases changes are of a nonspecific nature resulting from anoxia and reduction of renal blood flow.

INTRODUCTION

The previous articles in this series[1-4] have dealt with the effect of canine babesiosis on the liver. While hepatic damage tends to produce more spectacular clinical signs, laboratory appraisal of the disease has made it very clear that the kidney is also involved in the morbid processes.

In the clinical field it has frequently been found that older dogs with a depleted supply of functional nephrons tend to make a more tardy recovery from the disease than do younger animals. Laboratory examination of urine gives evidence of marked kidney damage ranging from acute nephritis through subacute forms to chronic inflammatory changes. At the same time nitrogen retention, at times irreversible, is shown by elevation of blood urea nitrogen figures to well above normal.

For the purpose of evaluation of kidney function it was not considered feasible to subject patients to lengthy clearance procedures. Blood urea nitrogen (B.U.N.) determination was selected in spite of its limitations as a suitable parameter for indicating deteriorating kidney function during the progress of and reflecting the intensity of effect of the *Babesia* infection.

Nitrogen retention[5] in renal disease depends in general on the nature and extent of the renal lesion and upon extrarenal factors including prerenal deviation of water (oedema, vomiting, diarrhoea or fever) and excessive protein catabolism.

Of these, in babesiosis, the renal lesion is the one to be studied. Oedema is only an occasional feature of the disease[6]. Vomiting and diarrhoea are not seen very often. Most affected dogs are typically off their feed, so that with the fever generally present, protein catabolism of the animal's own tissues is for practical purposes a constant feature.

Blood urea nitrogen figures in a considerable number of cases were thus selected and the results compared with the situation found in human malaria.

MATERIALS AND METHODS

As in the earlier studies most of the subject material consisted of cases of natural infection with *B. canis* brought to the Onderstepoort outpatient clinic for diagnosis and treatment. These were divided into three more or less arbitrary categories: -

Category I: early acute cases with pale pink mucous membranes.

Category II: Cases showing great mucosal pallor, but *no icterus*.

Category III: Cases showing any degree at all of icterus.

As before, blood in most cases was collected with potassium oxalate, and later with heparin as an anticoagulant. Blood urea nitrogen (B.U.N.) was estimated by the method of Hench and Aldrich[7] based on the mercury combining power of

blood. This is derived from the principle that mercury combines with such products as urea, creatinine and uric acid when a solution of a mercuric salt is added to a solution containing these nitrogenous substances (in this case a protein-free filtrate of blood) up to the point that the mercury combining power is satisfied. The excess mercury then appears in the solution and is demonstrated by the appearance of a reddish-brown, powdery precipitate when a drop of the solution to be tested is added to a drop of saturated sodium carbonate solution on a white spot plate.

While this method is not as accurate as the urease procedure it is sufficiently so to meet clinical requirements and has therefore gained wide acceptance in clinical laboratories.

Results

The findings are plotted graphically as a scatter diagram divided into three portions corresponding to the three categories. See Figure (1).

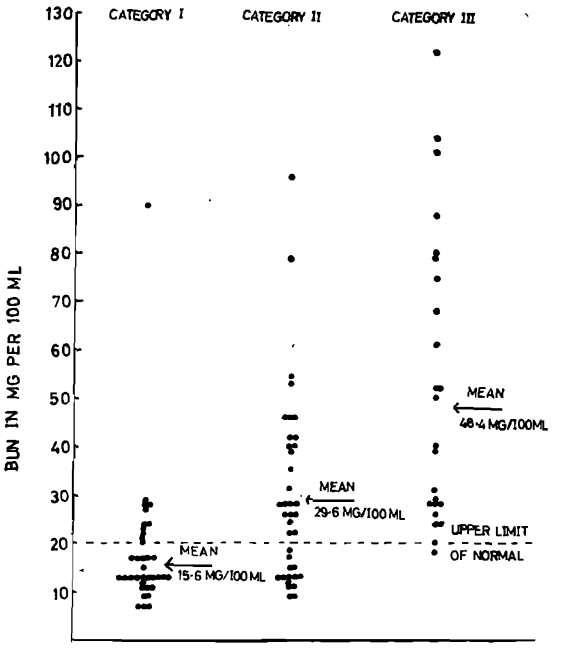
The majority of values found in the early acute cases are within the normal range, usually taken to have an upper limit of about 20 mg per 100 ml. Figures between 20 and 25 are not usually regarded as being particularly abnormal. The very high value of 90 in a single case was in a young dog in an advanced state of medical shock with massive haemoglobinuria and severe parasitaemia. Its inclusion was on the basis of "early acute" but it was in fact a peracute one. In spite of a blood transfusion and specific treatment it died within about ten hours.

In the second category the tendency to higher values is clear, with somewhat less than half of the observations within the normal range. The higher values take the mean up to nearly 30 mg per 100 ml.

Very nearly all the animals in the icteric (third) category showed nitrogen retention from mild to very severe degree. The mean B.U.N. of the 24 cases was 48.4 mg per 100 ml, considerably above the normal range.

Discussion

It is clear from the increasing levels of B.U.N. through the course of the disease that kidney involvement, and consequent nitrogen retention, is an important feature of babesiosis. Estimates of the percentage of the original complement of nephrons required to provide full functional capacity of the kidneys vary from 25 to 33. This functional reserve therefore allows the first category cases to reflect values mostly within the normal range when urine analysis already shows evidence of renal involvement. As the disease progresses however the reserve becomes depleted and a progressive rise of B.U.N. is evident.



FREQUENCY OF BLOOD UREA NITROGEN VALUES IN CANINE BABESIOSIS

Involvement of the kidney during the course of babesiosis was recognized by some of the early authors in this field from simple methods of urine examination. As long ago as 1902 Nocard and Motas[8] noted the presence of albuminuria at all stages of the disease and described the kidneys as being "congested" at autopsy. Graham-Smith[9] in a study of the morbid anatomy mentioned albumin and casts in most of his cases. Meyer[10] in 1912 referred to kidneys "which are doubtless primarily affected by piroplasmosis". Damage of kidney epithelia with the presence of casts and protein in the urine was further described by Fischer and Scheidemann[11] and Contis[12] in the third decade of this century. Most workers were however more interested in the observed presence of bile pigments.

Maegraith and co-workers[13] in 1957 gave an account of their definitive studies on pathological processes in *B. canis* infections. They used a highly virulent laboratory strain of the organism

and enhanced the severity of infection by passage through at least one puppy before infection of their experimental animals which were of various ages and breeds. In this way some of their cases became oliguric or even anuric and they gave B.U.N. figures "commonly ranging from 60 to 90 mg per cent" and in one case reaching 290. These values are generally in excess of those found in our field cases.

They gave a detailed account of the pathological changes found both macroscopically and histologically. Grossly they observed medullary congestion, sometimes congestion of the whole organ, and most constantly "great prominence of the vessels at the cortico-medullary junction, associated with local vascular congestion." Macroscopic changes were most marked in animals in which haemoglobinuria and anuria had occurred.

On histopathological examination they found shrunken glomerular tufts in anuric cases resembling the picture seen in blackwater fever. The tubular epithelium was regularly degenerated with shedding of debris into the lumen. Haemoglobin or its derivatives could be identified in granule form in the tubule cells and in casts in cases manifesting haemoglobinuria. Granular and hyaline casts were fairly regularly present in later stages of the disease. They moreover made the point that there was no correlation between haemoglobinuria and the severity of the nephritic condition.

Qualitatively these findings are in complete accord with our own experience in the examination of a very large volume of autopsy material. The above workers also found the general pattern to be very similar to that found in *falciparum* malaria, in blackwater fever and in cases of incompatible blood transfusion.

Urine examination shows the variability of the findings one may expect. Proteinuria is usual. The specific gravity reflects anything from, on the one hand, shock or relative failure of urine secretion, to a failure of urinary concentration on the other. Haemoglobinuria is irregularly present. Bilirubin is detected in the majority of cases, as are cellular, granular, and hyaline casts. As in the case of malaria none of the findings suggests anything of a specific nature. The presence or absence of large numbers of parasites in blood vessels in histological sections bears no relationship to the degree of nephritis, and, as Maegraith *et al.* have concluded, the explanation of the lesions must be found in the anoxia and "an overall reduction in the renal blood flow, sometimes, but not always, associated with some form of generalized shock."

In human medicine it was formerly thought that haemoglobin and myoglobin in plasma were directly responsible for necrotizing nephrosis as a result of obstruction of tubules by precipitation of these haem pigments in the tubules or of direct toxic action. It is however at present believed[5] that severe hypotension with intrarenal vasoconstriction and renal ischaemia are more important factors than the presence of haemoglobin. In babesiosis the important element of anoxia must be considered to be of major importance.

From the evidence which has been presented it is clear that, although the role of nephritis is considerable and is an important part of the disease picture, it is in the majority of field cases reversible, requiring no particular treatment after specific babesicidal therapy. It would depend to the greatest extent on the residual reserve capacity of the particular animal's kidneys at the time of infection and the degree of insult produced by the disease. An older dog already approaching the border-line of kidney decompensation and then subjected to infection will very likely die from kidney shutdown even after normally successful specific therapy. The proximate cause of death would, unlike the majority of cases of babesiosis, be uraemia. Supportive treatment aimed at this fact should certainly be instituted immediately when it becomes evident from B.U.N. determination and urine examination that this is necessary. The development of metabolic acidosis as a result of renal failure also contributes to the necessity of such measures, and its recognition and correction could be life-saving in cases that fail to respond to specific therapy in the normal way.

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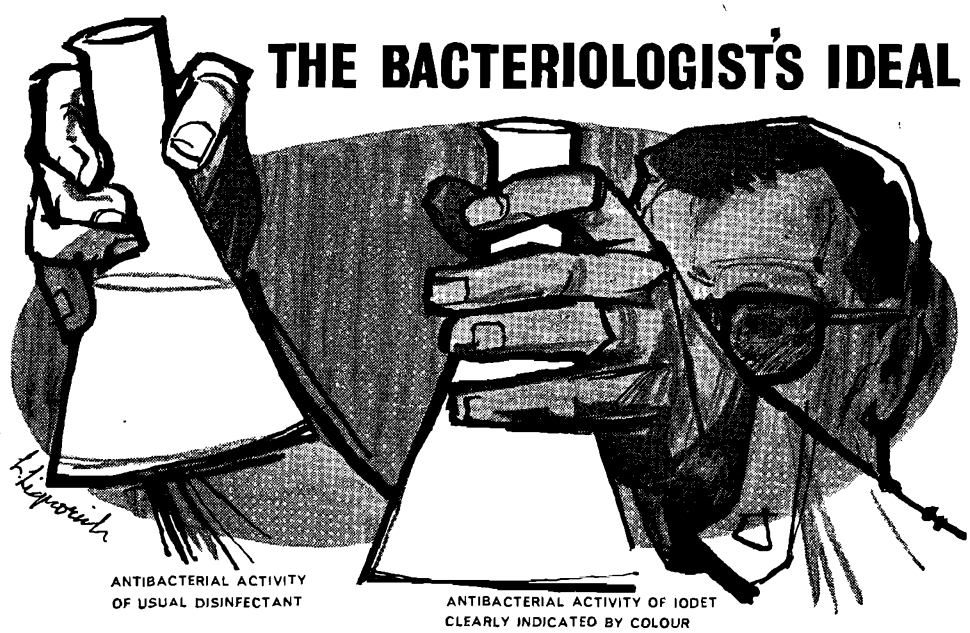

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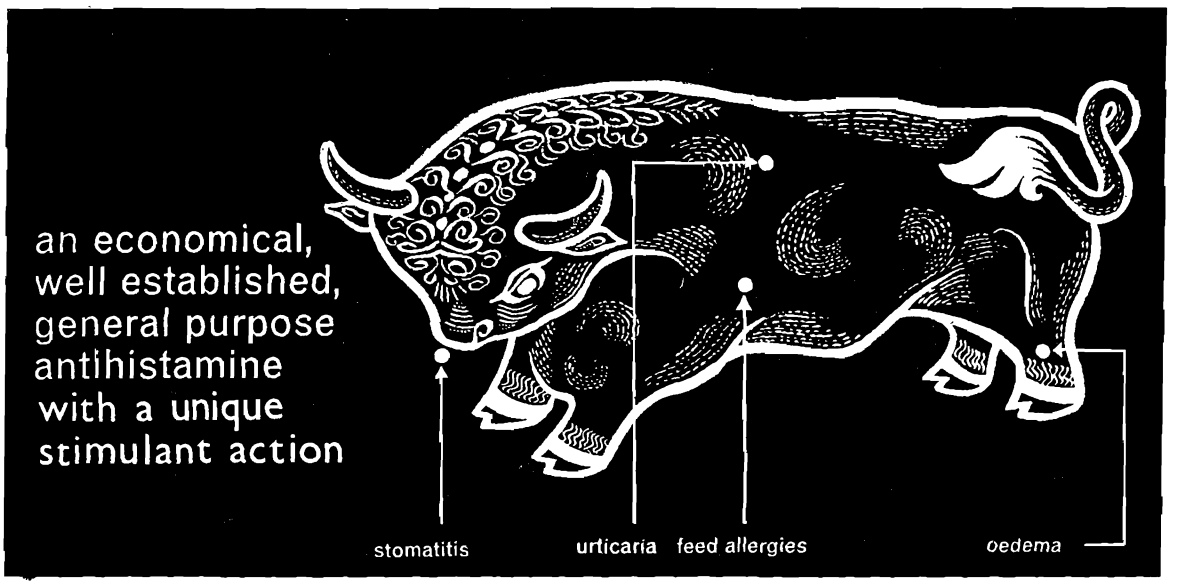

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BABESIOSIS IN ABORTED EQUINE FOETUSES: A REPORT ON TWO CASES IN SOUTH AFRICA

J. L. Du plessis and P. A. Basson.

Section of Pathology, Veterinary Research Institute, Onderstepoort.

Summary

Two cases of babesiosis in aborted equine foetuses are recorded. The histo-pathology of the kidney, which was characterised by the presence of numerous haemoglobin droplets in the tubular epithelium, is emphasized. The probability that, in both foetal babesiosis and erythroblastosis foetalis, erythrocytes pass through an abnormal placentation is discussed.

Introduction

The disease conditions that should feature in the differential diagnosis of icterus and anaemia in aborted equine foetuses and newborn foals are erythroblastosis foetalis (haemolytic icterus), equine rhino-pneumonitis virus infection and babesiosis.

It is generally accepted that the maternal antibodies against the foetal erythrocytes, in the case of erythroblastosis foetalis, gain entrance into the circulation of the foal only after ingestion of the colostrum. Priouzeau[1] states that transplacental transfer of antibodies may already occur prenatally and that foals or foetuses aborted during late pregnancy are born diseased. One of us has made observations which support this view. That some abnormality in the epitheliochorial placentation of the mare does play a deciding role in the pathogenesis of this disease is borne out by the fact that many mares which carry foals with incompatible erythrocytic antigens, do not manifest an increasing titre of isoantibody during pregnancy[2]. A placenta which is permeable to the foetal red cells, in cases where maternal-foetal bloodgroup incompatibility does lead to the haemolytic disease, could likewise allow antibodies to pass from the maternal to the foetal circulation.

Icterus, usually of a mild degree, is by no means an uncommon finding in aborted foetuses and newborn foals suffering from equine viral rhino-pneumonitis. Corner et al[3] state that icteric discoloration of the footpads and the ocular mucous membrane was a frequent finding in cases studied by them, while Westerfield and Dimock[4] made a similar observation and emphasized the footpads, abdominal organs and joint cavities as prominent sites of yellowish discoloration.

Congenital babesiosis and the transplacental transmission of this protozoan parasite in mares has been described by several authors, cited by Neitz[5]. Foetuses are either aborted in an icteric or anaemic state, or premature foals and those at fullterm are born diseased, showing symptoms of varying degrees of icterus, anaemia, severe prostration and reluctance to nurse.

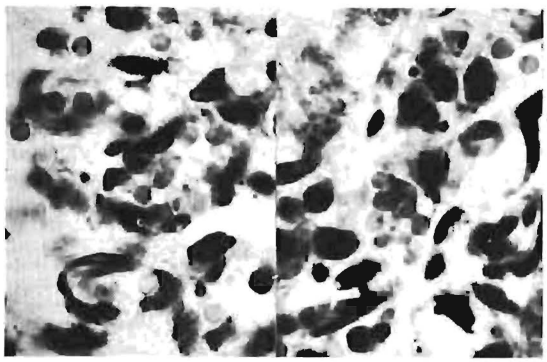
Babesiosis of newborn foals and aborted foetuses has been diagnosed a number of times in this country, but has not been recorded. The incidence is unknown. Two cases have been diagnosed from histological sections in this laboratory. It is the purpose of this report to record these findings and to emphasize the necessity of considering babesiosis in the differential diagnosis of icterus and anaemia in aborted and newborn foals.

Origin of Material

Formalin-preserved specimens of liver, lung, spleen and kidney in the one and liver, lung, spleen and myocard in the other case of icteric Thoroughbred foetuses were submitted by colleagues from the Cape Province. These tissues were embedded in paraffin-wax, sectioned at 3μ thickness with a sliding microtome and stained with haematoxylin and eosin. Pickworth's method for haemoglobin[6] was used as a special staining procedure.

The abortions occurred in two different areas where babesiosis is enzootic. In one of these areas an increased number of clinical cases of babesiosis had been diagnosed in imported stallions and maiden mares. In neither of the two cases did the dam show clinical evidence of the disease.

Fig. 1.



Photomicrographs of kidney showing several parasitized erythrocytes. HE X 1200.

Histopathology

Parasitized erythrocytes were observed in all the organs that were submitted, namely kidney, liver, spleen, lung and myocard (Fig. 1).

The most significant microscopic lesions were found in the kidneys. A severe nephrosis was present, evidenced by swelling and loss of architectural structure of the tubular epithelium particularly in the cortex and to a lesser extent in the medulla. A striking feature was the presence of varying numbers of haemoglobin droplets in the tubular epithelium of the cortex and to a limited extent in the outer zone of the medulla. There was a marked resemblance between these haemoglobin globules and hyalin droplets, the only difference being their staining ability, which was similar to that of the erythrocytes. In places the cytoplasm of all the epithelial cells of a tubule was densely packed by these globules. (Fig. 2). The identity of these droplets was established by means of Pickworth's haemoglobin method. It is interesting to note that similar droplets suspected to be haemoglobin were seen by Seibold[7] in the tubular epithelium of dogs suffering from babesiosis.

Additional histo-pathological lesions observed were cloudy swelling and hydropic degeneration in the liver, congestion and mild oedema in the lung and mild kariorrhectic changes in the red pulp and severe congestion of the spleen.

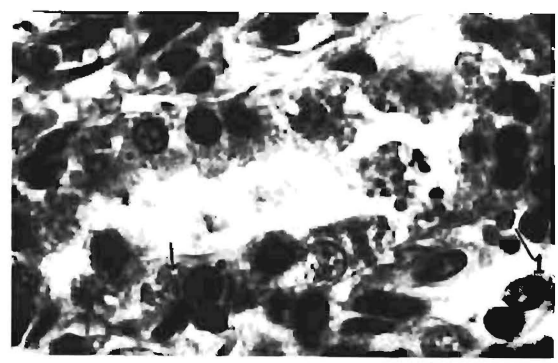
Discussion

The probability that an abnormality of placentation plays a decisive role in the pathogenesis of foetal and neonatal babesiosis is supported by the fact that only a relatively small number of foetuses and foals carried by mares premune to babesiosis fall prey to infection by this parasite. The presumption that foetal red cells gain entrance to the maternal circulation in erythroblastosis foetalis suggests that the placental bloodvessels for some reason or other become permeable to red cells, lending further support to the above hypothesis. It stands to reason that parasitized erythrocytes of the babesiosis-premune mare or extra-erythrocytic parasites can in a similar manner gain entrance into the foetal circulation. The direction of movement through the abnormal placenta would in this case be opposite to that of erythroblastosis foetalis.

The other possibility, that extra-erythrocytic *Babesia* parasites actively cross the intact placental barrier into the foetal circulation is difficult to visualize and cannot be substantiated by any references in the literature.

In considering the differential diagnosis of icteric and anaemic foetuses and newborn foals the necessity to examine a bloodsmear is obvious. Even in the absence of icterus this clinical procedure should consistently be followed in diseased foals, as not all such cases need necessarily show icterus.

Fig. 2.



Photomicrograph of the kidney, showing haemoglobin droplets (arrow) in the tubular epithelial cells. Parasitized erythrocyte,(↑). HE X 1200.

ACKNOWLEDGEMENTS.

The authors wish to thank the Chief, Veterinary Research Institute, for his permission to publish this report. Submission of specimens by Drs. R. C. Rous and G. L. Faull is acknowledged with thanks.

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BOOK REVIEW

THE CLINICAL ASPECTS OF SOME DISEASES OF CATS by Joan O. Joshua, FRCVS. First published December, 1965 by Heinemann. U.K. price 40/-. Size 14 x 21 in. 266 pages. Hard cover, cloth bound.

This book is the first of a series of veterinary books that will be published by Heinemann. It is of a handy size, clearly printed on a matt paper and is notable for the absence of typographical errors.

It is stated in the preface that the purpose of the book is to present clinical observations on the common ailments of cats as seen by the writer during 25 years of practice.

The experienced clinician will find many of his own observations confirmed in this work and the new graduate will acquire a good grounding in feline practice (painlessly!).

The few debatable points are as follows: The author advocates the subcutaneous administration of fluids; the topical use of antibiotics in infected tissues, wounds and body cavities and the use of Depropanex to relax stricted muscle of the male urethra. The role of vitamins in therapy is probably overemphasised.

In spite of the modest scope implied by the title most of the feline diseases are adequately dealt with. A specific discussion of the shock syndrome and its management as well as the metabolic disturbances of neuters must be considered for future issues.

The facts presented are backed by adequate references. Where the author expresses a private preference or opinion without tangible proof the reader is informed.

The work covers feline behaviour, housing, cat shows, quarantine, diet clinical examination, anaesthetic methods, surgery, medical care, infectious and non specific diseases, injuries, geriatrics and poisoning. This expansive field is presented in a bright readable style and in an orderly sequence. Four chapters were prepared by collaborating authors.

This book will be of great use to the practitioner. The references given will enable those with access to a library to obtain basic information about original work done on the conditions described. This work is likely to remain a standard treatise on feline disease for a very long time.

— P. le R.

DETECTION OF LEPTOSPIRAL ANTIBODIES BY MEANS OF THE *INDIRECT FLUORESCENT ANTIBODY METHOD*

J. L. Du Plessis.

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Summary

Results of 44 serum samples subjected to the indirect fluorescent antibody (IFA) test compared favourably with those obtained by the microscopic agglutination (MA) test and reflected a definite correlation between the two tests. Ninety-one and 93 per cent of sera examined reacted to the MA and IFA tests respectively and 75 per cent of sera gave MA titres above 1:100.

The main advantages of the IFA test are the following: 1. It is group specific and therefore valuable as a screening method. 2. It can be carried out in small laboratories without elaborate equipment being required. 3. Exposure of laboratory workers to live *Leptospira* cultures is limited to a minimum.

Introduction

The detection of agglutinating antibodies plays a major role in the sero-diagnosis of leptospirosis. The microscopic agglutination (MA) test with live leptospirae is universally employed as the most dependable serological test and was advocated by Babudieri[1] as having not only the greatest sensitivity, but also the highest degree of serotype specificity.

Various macroscopic agglutination tube tests as well as plate tests have been described[2 3 4 5]. These tests are less sensitive than the MA test, the titres as a rule being five to ten times lower. However, the advantage is that they can be carried out with greater ease and rapidity.

Another rapid microscopic agglutination test has been described by Brede[6]. This is a qualitative test involving the detection of leptospiral antibodies in blood dried on discs of blottingpaper. It is type-specific, gives an indication of the actual antibody titre and is dangerous to laboratory personnel, who are exposed to live organisms.

The indirect fluorescent antibody (IFA) technique is being employed as a sero-diagnostic tool in an increasing number of infectious diseases. In malaria this technique was found to be a specific and sensitive method of determining antibody levels[7], and past infections of human malaria[8].

Antibody titres against *Toxoplasma gondii* obtained by means of the IFA technique, were in agreement with those of the dye test at both low and high levels of antibody[9].

Comparing the relative sensitivity of the *Treponema pallidum* immobilization (TPI) procedure with that of the fluorescent treponemal antibody (FTA) test for syphilis, Fife, Bryan Sanders and Muschel[10] found that the FTA test was more sensitive and at least as specific as the TPI test.

Fluorescein-conjugated leptospiral antibodies have been successfully employed to demonstrate *Leptospira canicola* in hamster kidney sections and smear preparations[11]. This method has likewise been used to detect *Leptospira pomona* in the urine of experimentally infected calves[12] as well as various *Leptospirae* in different tissues collected from both artificially and naturally infected laboratory, domestic and wild animals[13].

The purpose of this paper is to describe the detection of leptospiral antibodies in serum by means of the IFA technique and to compare the results obtained with those of the MA test.

Materials and Methods

Sera. Forty-four serum samples obtained at random from 14 dogs, 11 pigs and 19 cattle, were subjected to both the MA and the IFA test.

Preparation of antigen smears for the IFA test. Dense, 10-14day old cultures of *Leptospira,* grown in Korthoff's medium at 28°C, were used to prepare the smears. The serotypes listed in tables 1-3 were employed. Four equally spaced circles ap-

proximately five mm in diameter were drawn on clean glass slides by means of a diamond pencil. A platinum loop two mm in diameter was used to transfer sufficient culture material to cover one circle at a time, in order to obtain an average of 40 to 60 leptospirae per field, under the 40X microscope objective. The smears were allowed to dry in air at room temperature, marked, wrapped in tissue-paper and aluminium foil and stored at - 20°C until used.

In a preliminary experiment to determine whether the age of the culture would influence the results, a number of smears were made from cultures after six, 14 and 21 days' growth. A preparation from each of these was tested with a number of sera. It was found that six and 14 day cultures were more suitable than the older cultures. For this reason smears were prepared from six to 14 day cultures throughout the course of the investigation.

Anti-species conjugates. Commercial preparations of fluorescein conjugated rabbit anti-canine*, anti-bovine* and anti-porcine** globulins were employed.

Method of the IFA test. Each individual culture smear of a number of serotypes was marked according to the dilution of test serum to be applied to it. The smears were fixed in acetone for ten minutes at room temperature, air-dried and placed in a moist chamber.

Two-fold serial dilutions of the serum sample to be tested were made in normal saline. Approximately 0.02 ml of each dilution was placed onto the appropriately marked circle, avoiding confluence of neighbouring drops.

A 1:20 dilution of pre-colostrum serum of the animal species concerned was placed on one antigen smear of each serotype in each test as a control.

After 30 minutes at room temperature in the moist chamber, the smears were gently rinsed in two changes of 0.02 M phosphate buffer for 15 minutes. The slides were left on their sides for a few minutes in order to remove excess buffer and were then gently blotted and replaced in the moist chamber.

The appropriate anti-species conjugated globulin was diluted 1:5 with distilled water and a drop, sufficient to cover the outline of the smear, was placed on each circle. After a further period of 30 minutes at room temperature the superfluous conjugate was removed by again rinsing in two changes of buffer for 15 minutes. Smears were mounted in buffered FA mounting fluid under a cover-slip.

Preparations were then examined by fluorescence microscopy, using a standard Zeiss binocular microscope with a mercury-vapour 75-watt burner and a BG-12 ultra-violet filter in conjunction with a protective Zeiss filter. A darkfield condensor and a 40X objective were employed throughout the experiment.

An arbitrary estimation of the number of organisms showing fluorescence was made and the highest dilution at which ten per cent or more of the organisms showed fluorescence, was taken as the endpoint. Organisms were considered to exhibit fluorescence if they were clearly distinguishable as leptospirae, showing a yellow-green fluorescence. In the absence of fluorescence, organisms were vaguely visible, merged with the background and were detected with difficulty. It was found essential to examine several representative areas covering the entire smear.

Non-specific staining. In a preliminary trial conjugate absorbed with canine liver powder was compared with unabsorbed conjugate. No non-specific fluorescence was observed in case of the former and conjugates were therefore not treated with tissue powders in the subsequent tests.

Agglutination tests. The MA test, performed according to standard procedure, was conducted simultaneously with the IFA test, using the same serum dilutions.

Results

The results of the MA and IFA tests, performed on the 44 sera, are presented according to animals species in tables 1-3.

Absence of sero-specificity of the IFA test. It is evident from tables 1-3 that the IFA test is group specific and not serotype specific. Each serum sample subjected to this test reacted with virtually equal intensity with more than one specific antigen. In serum number 36, for example, the responsible serotype, according to a MA titre of 1:1280, was *L. pomona*. IFA titres of 1:1280 were obtained with antigens prepared from *L. pomona*, *L. icterohaemorrhagiae* and *L. hyos* and titres of 1:640 in case of *L. canicola* and *L. hebdomadis*.

*The Sylvana Company, Millburn, New Jersey.
**Difco Laboratories.

TABLE 1.—RECIPROCALS OF MA AND IFA TITRES OF 14 CANINE SERA AGAINST SEROTYPES INDICATED.

Serum No.	L. pomona		L. canicola		L. icterohaemorrhagiae		L. hyos		L. sejroe		L. hebdomadis		L. saxkoebing		L. australis A		L. australis B		L. ballum		L. bataviae	
	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA
12	0	320	5,120	640	80	640	0	—*	0	—	0	—	0	—	0	—	0	—	0	—	0	320
14	0	160	640	160	0	160	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	80
22	0	—	320	320	0	160	0	—	0	—	0	320	0	—	0	—	0	—	0	—	0	—
45	0	160	320	320	0	—	0	80	0	—	0	—	0	—	0	—	0	—	0	160	0	—
49	0	0	0	0	0	0	0	—	0	—	0	0	0	—	0	—	0	—	0	—	0	0
50	0	0	0	0	0	—	0	—	0	—	0	0	0	—	0	0	0	0	0	—	0	—
53	0	—	20	80	0	80	20	—	0	—	0	80	0	—	0	40	0	—	0	—	0	160
54	20	—	20	80	0	160	0	40	0	—	0	80	0	—	0	—	0	—	160	—	0	80
55	0	2,560	5,120	2,560	40	2,560	0	—	40	—	0	—	0	—	0	—	0	—	0	—	0	2,560
59	0	160	2,560	320	20	320	0	—	0	—	0	160	0	—	0	—	0	—	0	—	0	—
61	0	640	2,560	640	80	1,280	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	1,280
62	0	640	2,560	640	40	640	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	1,280
66	0	320	2,560	640	20	320	0	—	0	—	0	640	0	—	0	—	0	320	0	—	0	—
67*	0	—*	20,480	20,480	0	10,240	0	—	80	10,240	0	10,240	0	—	0	—	0	—	640	10,240	1,280	10,240

* — = IFA test not done.

TABLE 2.—RECIPROCALS OF MA AND IFA TITRES OF 11 PORCINE SERA, AGAINST SEROTYPES INDICATED.

Serum No.	L. pomona		L. canicola		L. icterohaemorrhagiae		L. hyos		L. sejroe		L. hebdomadis		L. saxkoebing		L. australis A		L. australis B		L. ballum		L. bataviae	
	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IF
7	10,240	2,560	40	1,280	0	1,280	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
21	10,240	1,280	640	1,280	320	640	20	—	0	—	0	—	0	—	0	—	0	—	0	—	0	2,560
36	1,280	1,280	320	640	0	1,280	0	1,280	0	—	0	640	0	—	0	—	0	—	0	—	160	—
37	10,240	1,280	640	640	0	—	0	—	0	—	0	—	0	—	0	—	0	640	0	—	0	1,280
38	2,560	640	160	320	0	640	0	—	0	—	0	320	0	—	0	—	0	—	0	—	80	320
39	10,240	1,280	320	640	0	—	0	640	0	—	0	—	0	—	0	—	0	—	0	640	0	1,280
56	40	320	320	320	0	640	0	—	80	—	0	—	0	—	0	—	0	—	160	640	0	—
57	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	0	0	—	0	—	0	—
58	0	320	0	640	40	640	0	320	40	320	0	640	0	—	0	—	0	—	160	—	0	320
60	0	40	0	80	0	80	0	—	20	—	0	—	0	—	0	—	0	—	80	80	0	—
65	10,240	160	2,560	80	40	80	0	—	80	—	0	160	0	—	0	—	0	—	0	—	40	80

TABLE 3.—RECIPROCALS OF MA AND IFA TITRES OF 14 BOVINE SERA, AGAINST SEROTYPES INDICATED.

Serum No.	L. pomona		L. canicola		L. icterohaemorrhagiae		L. hyos		L. sejroe		L. hebdomadis		L. saxkoebing		L. australis A		L. australis B		L. ballum		L. bataviae	
	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA	MA	IFA
10	0	—	0	—	0	640	160	320	640	1,280	0	—	0	—	0	—	0	—	0	—	0	—
11	0	—	0	—	0	320	20	160	320	320	0	—	0	—	0	—	0	—	0	—	0	—
15	0	80	0	80	0	160	0	—	0	160	0	160	40	40	0	80	0	—	160	160	0	—
16	0	—	0	40	0	80	0	—	0	—	0	—	0	—	0	—	0	—	80	80	0	—
17	0	40	0	—	0	80	0	—	0	—	0	40	20	—	0	—	0	—	80	80	0	—
18	0	—	0	80	0	160	0	80	0	160	0	80	40	320	0	—	0	—	40	320	0	320
24	0	—	0	—	0	40	0	20	0	—	0	—	0	—	0	—	0	—	0	—	40	40
25	0	—	0	160	0	160	0	80	0	—	0	—	0	—	0	—	0	—	160	160	0	—
26	0	—	0	—	0	320	0	160	0	—	0	—	0	—	0	—	0	—	320	320	80	—
28	80	—	0	—	0	—	0	320	0	—	0	—	0	—	0	—	0	—	160	320	0	320
29	0	—	0	—	0	—	0	160	0	—	0	—	0	—	0	160	0	—	320	320	80	—
30	0	—	0	—	0	—	0	40	0	—	0	—	0	—	0	—	0	—	40	80	40	80
42	20	320	0	160	0	80	640	160	0	—	0	—	0	—	0	—	0	—	0	—	0	—
43	1,280	320	0	—	0	—	20	320	0	—	0	—	0	—	0	—	0	—	40	160	0	160
44	20	160	40	80	0	—	0	160	80	80	0	—	0	—	0	—	0	—	1,280	160	40	160
47	0	—	80	160	20	320	320	320	0	—	0	—	0	—	20	320	40	160	80	160	0	—
48	0	20	0	20	0	—	0	—	0	—	0	20	0	—	0	—	0	—	0	—	0	20
63	640	320	20	320	40	320	40	—	0	—	0	—	0	—	0	—	0	—	20	—	0	—
64	2,560	640	40	320	20	320	0	—	80	—	0	640	0	—	0	—	0	—	40	—	0	—

Each of the 44 sera was not tested against the 11 antigens listed, but at least three different serotype smears were employed in each test and every antigen was used at least twice during the course of the investigation. In no instance did any one particular antigen fail to react when other antigens gave a positive result.

determined. In this way the tests are complementary. A similar procedure can be followed with animals kept under quarantine.

Indirect fluorescent antibody studies in malarial infections also show evidence of non-specificity. Thus, considerable cross-reactivity between human and simian malarial parasites has been demonstrated by Voller[14] and Tobie, Kuvin, Contacos, Coatney and Evans[15]. In addition Kuvin and Voller[8] observed cross-reactivity, with essentially the same antibody titres, between *P. falciparum* and the simian parasite, *P. cynomolgi bastianelli.*

TABLE 4.—TABLE INDICATING CORRELATION BETWEEN MA AND IFA SERUM TITRES.

	Sera with MA titres equal to IFA titres	Sera with MA titres higher than IFA titres	Sera with IFA titres higher than MA titres
Total	18/44	18/44	7/44
Percentage	41	41	16

Correlation between MA and IFA tests. The correlation between the MA and IFA test results is reflected in table 4.

With the exception of serum samples 14, 42 and 63 the 18 cases, in which the MA titre was higher than the IFA titre, fall into a group in which the agglutination titre was 1:1280 or higher.

DISCUSSION

In contrast to the serotype specificity of the MA test, the group reaction exhibited by the IFA test has the decided advantage that this test can be used as a screening test for the diagnosis of leptospirosis. As a result of its limited cross-reactivity, employment of the MA test necessitates the maintenance of cultures of a full range of *Leptospira* serotypes and the testing of a serum sample against all the serotypes of *Leptospira* possibly present in a country.

The agglutination plate test and all other rapid agglutination tests require laborious testing against a wide range of serotypes before a sample can be regarded as being negative, whereas, according to the results obtained here, a single serotype antigen in the IFA test will show up antibodies against a wide range of Leptospira serotypes. In order to determine the species concerned, a positive IFA test must subsequently be followed by the MA test. If a MA titre lower than that of the IFA test is obtained, one should consider the possibility that a serotype not included in the MA test, was responsible for the infection.

In determining the incidence of leptospirosis in large numbers of cattle and swine, the IFA test should prove valuable to detect reactors. By subjecting the IFA positive sera to the MA test as indicated above, the serotypes concerned can be

Despite considerable variation between MA and IFA titres, the results indicated a high percentage of correlation betwen the two tests. In no instance was the IFA test negative when a positive MA reading was obtained.

It is evident that the IFA titres are generally lower than the MA titres, especially in the range of MA titres of 1:1280 and higher.

Two exceptions to this finding were encountered. According to available clinical and clinicopathological evidence, serum No. 67 was obtained from a dog eight to ten days after the acute phase of leptospirosis. The results in this case would appear to indicate that antibodies demonstrable by the IFA test are at least as high as the agglutinating antibodies in this stage of the disease, and the impression is gained that subsequent to infection antibodies demonstrable by the IFA test decrease more rapidly than do agglutinating antibodies.

If it can be confirmed that fluorescent antibody titres are highest immediately subsequent to the acute phase of leptospirosis, as demonstrated by serum 67, a comparison between the MA and the IFA titres may provide useful evidence on the lapse of time subsequent to infection.

There are two possible reasons why certain sera showed higher titres in the IFA test than in the MA test. Antibodies detectable by the IFA method may, for unknown reasons, in some instances be

present at higher levels than agglutinating antibodies. However, a more feasible explanation is that a Leptospira serotype not included in the MA test was responsible for the infection in these cases.

In this study the high percentage of sera reacting to both the MA and the IFA tests is noteworthy. Although all the sera, except those from four newborn animals, were collected at random, 91 per cent proved to contain agglutinating antibodies, and 93 per cent antibodies detectable by means of the IFA test. A survey of the literature points to considerable differences of opinion on what should be considered the lowest agglutinating titre of significance in leptospirosis. Babudieri[1] states that only titres above 1:100 should be regarded as significant. In this study 75 per cent of sera exceeded this figure.

In conclusion the advantages of the IFA test can be summarised as follows: 1. It is valuable as a screening method because it is group specific in contrast to the agglutination tests which are serotype specific. 2. The IFA test can be carried out in smaller laboratories without elaborate equipment being required. Standard microscopes fitted with ordinary ultra-violet apparatus can be used; commercially prepared fluorescein labelled reagents are easily procured and large numbers of antigen smears may be prepared from small volumes of cultures and these can be stored at $-20°C$ for as long as six months. 3. Final smear preparations need not necessarily be read immediately but, if required, may be stored at 4°C for several days before examination. 4. The hazard of exposure to live cultures by laboratory workers is limited to a minimum, as stocks of smears need only be replenished every few months.

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NEUROLEPTIC NARCOSIS OF LARGE WILD HERBIVORES IN SOUTH AFRICAN NATIONAL PARKS WITH THE NEW POTENT MORPHINE ANALOGUES M-99 AND M-183.

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SUMMARY

The use of two of a series of bridged-ring oripavine derivatives (M-99 and M-183 Reckitt) for the immobilisation and capture of hoofed wild animals is described.

These substances are sometimes effective without the addition of synergists, as in the case of square-lipped rhino and elephant, but as a rule they are administered in combination with a tranquilizer and hyoscine.

The technique of neuroleptanalgesia has decided advantages over the majority of earlier drug-immobilising procedures and has proved highly successful when applied to a series of 439 animals, involving 16 different species, in South African National Parks. Mortality arising directly from drug reactions has been negligible, and of the order of 2-3 per cent.

The results of different drug combinations, which have been evolved for the capture of the different species, are discussed, and a composite table of dosage ranges is provided.

INTRODUCTION

The increased demand in recent years for more refined methods of field immobilisation and restraint of wild animals, for the purpose of veterinary and ecological research in situ, has compelled investigators to cast their net even wider in their search of suitable drugs.

The early range of drugs employed for incapacitating wild animals in the field included a wide range of muscle relaxants, reflex inhibitors, central nervous system depressants etc.[21 22 23 24]. These were applied, with varying degree of success, to a wide range of wild animals, but with few exceptions, they had the common disadvantage that their successful effect was to a large extent dependent upon accurate weight determination of the subject. This proved to be an insurmountable obstacle in the case of, particularly heavy animals. The action of the majority of these drugs was also irreversible, and in many instances, the large bulk of drug required to bring about the desired effect militated against its routine use in the field.

It was only when combinations of neuroleptic or ataractic and analgesic drugs with wide therapeutic index were adapted for animal immobilisation, that the high mortality rate incurred with older drug mixtures could be significantly reduced.

The pioneer work of Harthoorn[5] on the square-lipped rhinoceros, using a combination of morphine or diethylthiambutene (Themalòn), hyoscine hydrobromide and a suitable tranquilizer, set the stage for the first really successful series of immobilising experiments on a particular species of wild animal, without fear of overdosage and resultant losses.

An important step forward was the fact that the narcotic action of one of the constituent drugs in the mixture could be reliably reversed, at any stage, through the intravenous or intramuscular injection of an antidote (Nalorphine hydrobromide).

One serious handicap which prevented the general application of neuroleptic narcosis in the animal field, was the large bulk of drug (analgesic) required to immobilise even a medium-sized ungulate in the wild state.

Different species also displayed varying reactions to the effects morphine, diethylthiambutene and other synthetic morphines, and a variety of tranquilizers had to be tested to find the correct combination of analgesic and neuroleptic agent which would bring about the proper state of central depression without an initial phase of hyper-excitement.

The advent on the scene of the bridged-ring oripavine derivatives M-99 and M-183 — thebaine-derived analgesics with morphine-like action, but extremely high potency — eliminated most of these practical difficulties.

After exhaustive field testing by a number of workers, it can safely be claimed that drug combinations including M-99 or M-183 are today without peer in the field of wild animal immobilisation, and these should be the drugs of choice for the capture of all large and medium-sized ungulates.

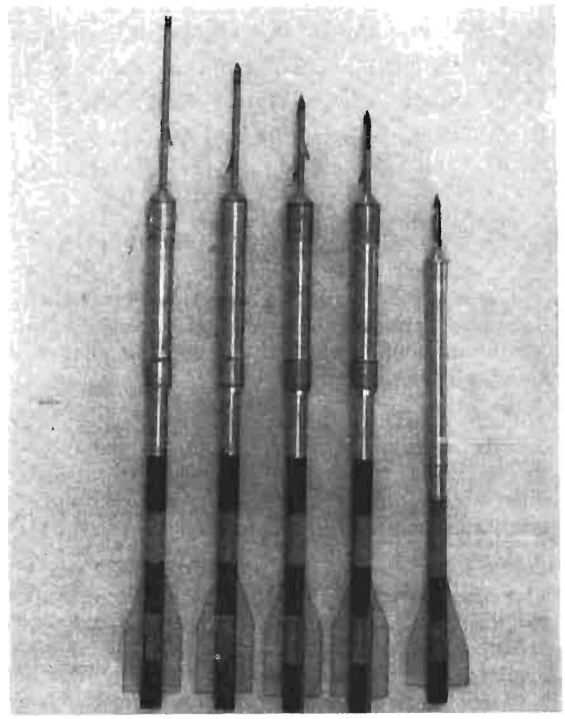
The successful application of M-99 drug mixtures for the restraint of particular hoofed wild animals has been reported on by Harthoorn and Player[10] — square-lipped rhinoceros; King and Klingel[14] — several species of equines; King and Carter[13] — black rhinoceros and Pienaar et al.[18] — African elephant. The initial series of experiments with M-99 in the Kruger Park, during which 7 different species of ungulates were successfully captured (with minor loss), was reported on by Harthoorn and Bligh[9].

It is the purpose of this paper to comment on the results of the protracted series of field trials with M-99 and M-183 which were initiated by us in December, 1963, and which eventually involved the capture of some 439 animals of 16 different species.

Material and Methods

With few exceptions, all the animals immobilised in this series, were injected by means of dart syringes (fig.) (i)), which were propelled by a powerful cross-bow (fig. (ii)), which was described by us in earlier papers[21] . For close-range work the Palmer Cap-chur pistol was found useful. Both the Palmer gas-propelled and powder-charged guns were, in our experience, not consistently accurate at long ranges, and have the added serious disadvantage that the loud report when fired, promotes the flight reaction of not only the darted beast, but also of associated animals in the herd. In comparison, the Van Rooyen cross-bow* is silent, causes no disturbance of the hunted animals and gives consistently accurate results at all ranges up to 120 yards, when used in combination with a good quality rangefinder**, and loaded with 3 cc. capacity dart syringes.

Fig. i



We also do not agree with Harthoorn[8] that a good quality cross-bow used in this manner, is essentially a specialist weapon. In fact, the converse is true, and cross-bows are at present used routinely by our game officers in preference to the 'Cap-chur' guns.

Animals, such as elephants, were sometimes stalked on foot, but as a rule darting was done from a vehicle (Land Rover of which the left front door and windscreen had been removed).

The following drugs were employed during the course of this study:

*Manufactured commercially by Mr. G. L. van Rooyen of "Southfields", P.O. Greytown, Natal, Republic of South Africa.

**Such as the 'Wild' hunter's range finder. (Manufactured by Wild Heerbrugg Ltd., Switzerland).

M-99

M-99 (Reckitt) is the code-name for the experimental drug 7oc-(1-R-hydroxy-1-methylbutyl)-6, 14-endoetheno-tetrahydro-oripavine hydrochloride (Synonym: Propylorvinol hydrochloride); currently manufactured and distributed in small quantities for biological research purposes only by Reckitt and Sons Ltd., Hull, England. This bridged-ring oripavine derivative is an analgesic of extremely high potency and may exhibit an activity 5,000 — 10,000 times greater than morphine.

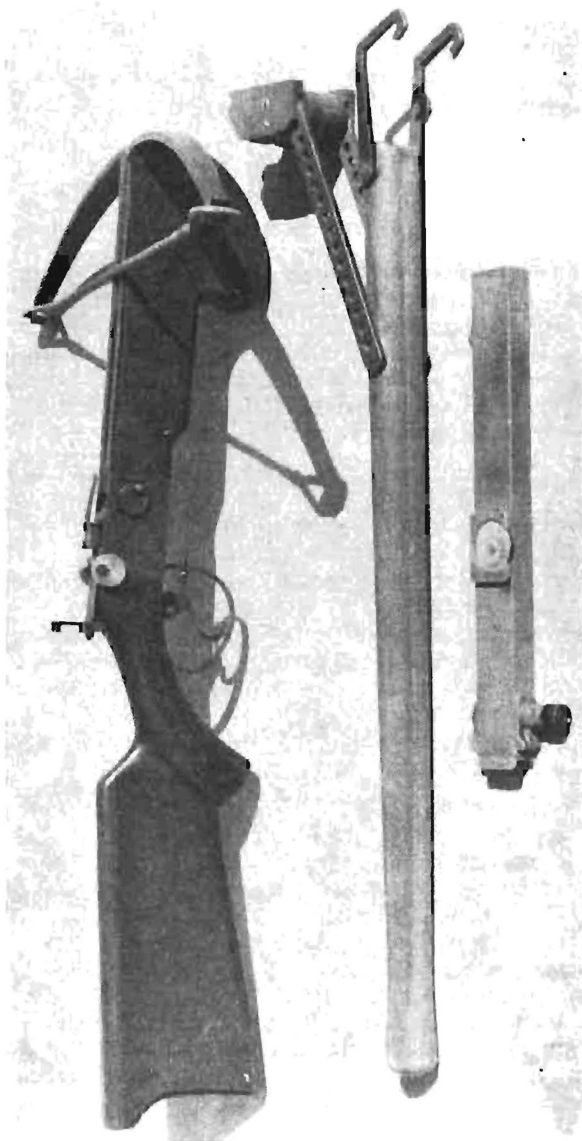
The small bulk of drug needed to produce the same effect as morphine or diethylthiambutene (Themalon), is an extremely valuable characteristic, and makes it possible to contain the total dose for even the largest animal (mature elephant bulls) in a 2 or 3 cc. capacity dart syringe. M-99 is rapidly absorbed after intramuscular administration and a central narcotic and analgesic state with elimination of fear and anxiety is induced within minutes in most species. The substance is sparingly soluble in water but stable aqueous solutions containing 4-5 mgm/ml. of the powdered base can be prepared, provided the water is acidified with N/1 HCl to pH4. M-99 is much more soluble in Dimethyl sulphoxide (D.M.S.O.*), an organic solvent with remarkable spreading properties. Solutions containing 10 mgm. or more of M-99 per ml. of solution may easily be prepared using D.M.S.O., and this was the technique employed when preparing solutions for the capture of elephant. M-99 in D.M.S.O. solutions should be treated with extreme care, as it is readily absorbed through the skin, but have the added advantage that induction is even more rapid than with watery solutions, and the addition of hyalase to the drug mixtures becomes unnecessary. Both aqueous and D.M.S.O. solutions of M-99 are readily miscible with other substances such as hyoscine hydrobromide, sernylan and most tranquilizing drugs.

M-99 has a wide therapeutic index and a safety margin of several hundred per cent in the case of most species. Dosage rates do not vary much from one species to another, and the action of the drug is rapidly and reliably reversed by the administration of the usual morphine antagonists such as Nalorphine hydrobromide and Lorfan, as well as the antagonist in the M-series of drugs, *M-285*.

Other advantages of M-99 are its lack of severe side reactions (there is a varying degree of respiratory depression and tachycardia), and the fact that most postural reflexes are maintained.

Darted animals usually go down on their briskets and maintain a position of sternal recumbency. This is to the advantage of ruminants as ruminal movements are inhibited under the influence of M-99. Expulsion of gas by eructation is possible if the animal maintains this favourable position, and bloating is not a serious complication. Elephants lying in a position of sternal recumbency

Fig. ii



*It has recently been found that D.M.S.O. may cause eye disturbances in a number of experimental animals subjected to prolonged contact with this substance.

soon develop symptoms of serious respiratory distress and it is essential that they should be assisted manually into a laterally recumbent position as soon as possible before a fatal state of anoxia is allowed to develop[18].

M-183

M-183 (Reckitt) is essentially the acetylated form of M-99 i.e. 3-0-acetyl-7œ-(1-R-hydroxy-1-methylbutyl)-614-*endo*etheno-tetrahydro-oripavine hydrochloride (Synonym: Acetyl-propylorvinol hydrochloride).

Clinical tests have revealed that the acute toxicity of M-183 is considerably less than that of M-99 in the case of rats and mice.

Our field trials with M-183 appear to bear out these findings in the case of many wild ungulates. It was a general finding that a dosage rate of M-99 which was just high enough to cause the collapse of an immobilised animal, was insufficient if M-183 was employed, and the stricken animals remained on their feet.

This was found particularly advantageous in the case of giraffe, and in our experience M-183 is quite definitely preferable to M-99 for the capture of these animals. M-99 causes severe tachycardia and a fall in blood pressure which may be rapidly fatal, particularly in undernourished giraffe. Several cases were experienced where giraffe collapsed in their stride and died while under influence of M-99. When M-183 was substituted for M-99, these toxic symptoms were eliminated to a large degree, and a series of more than 50 giraffe was captured without further loss.

It is today general practice in the Kruger Park to employ M-183 rather than M-99 for the capture of animals in poor condition, or in cases where captured animals are immediately subjected to the additional stress of long journeys, etc. It must be stressed that, except perhaps in the case of giraffe, this is not absolutely necessary, and a similar effect may possibly be achieved by lowering the dosage rate of M-99 somewhat. It is useful to know, however, that one can employ M-183 at the same dosage rate as M-99 with the assurance of an additional margin of safety.

M-183 is more soluble in water than M-99 and aqueous solutions containing 4 mgm/ml. solution were generally used by us. Cognisance should be taken of the fact however, that M-183 on sterilisation, and especially by autoclaving, is liable to hydrolyse partially and to give a mixture of M-183 and M-99.

Nalorphine hydrobromide.

Nalorphine hydrobromide or N-allylnormorphine hydrobromide is the morphine-antagonist which has been routinely employed in the Kruger Park experiments as an antidote for M-99 and M-183. The proprietary brand used was 'Lethidrone' (Burroughs-Wellcome).

Nalorphine rapidly reverses the morphine-like depression caused by the M-drugs when administered intravenously, and more slowly when an intramuscular injection is given. The dosage rate of nalorphine varies with the size of the animal and not so much with the dose of narcotic. Whereas 100 mgms. of nalorphine is normally sufficient to reverse the action of 2 mgms. M-99 in a captive zebra or wildebeest, 500 mgms. or more may be necessary to counteract the effect of a similar dose in the case of an adult square-lipped rhinoceros.

As is pointed out by Harthoorn[8], this is possibly due to the fact that M-99 is highly selective for the particular receptor centres of the central nervous system, and therefore suffers less from dilution in the animal body than its antagonist.

M-285

M-285 (Reckitt) is N-cyclopropylmethyl-7oc-(1-hydroxy-1-methylethyl)-6,14-endoetheno tetrahydro -nororipavine hydrochloride. (Synonym: N-cyclopropylmethyl-19-methyl-norорvinol). This substance is a highly potent specific morphine antagonist, but in contrast to Nalorphine hydrobromide, its action is very much less weight dependent. This is particularly true when it is employed to reverse the narcotic action of the M-drugs in large animals. It is probably, like M-99, more specific for the receptor sites in the central nervous system than nalorphine, and this characteristic makes it an essential requisite for the reversal of M-99 narcosis in elephants. The prohibitively large quantities of nalorphine which is necessary to antagonize the action of 4-7 mgm. M-99 in adult elephants (2 gms. and more) rules it out as a routine antidote. By contrast, only 40 mgms. of M-285 is necessary to effectively perform this function.

Scopolamine (Hyoscine hydrobromide).

Hyoscine hydrobromide is an alkaloid with parasympatholytic action somewhat similar to Atropine. It also has central depressant effects however, and has a potentiating action on ataractic and narcotic drugs and may counteract respiratory depression.

It has been found by us to be an essential adjuvant to drug mixtures employed for the capture of giraffe and even zebra, but for most other species it is not essential (although without it, the latent period after darting and before capture is extended). In some, like elephant, it might even be toxic, and is best left out[18].

Hyoscine hydrobromide is usually administered at a dosage rate which varies from 1-5 mgm/100 lbs. body weight.

Sernylan (Phencyclidine).

Sernylan (Parke Davis) is 1-(1-phenylcyclohexyl) piperidine monohydrochloride and is a centrally

Fig. 111

The crystalline substance is highly soluble in water, and aqueous solutions containing 100 mgm/ml. of the drug were prepared by us.

A disadvantage of hyoscine is that it causes a prolonged dilatation of the pupil and paralysis of the ciliary muscles. This causes photophobia and the animal is incapable of focusing on nearby objects. If released in such a semi-blinded state, its chances of survival must be reduced.

acting drug, the action of which varies according to dosage level.

At low dosages it causes a cataleptic state and at higher levels a condition resembling anaesthesia.

It may possibly be classified with the so-called 'Major' tranquilizers of Marsboom and Mortelmans[16], which also include the butyrophenones dehydrobenzperidol, fluanisone and others.

Harthoorn[7] considers that the term 'neuroleptic' should properly be reserved for this group of drugs which have a more intense akinetic activity than the true tranquilizers (ataractics), and which may produce a catatonic state which permits no concerted movement.

This is probably the correct approach, as sernylan, and even some of the butyrophenones employed by us, produce no state of true sedation. They certainly potentiate the action of M-99 and related drugs and effect the immobilisation of highly excitable ungulate species such as kudu, eland, and nyala, which in their absence remain ambulatory even under influence of large doses of M-99. Low dosage levels of sernylan should be administered in combination with M-99 (i.e. not more than 100 mgm/500 lbs. body weight), or the animal will fail to rise when the action of the M-99 is reversed with an antagonist.

It is also desirable to include a suitable tranquilizer in this mixture as Sernylan produces little or no sedation and the animal may thrash about severely and injure itself in the state of incoordination produced by the combined effect of M-99 and Sernylan.

Sernylan is highly soluble in water and stable aqueous solutions containing 100-200 mgm/ml. of the drug were prepared.

Fluanisone (R2028 base).

Fluanisone (Janssen) is the proposed name for 1-(3-(4-fluorobenzoyl)-propyl)-4-(2-methoxyphenyl)-piperazine. This butyrophenone derivative is, like the related Droperidol and Haloperidol (Janssen), a true neuroleptic drug of high potency. It is a strong inhibitor of learned reflexes, thus producing a typical state of catalepsy[16]. As such, dehydrobenzperidol (Droperidol) is 400 times more active in dogs than chlorpromazine and chlorprotixene, and 10 times more active than haloperidol. Droperidol has the shortest, and haloperidol the longest duration of action in this series. As in the case of Sernylan, aqueous solutions of Fluanisone are rapidly absorbed and hasten the induction of narcosis by narcotic or analgetic/cataleptic agents such as M-99.

At the dosage levels employed by us, Fluanisone does not cause any of the undesirable side effects of Sernylan, such as loss of balance, gnashing of the teeth etc.

In combination with M-99 and hyoscine hydrobromide, it induces a state of truly remarkable tractability in zebra, which persists for hours even after the morphine antagonist is administered, and the animal rises to its feet. In ruminants, however, fluanisone does not allay fear or nervous states as well as some phenothiazines, and it was noticed that buffalo, wildebeest and waterbuck, for instance, remained sensitive to handling. The potentiating action on M-99 in ruminants is as great as that of Sernylan however, and there is the added advantage that fluanisone causes no disturbance of heat regulatory mechanisms in this group.

Small synergistic doses of suitable phenothiazines would constitute an ideal combination with fluanisone or droperidol and M-99 for the capture of most species of heat-sensitive ruminants. This is highly desirable, as the usual doses of phenothiazines employed for the capture of these ruminants very often cause serious (often fatal) heat regulatory disturbances, particularly on hot days, in such species as waterbuck, buffalo, wildebeest, sable and others.

Fluanisone and Droperidol are both water-soluble drugs and stable aqueous solutions containing up to 40 mgm/ml. of these drugs were prepared by dissolving the requisite amounts in 1.5% Tartaric acid containing 0.05% Methylparaben and 0.005% Propylparaben as preservatives.

Tranquilizers.

A variety of tranquilizing or ataractic drugs were tested, and of these the phenothiazine derivatives chlorpromazine hydrochloride (Largactil, May and Baker), acetylpromazine (Boots) and trifluo-promazine (Siquil, Squibbs) were found most useful. Acetylpromazine because of its rapid absorption and fast action found the widest application, and is generally used in combination with M-99 (with or without Scopolamine) for the immobilisation of most ungulate species.

It produces very satisfactory sedation, and in combination with M-99 brings about a narcotic and analgesic state during which the animal is insensitive to pain and completely tractable. Animals have been branded (see fig. (iii)), castrated, and even partial hysterectomies have been performed under the influence of this drug mixture, after some additional local anaesthesia.

M-99 has a remarkable potentiating effect on tranquilizing drugs such as Acetylpromazine. Dosages of these phenothiazines which would normally not have the slightest visible influence on an animal when administered alone, effect a marked degree of tranquilization when injected in combination with M-99 or M-183. A total dose

of 50-60 mgms. of Acetylpromazine, for instance, is sufficient to produce a satisfactory state of sedation in even the largest elephant bull and higher doses induce a soporific reaction and a somnolent state from which the animal refuses to rise after the M-99 antagonist is administered[18].

It seems logical to conclude that M-99 plus acetylpromazine (or related neuroleptic agents) form true neuroleptanalgesic combinations under the influence of which even surgical intervention is possible in many species — a procedure which would not be possible with either drug alone.

Acetylpromazine causes toxic symptoms in many ruminants, even at fairly low dosage levels, and cognisance should be taken of the fact that serious, and often fatal, heat regulatory disturbances may follow its administration, particularly on hot days. The torticollis reported in waterbuck by Short and Spinage[19 20], is most likely also due to the effects of Acetylpromazine and is not a toxic symptom of M-99 per se.

In the case of highly-strung and nervous animals, such as kudu, eland, nyala, sable and others, it is advisable to use a tranquilizer of more potent, if slower, action. For this purpose, both chlorpromazine hydrochloride or trifluopromazine may be employed, and the latter has the added advantage that its influence on heat regulation is less drastic than that of acetylpromazine.

Discussion of Results

The reaction of ungulates to M-99 drug mixtures has been adequately reported on by Harthoorn and Bligh[9] and others, and will not be recapitulated.

A better purpose will be served by a discussion of drug mixtures applicable to individual species and the variation in dosage levels necessitated by differences in weight and sex of individuals.

(i) *Impala* (*Aepyceros melampus melampus* (Lichtenstein)).

A substantial number of impala has been successfully captured with the aid of the drug-immobilising technique. (See fig. (iii)). The following combination may be used for adult animals ranging from 100-165 lbs. in body weight.

0.5 mgm. M-99.
5 mgm. Acetylpromazine maleate.
5 mgm. Hyoscine hydrobromide.

Impala are rather sensitive to the action of M-99, and at this dosage rate they will usually lapse into a coma and die from anoxia within 30 minutes if no remedial measures are applied. The intravenous injection of 10 mgms. Nalorphine hydrobromide immediately after capture, is normally sufficient to prevent any such occurrence.

In more open country, the dose of M-99 may well be reduced to 0.25 mgm., and although the animal will remain ambulatory for a longer period*, there is no danger of excessive respiratory depression developing.

Total number of impala immobilised: 47 (33 males, 14 females).

Mortality: 2.

(ii) *Blue wildebeest* (*Connochaetes* (*Gorgon*) *taurinus taurinus* (Burchell)).

Wildebeest have been captured with almost infallible certainty and negligable loss with the following mixture (see fig. (iv)):

Adults (450 — 650 lbs.): M-99 — 2.0 mgms.
Acetylpromazine maleate — 20 mgms.
Hyoscine hydrobromide — 20 mgms.

1-2 *year old young* (200 — 450 lbs.): M-99 — 0.5 to 1.0 mgm.
Acetylpromazine maleate — 10 mgm.
Hyoscine hydrobromide — 10 mgm.

Fig. iv

In view of the successful application of Fluanisone in such cases where phenothiazine derivatives may cause toxic symptoms at higher dosage

*The addition of the enzyme Hyaluronidase (1500 i.u.) to the immobilising mixture, usually facilitates a more rapid induction.

levels, it may be desirable to reduce the Acetylpromazine dose by half and substitute an equivalent dose of Fluanisone.

The drug mixture for adult wildebeest would then read: M-99 — 2 mgms., Fluanisone — 10 mgms., Acetylpromazine — 10 mgms.

Total number of wildebeest immobilised: 124 (75 males, 49 females).

Mortality: 8. (Not all due to drug action).

(iii) *Zebra* (*Equus* (*Hippotigris*) *burchelli antiquorum* H. Smith)

The same drug-mixtures and dosage levels applicable to wildebeest above, may also be employed for the capture of adult zebra (550 — 750 lbs. body weight). (See fig. (v). In the case of these animals, Fluanisone is definitely preferable to Acetylpromazine or other phenothiazines, and induces excellent tranquilization even during the recovery phase post-nalorphine administration. This is particularly desirable when zebra have to be crated immediately for transport. Crates have to be fitted with padded shoulder supports to prevent the animal from moving forwards in characteristic manner during the recovery phase and injuring or breaking its neck.

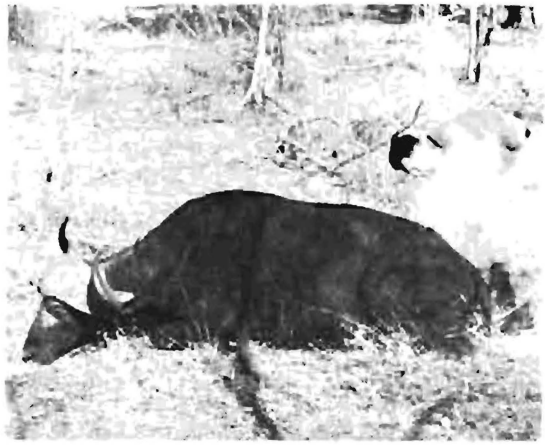
Zebra foals of 1-2 years old have also been most successfully captured with a mixture comprised of:

M-183 — 1.0 mgms.
Fluanisone — 10 mgms.
Hyoscine hydrobromide — 10 mgms.

Darted animals usually exhibit first signs of ataxia within 3 minutes and could be caught and handled in less than 10 minutes.

Fig. v

Fig. vi



Total number of zebra immobilised : 106 (60 males, 46 females).

Mortality: 7. (Only 2 directly due to drug action).

(iv) *Tsessebe* (*Damaliscus lunatus lunatus* (Burchell)).

A single tsessebe bull (estimated body weight 350 lbs.), was successfully captured and subsequently marked, using a mixture of 1.0 mgm M-99, 10 mgm. Hyoscine hydrobromide and 10 mgm. Acetylpromazine. The latter could well be substituted by Fluanisone 5 mgm. and Acetylpromazine 5 mgm.

(v) *Buffalo* (*Syncerus caffer caffer* (Sparrman)).

An effective and safe immobilising mixture for adult buffalo is the following (see fig. (vi)).

Adult bulls (1,500 — 2,000 lbs.) : 4 to 6 mgm. M-99.
Fluanisone 30 mgm.*
Acetylpromazine 20 mgm.
75 — 100 mgm. Hyoscine hydrobromide (Optional).

Adult cows (1,000 — 1,500 lbs.) : 3 to 4 mgm. M-99.
20 mgm. Fluanisone.
15 mgm. Acetylpromazine maleate.
50 mgm. Hyoscine hydrobromide (Optional).

* Buffalo have previously been successfully captured using M-99 with Acetylpromazine (20-25 mgms.) *or* Fluanisone (30-40 mgm.) alone, but in view of the synergistic action of the neuroleptic

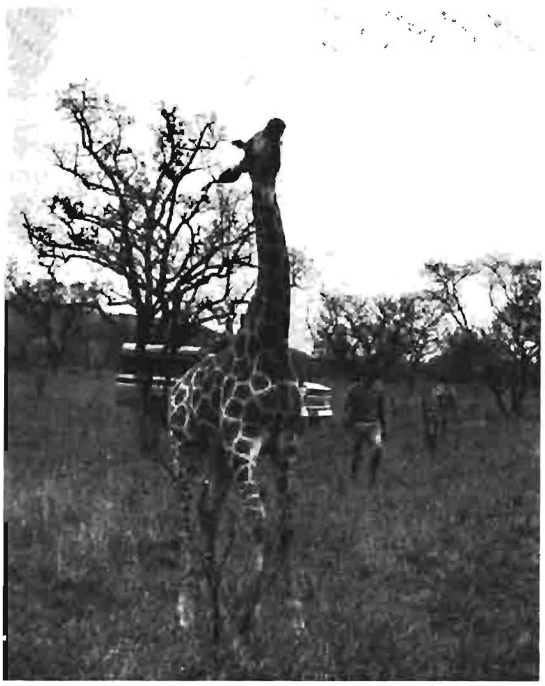
drugs and the unsatisfactory sedation achieved with Fluanisone alone, it is considered advisable to use a combination of the two drugs, both at a lower dosages level. In such cases the addition of hyoscine hydrobromide may well be redundant.

200 — 400 mgm. Nalorphine hydrobromide is the usual dose of antagonist administered. It is customary to inject some ¾ of the total dose of Nalorphine intravenously and the rest intramuscularly, to form a depôt against the needs of the immediate future.

Total number of buffalo immobilised : 19 (9 bulls, 10 cows).

Mortality: 0.

Fig. vii



(vi) *Giraffe* (*Giraffa camelopardalis giraffa* (Boddaert)).

The oripavine derivative M-183 is a safer drug to use for the capture of giraffe than the related more potent M-99. The onset of its reaction is more gradual than that of M-99, and its effect is less drastic on cardiac function and respiration.

M-99 often causes a sudden fall in blood pressure, which may or may not be associated with acute cardiac failure. This is particularly true for giraffe in poor condition, and once they collapse, death follows almost inevitably.

It is essential to administer a dose of narcotic that will keep the animal ambulatory, as giraffe experience great difficulty in rising from the ground in a bemused state. They often exhaust themselves so much in their efforts to rise that they eventually succumb completely and die. In view of the risk of fatal hypotension, it is also essential to keep the animal on its feet.

While walking about in a condition of 'twilight sleep', it can easily be roped and led into a crate mounted on the back of a low trailer. (See fig. (vii)). Once in the crate, the morphine antagonist (100-200 mgm. Nalorphine) is immediately injected into the jugular vein, and 100-200 mgm. hydrocortisone (Vecortenol. Ciba) and some 12,000,000 i.u. long-acting penicillin are administered intramuscularly.

As soon as the animal's blood pressure returns to normal, which may be deduced from the prominence of the *Vena facialis,* the animal may be transported to the holding pen and released.

A completely safe and reliable drug combination for the capture of young giraffe in the 600 — 1,200 lbs. class, is:

M-183 — 2 mgms.
Acetylpromazine maleate — 20 mgms.
Hyoscine hydrobromide — 50 mgms.

For adult animals (1-1½ tons), the dose of M-183 would have to be increased to 4 or 5 mgms.

If giraffe have to be transported over long distances, it is very advisable to keep them in a holding pen for some time, until they are quite tame and will feed from the hand. This is often accomplished within 7-10 days. Giraffe should be transported individually in crates large enough to permit the animal to lie down and rise without difficulty. Frequent stops should be made en route, and the animals allowed to rest, to prevent fatal trauma in the extensor muscles of the fore legs[25].

Over smaller distances giraffe may be transported in smaller crates, provided they are trussed in a special harness, as is described by Riney and Kettlitz[17].

Total number of giraffe immobilised: 73. (35 bulls, 38 cows).

Mortality: 8. (Not all due to drug action).

(vii) *Hippopotamus* (*Hippopotamus ampbibius capensis* Desmoulins).

Drugs of the M-series, morphine and even diethylthiambutene (Themalon) in combination with chlorpromazine or acetylpromazine and hyoscine, are suitable for the capture of hippopotami on dry land, but are practically useless when the animals are in the water. The onset of the drug reaction is too rapid and the animals become completely immobilised, sink and drown.

On land, adult hippos (3,000 — 4,500 lbs. body weight) may be successfully immobilised with 4.0 — 5.0 mgms. M-99 without any adjuvants.

In the water, however, the only drug combination, which keeps the affected hippo buoyant for a sufficient length of time to allow a net to be brought in position and to haul it on to dry land before sinking, is Sernylan (Parke Davis), and a suitable tranquilizer[24].

A Sernylan-Chlorpromazine mixture gave very satisfactory results in the Kruger Park, and a number of hippo were successfully captured at a dosage rate of Sernylan 0.125 — 0.16 mgm/lb. and Chlorpromazine 0.25 — 0.4 mgm/lb. Chlorpromazine could conceivably be substituted with Trifluopromazine or Acetylpromazine.

Total number of hippo immobilised with M-99: 2.

Mortality: 1.

(viii) *Square-lipped Rhinoceros* (*Ceratotherium simum simum* (Burchell)).

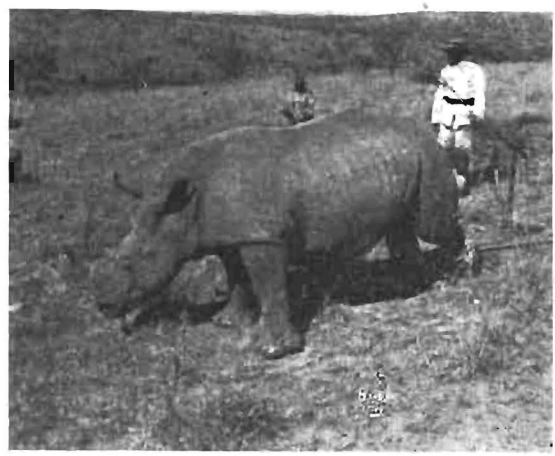
Circumstances have necessitated the capture of only 3 white or square-lipped rhino in the Kruger Park, but the long series which have been successfully immobilised in the Natal Parks[10], proved that adult beasts of this species (ranging from 3,000 — 5,000 lbs. body weight) may be safely and reliably restrained by the injection of 1.5 — 3.0 mgms. M-99, with or without adjuvants. (See fig. (viii)).

(ix) *Elephant* (*Loxodonta africana africana* (Blumenbach)).

Elephants are much more sensitive to the action of neuroleptic-narcotic mixtures than most other species. Compared with the dosage rate for M-99 in the case of most ruminant species (2.0 — 4.0μ gm./lb.), that for elephant is very much lower (0.47 x 0.67μ gm./lb.).

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 group of adult elephant bulls (weighing 12,000 — 15,000 lbs.), and 5-6 mgms. for the smaller class adult bulls and largest cows (7,000 — 12,000 lbs. body weight). (See fig. (ix)).

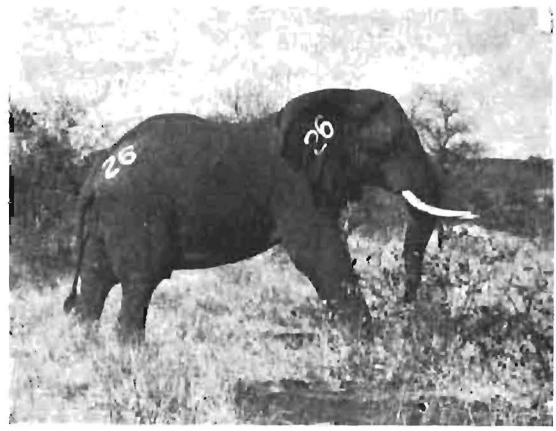
Fig. viii



M-99 is administered in combination with Acetylpromazine (50-60 mgms. (total dose) for the largest bulls and 40-50 mgms. for the smaller adult bulls). The latter may well be substituted by Fluanisone with even more satisfactory results.

Hyoscine hydrobromide apparently causes toxic reactions in elephant and it is best omitted from drug mixtures.

Fig. ix



Large amounts of Nalorphine are necessary to antagonise the effect of M-99 in these massive beasts and the antagonising action is to some degree weight dependent.

On the other hand, highly dependable reversal of narcosis is obtained in elephant with norori-pavine hydrochloride (M-285), and the optimum dose of antidote in the case of beasts immobilised with 5-8 mgms. M-99, seems to be in the region of 40-60 mgms. M-285. Elephants which go down in a sternal position when succumbing to the drug reaction, should be pulled over on their sides by means of a rope and truck, in the manner described by Pienaar et al[18], as soon as possible, in order to prevent fatal respiratory and circulatory collapse.

Total number of elephants immobilised: 34 (all bulls).

Mortality: 2.

(x) *Warthog* (*Phacochoerus aethiopicus sundevalli* Lönnberg).

An effective immobilising dose of M-99 for adult warthog (140-220 lbs.), is 1.0 — 1.5 mgms., in combination with 5-10 mgms. Hyoscine hydrobromide and 20 mgm. Acetylpromazine (or Fluanisone).

Total number of warthog immobilised: 2 (Boars).

Mortality: Nil.

(xi) *Waterbuck* (*Kobus ellipsiprymnus ellipsiprymnus* Ogilby).

A number of waterbuck have been successfully captured in the Kruger Park with neuroleptic-narcotic mixtures, but the therapeutic index is not particularly favourable in this species, and losses have been experienced elsewhere from heat-stroke and collapse, torticollis, cardiac failure, etc. Adult bulls (475 — 600 lbs.) have been captured with 3 — 3.5 mgm. M-99 and adult cows (350 — 500 lbs.) with 2 — 2.5 mgms. M-99, in combination with Acetylpromazine 20 mgms. and Hyoscine hydrobromide 20-30 mgms. (See fig. (x)). Until such time as Fluanisone or one of the other related butyrophenones prove to be a satisfactory substitute for Acetylpromazine (which causes the toxic reactions), it would be advisable to capture waterbuck with Succinyl-choline (Suxamethonium) at a dosage rate of 0.7 mgm./lb. in combination with Atropine or Hyoscine hydrobromide (5 mgm./100 lbs.).

Fig. x

Total number of waterbuck immobilised : 5 (4 males, 1 female).

Mortality: Nil.

(xii) *Red hartebeest* (*Alcelaphus buselaphus caama* (Cuvier)).

As in the case of wildebeest and tsessebe, red hartebeest may be captured with splendid success, using neuroleptanalgesic techniques.

Adult bulls (350 — 450 lbs.) require 1.0 mgm. M-99 and adult cows (280 — 380 lbs.) only 0.75 mgm. M-99 in combination with 10 — 15 mgm. Acetylpromazine and 10 mgm. Hyoscine hydrobromide. Fluanisone may be substituted for half the dose of Acetylpromazine and the Hyoscine may be omitted.

The dosage rates for hartebeest bulls may also be successfully applied to adult bontebok (280 — 350 lbs.) *Damaliscus dorcas dorcas* (Pallas), but here again the Acetylpromazine dose should be cut to the minimum and substituted with Fluanisone to prevent unwanted side reactions.

Total number of red hartebeest immobilised: 5 (4 males, 1 female).

Mortality: Nil.

(xiii) *Kudu* (*Tragelaphus strepsiceros strepsiceros* (Pallas)).

Kudu, eland, nyala and their kin fall in the group of highly excitable animals, the behaviour of which upon darting indicate the need for a

more potent tranquilizing agent. The usual combinations of M-99 with acetylpromazine and hyoscine do affect these animals, but they remain ambulatory and keep on the move with a persistent trotting gait. Their sense of hearing is not impaired and they are easily startled and put to flight even in their bemused state. It is often very difficult to capture them unless they may be fortuitously roped.

Fig. xi

The most satisfactory drug combination for kudu used by us to date, and which does immobilise the animals, is the following. (See fig. (xi)).

Adult bulls (550-650 lbs.): M-99 — 4 mgms.
Sernylan — 75 to 100 mgm.
Trifluopromazine (Siquil) — 50 mgm.

Adult cows (280-400 lbs.): M-99 — 2.5 to 3 mgms.
Sernylan — 50 mgms.
Trifluopromazine — 50 mgm.

Hyoscine hydrobromide may also be added to this mixture at a dosage rate of 5 mgm./100 lbs. body weight, but is best omitted if the animal is to be released immediately after capture.

It seems likely, in the light of experience with other ungulate species, that the Sernylan in the above drug combination could be replaced by Fluanisone (40 — 50 mgms. total dose for bulls and 30 — 40 mgms. total dose for cows), with even more satisfactory results.

Number of kudu immobilised: 13 (10 bulls, 3 cows).

Mortality: 1.

(xiv) *Eland* (*Taurotragus oryx oryx* (Pallas)).

The same drug combination and dosage level employed for adult kudu bulls, may also be used for the capture of adult eland cows (500 — 850 lbs.). For adult bulls, weighing from 1,200 to 2,000 lbs., the dose of M-99 must be increased to 5 or 6 mgms., and that of Sernylan to 100 or 150 mgms. (alternative Fluanisone 50-60 mgms.). Trifluopromazine should also be used instead of Acetylpromazine. (See fig. (xii)). — Page 289.

Number of eland immobilised: 2 (1 male, 1 female).

Mortality: Nil.

(xv) *Sable* (*Hippotragus niger niger* (Harris)).

A provisional dose for adult sable antelope (450 — 550 lbs.), in the light of limited data available, would be: (See fig. (xiii)).

M-99 or M-183 — 2.0 mgms.
Hyoscine hydrobromide — 20 mgms. (Optional).
Trifluopromazine — 20 mgms.
Fluanisone — 10-20 mgms.

These dark-skinned animals develop toxic symptoms, associated with heat stroke, when injected with Acetylpromazine, and for this reason a low dose of Trifluopromazine in combination with Fluanisone is recommended.

A similar drug combination is proposed for the capture of Roan antelope (*Hippotragus equinus equinus* (Desmarest)), but for adult bulls, which

Fig. xiii

may weigh 600 lbs. and more, it may be necessary to increase the dose of M-99 to 3.0 mgms.

Number of sable immobilised: 2 (1 bull, 1 cow).

Mortality: 1.

Number of roan immobilised: 1 (Young calf).

Mortality: Nil.

Discussion

It dose not fall within the scope of this paper to go into a detailed analysis of dose response curves, and with few exceptions, we have not as yet succeeded in establishing the minimum effective dose and LD-50 for M-99 or M-183 in our subject species. The table of optimum dosage levels provided below for 16 different species, will, in our opinion, form a practical guide on which more detailed studies can be based.

Fig. xii

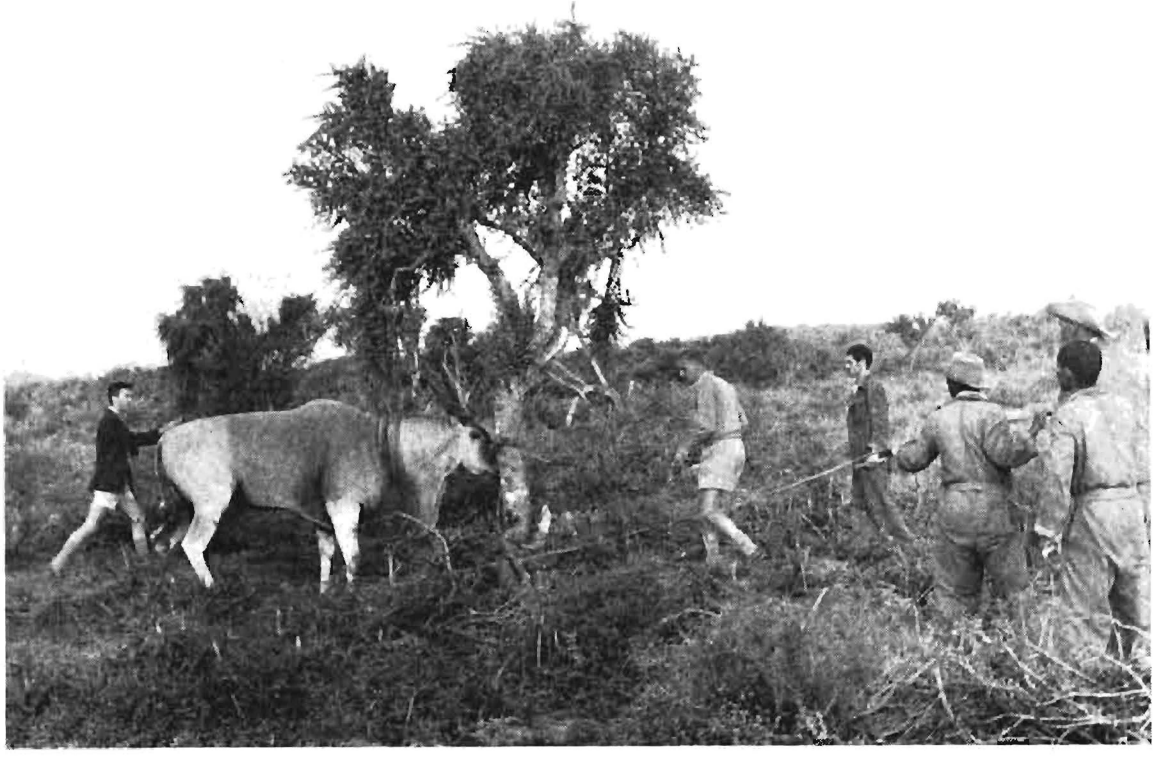


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TABLE 2.

OPTIMUM DOSAGE RATES OF M-99 AND M-183 (IN MG/KG) IN NEUROLEPTANALGESIC MIXTURES FOR 16 SPECIES OF WILD HOOFED ANIMALS IN SOUTH AFRICAN NATIONAL PARKS.

Species	Sex	Range adult body weight in Kg	Dosage rates in µg/Kg.	
			M-99	M-183
Elephant	♂	5443–6804	1.03– 1.47	
	♂	3175–5443	0.91– 1.89	
	♀	3175–5443	0.91 –1.89	
Square-lipped Rhinoceros	♂	1361–2268	0.88— 2.2	
	♂ & ♀	1134–1814	0.82— 2.2	
Hippopotamus	♂	1588–2041	2.45— 3.15	
	♀	1361–1724	2.32— 2.93	
Giraffe	♂ & ♀	907–1361		2.94— 5.51
	Young ♂ & ♀	272–544		3.68— 7.35
Warthog	♂ & ♀	64– 100	10.00—23.44	
Zebra	♂ & ♀	249– 340	5.88— 8.03	5.88— 8.03
	Young ♂ & ♀	113– 159	6.29— 8.85	6.29— 8.85
Impala	♂ & ♀	45– 75	5.55—11.11	5.55—11.11
Blue wildebeest	♂ & ♀	204– 295	6.77— 9.80	
	Young ♂ & ♀	91– 204	4.90—10.99	
Red Hartebeest	♂	158– 204	4.90— 6.32	
	♀	127– 172	4.36— 5.91	
Tsessebe	♂& ♀	113– 158	4.75— 8.85	
Buffalo	♂	590– 907	4.41—10.17	
	♀	454– 680	4.41— 8.81	
Waterbuck	♂	215– 272	11.02—16.28	
	♀	158– 227	8.81—15.82	
Kudu	♂	249– 295	13.56—16.06	
	♀	127– 181	13.81—23.62	
Eland	♂	544– 907	5.51—11.03	
	♀	227– 386	10.36—17.62	
Sable antelope	♂ & ♀	204– 249	8.03— 9.80	8.03— 9.80
Roan antelope	♂ & ♀	204– 272+	7.35—14.71	7.35—14.71

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TABLE 1.—DOSAGE RATES OF DRUGS USED FOR NEUROLEPTIC NARCOSIS IN 16 SPECIES OF HOOFED WILD ANIMALS IN SOUTH AFRICAN NATIONAL PARKS.

Species	No. of successful cases	Mortality	Sex	Range Adult Body weight lbs.	DOSAGES (Total average dose for adult animals)									
					Neuroleptic (Major Tranquilizer)		*Ataractic* (Tranquilizer)			*Narcotic*		*Parasympatholytic*	*Morphine antagonist*	
					Sernylan mgm.	Fluanisone mgm.	Acetylpromazine mgm.	Trifluopromazine mgm.	Chlorpromazine mgm.	M-99 mgm.	M-183 mgm.	Hyoscine Hydrobr. mgm.	M-285 mgm.	Nalorphine hydrobr. mgm.
Elephant (*Loxodonta africana africana*)	34	2	♂ ♂ ♀	12,000–15,000 7,000–12,000 7,000–12,000			50–60 40–50 40–50			7–8 5–6 5–6			60 40 40	1500–4000 (Not recommended)
Square-lipped Rhinoceros (*Ceratotherium simum simum*)	3	1	♂ ♂ & ♀	3,000– 5,000 2,500– 4,000			40 (optional) 40 (optional)			2–3 1.5–2.5		100 (optional) 75 (optional)		250–500 250–500
Hippopotamus (*Hippopotamus amphibius capensis*) (on land)	2	1	♂ ♀	3,500– 4,500 3,000– 3,800			40 (optional) 40 (optional)			5 4		100 (optional) 100 (optional)		250–500 250–500
Giraffe (*Giraffa camelopardalis giraffa*)	73	8	♂ & ♀ ♂ & ♀	2,000– 3,000 Young 600– 1,200			40 20				4–5 2	100 50		250–500 100–200
Warthog (*Phacochoerus aethiopicus sundevalli*)	2	—	♂ & ♀	140–220		10	20			1.0–1.5		5–10		50–100
Zebra (*Equus burchelli antiquorum*	106	7	♂ & ♀ ♂ & ♀	550–750 Young 250–350		20 10	Alternative to Fluanisone 20 10			2 1	Alternative 2 1	20 10	5	100 50–100
Impala (*Aepyceros melampus melampus*)	47	2	♂ & ♀	100–165			5			0.25–0.5	Alternative 0.25–0.5	5		10 (immediately) +40
Blue wildebeest. (*Connochaetes (Gorgon) taurinus taurinus*)	124	8	♂ & ♀ ♂ & ♀	450–650 Young 200–450		20 (or 10+10 Ac. prom.) 10	20			2 1		20 (optional) 10 (optional)		100 50–100
Red hartebeest (*Acelaphus buselaphus caama*)	5	—	♂ ♀	350–450 280–380		10 10	15 10			1.0 0.75		10 (optional) 10 (optional)		100 75–100
Tsessebe (*Damaliscus lunatus lunatus*)	1	—	♂ & ♀	250–350		10 (or 5+5 Ac. prom.)	10			0.75–1.0		10 (optional)		100
Buffalo (*Syncerus caffer caffer*)	19	—	♂ ♀	1,300– 2,000 1,000– 1,500		40 (or 30+20 Ac. prom.) 30 (or 20+15 Ac. pr.)	20 20			4–6 3–4		75–100 (optional) 50–100 (optional)		200–400 200
Waterbuck (*Kobus ellipsiprymnus ellipsiprymnus*)	5	—	♂ ♀	475–600 350–500		Preferable to Ac. pr. alone. *20+10 Ac. pr. *20+10 Ac. prom	20 20 Not recommended			*3.0–3.5 *2.0–2.5		20–30 (optional) 20–30 (optional)		200 100–200
Kudu (*Tragelaphus strepsiceros strepsiceros*)	13	1	♂ ♀	550–650 280–400	75–100 50	Alternative to Sernylan *50 *40	Not recommended	50 50	Alternative to Trifluopromazine. 1.5–2.0 mgm/lb. body weight	4 2.5–3		50 (optional) 30 (optional)		200 100–200
Eland (*Taurotragus oryx oryx*)	2	—	♂ ♀	1,200– 2,000 500–850	100–150 75–100	Alternative to Sernylan. 50-60 *50	Not recommended	50–100 50		5–6 4		100 (optional) 50 (optional)		200–400 200
Sable antelope. (*Hippotragus niger niger*)	2	1	♂ & ♀	450–550		*20 (or 10) +20 Trifluopromazine	Not recommended	20–30		2	Alternative 2	20 (optional)		200
Roan antelope (*Hippotragus equinus equinus*)	1	—	♂ & ♀	450–600+		*20–30 (or 15+ 20 Trifluopromazine)	Not recommended	20–30		2–3	Alternative 2–3	20 (optional)		200–300

*The dosages marked with an * are subject to further confirmation.

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FIRST AID FOR SMALL ANIMALS

K. C. Summer. John Wright & Sons Ltd., Bristol, 1965. Pages 144. Nine illustrations. English price 15s.

Veterinarians are often asked by pet owners about publications which will assist them in taking better care of the health of their dogs. This well written little book can be recommended for this purpose.

The author, a veterinarian, has divided the book in two parts. The first part describes in simple language sufficient anatomy and physiology to enable the first-aid worker to know why certain actions are taken and others avoided. The second part deals with application of the knowledge gleaned from the first part in such a way that first aid can be rendered without encouraging the owner to indulge in treatments beyond his scope or comprehension. The line drawn illustrations assist in clarifying the text on some anatomical systems and methods of bandaging.

Veterinarians can, without apprehension recommend this book to their clients, and also use it as a simple manual of instruction for their lay staff in their surgeries and hospitals.

— K. v.d. W.

THE USE OF TRANQUILLIZERS, MUSCLE RELAXANTS AND ANAESTHETICS AS AN AID IN THE MANAGEMENT OF WILD CARNIVORES IN CAPTIVITY—TWENTY FIVE CASE REPORTS

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SUMMARY

Results obtained with the use of different anaesthetics, tranquillizers and muscle relaxants on carnivorous animals of seven different species, are recorded in this report.

INTRODUCTION

The use of muscle relaxants, tranquillizers and anaesthetics has greatly increased the safety and ease with which wild carnivores can be handled and has widened the scope of their study and treatment. Thorough clinical examination, including the use of x-ray and other modern aids is now possible as are the application of major surgical techniques. As the literature in this field is still very restricted it is felt that the experiences here recorded may be of value.

MATERIALS AND METHODS

Animals. With the exception of one cheetah, all the animals mentioned in this report, belonged to the National Zoological Gardens of South Africa.
Drugs. The following chemical compounds were used:

Sernylan (Parke Davis), 1-(-1-Phenylcyclohexyl) piperidine hydrochloride is a drug with tranquillizing and anaesthetising properties (van Niekerk and Pienaar, 1963)[1]. 'In a great variety of animals, the drug produces a quiet and cataleptoid state and, at increasing dose levels, general anaesthesia.' (Kroll, 1962)[2]. This drug may be administered orally or by intramuscular or intravenous injection. Kroll (1962)[2] found Sernylan adequate without the additional administration of muscle relaxants and tranquillizers. Pienaar, van Niekerk, Young, van Wyk and Fairall (1966)[3], found the inclusion of a suitable tranquillizer in the drug mixture desirable. When a relatively low dose of Sernylan is administered without the addition of a tranquillizer, the animal may injure itself in the state of inco-ordination, produced by Sernylan.

Largactil (May Baker), chlorpromazine hydrochloride is a well known tranquillizer with a relatively long lasting effect. Largactil proved to be effective and useful for the tranquillization of wild carnivores and may be administered by oral or parenteral routes. This phenothiazine derivative has also been found very suitable for the conditioning of newly caught animals, by virtue of its soporific effect (Harthoorn, 1960)[4].

Acetylpromazine (Boots), acepromazine maleate, is another phenothiazine derivative which has been used with success in the tranquillization of wild animal species. The rapid absorption and fast action of this ataractic drug makes it a valuable constituent in drug mixtures, for the chemical immobilisation of a variety of free living wild ungulate species (Pienaar et al., 1966)[3]. At relatively high dosage levels, acetylpromazine was observed to cause posterior paresis in tranquillized animals.

Flaxedil (May Baker), gallamine triethiodide, is a muscle relaxant which blocks the transmission of nerve impulses at the neuromuscular junction by reducing the muscle-end-plate potential and inhibiting the physiological action of acetylcholine. (Harthoorn, 1960)[4]. This action of flaxedil may be reversed with the subsequent administration of a suitable antidote.

Prostigmin Vet. (Roche), neostigmine has potent cholinergic stimulating properties and is capable of reversing the paralysing effect of gallamine triethiodide. This drug is usually administered at a dosage rate of 0.02 mg/Kg.

Sagatal (May Baker), pentobarbitone sodium is a non-volatile anaesthetic drug, commonly used for anaesthesia in domestic dogs and cats. Barbi-

turate anaesthetics were also employed for anaesthetising wild carnivores. Clifford, Stowe and Good (1960)[5] anaesthetized lions with pentobarbital, subsequent to premedication with meperidine and promazine. These authors maintain that pentobarbital is a dangerous anaesthetic when used to abolish all reflexes in lions. Cabrera (1965)[6] also anaesthetized lions with pentobarbital sodium but used dimetilamin, 3 propil-10 phenotiazin as an "inductor" before administration of the barbiturate. In the Pretoria zoo, carnivores were anaesthetized with pentobarbitone sodium, without prior premedication. The animals had been restrained mechanically before the intravenous injection of anaesthetics. It can be immagined, however, that intravenous injections on heavily tranquillized carnivores could be done in a much easier and safer way.

Brevane (Corn States labs.), methohexital sodium is another non-volatile anaesthetic and has a very short effect on the animal. This drug is administered by the intravenous route. When this drug had been used alone, recovery of the animal was usually accompanied by jerking movements of the legs.

Fluothane (I.C.I.), halothane is a very useful and safe volatile anaesthetic. It has been used with success on a variety of animal species.

R0.5-2807/B-21 (Roche) is an experimental tranquillizer which has only been used on a limited number of cases by the author. This drug appeared to have a marked "taming" effect on the one animal in which it was used but it unfortunately caused vomition.

Apparatus: The "Capchur" gun was supplied by the Palmer Chemical and Equipment Co., Atlantia, Georgia. The darts were fitted with barbed needles, which prevented them from being detached from the animal before the complete dose had been administered.

The squeeze cage is incorporated in the animal hospital section of the Rudolph Bigalke Institute in Pretoria and is capable of exerting a pressure of up to 600 lbs. per square inch. The animals were wedged between the movable wall of this restraint cage and its bars which separate the operator from the animal.

The catching net consisted of a handle and a steel ring to which a very thick canvas-bag had been attached.

Results

See tables.

Discussion

The use of this group of "chemical immobilizers" may be complicated by several factors. It is, for instance, difficult to assess the correct weight of a large carnivore visually. This factor makes the use of chemical agents with a narrow therapeutic index rather dangerous.

The mental and physiological status of an animal may also influence its response to chemical agents. Great variation in response to the same anaesthetic drug was experienced in the same animal on different occasions. One can therefore not always depend on a predetermined dose only, but should also take the response of the patient in consideration. The reaction of the animal to external stimuli, and the presence or absence of certain reflex movements should serve as a guide for the additional amount of anaesthetic to be administered.

Factors such as the availability of suitable facilities and the temperament and size of the animal should indicate the method of restraint to be used. The smaller carnivores are captured with catching bags, snares, nets and traps while the squeeze cage is often used for mechanical restraint of the larger species. Intravenous injections into the cephalic, recurrent tarsal or coccygeal veins of large carnivores can usually be accomplished, once they have been restrained in a suitable squeeze cage. Intraperitoneal, intramuscular or subcutaneous administration of sedative drugs is sometimes employed before further handling of these animals is attempted. Subcutaneous injection of small volumes of non-irritant chemical substances is sometimes done into the tail, after it has been pulled out of the cage. A syringe, attached at the end of a stick, is sometimes used for intramuscular injections. The larger carnivores should preferably be premedicated before the use of volatile anaesthetics.

Volatile anaesthetics may be administered in various ways. Apparatus used for this purpose vary from the old type "gas box" to more modern equipment. The animal hospital of the Pretoria Zoo has, for instance, a magnificent circle absorber circuit which can be used on animals of various species and sizes.

The value of Fluothane as an anaesthetic for use on wild animals cannot be overemphasized. Graham-Jones (1964)[7] used it with success on a Jungle cat, Puma, Ringtail coati, Arabian oryx and Crab-eating monkey. In the animal hospital of the Pretoria zoo this volatile anaesthetic was also found effective and safe for the induction and maintenance of general anaesthesia in several

mammalian and bird species, including the domestic rabbit, *Oryctolagus cuniculus,* the Black backed jackal, *Canis mesomelas,* Vervet monkey, *Cercopithecus aethiops pygerythrus,* Pied crow, *Corvus albus* and Giant eagle owl, *Bubo lacteus.*

Sagatal and Brevane are recommended for anaesthesia in wild carnivores, but it should be kept in mind that the standard dosage rate may not always be adequate and safe for different individuals.

A combination of Sernylan and a tranquillizer like Largactil or Acetylpromazine is recommended for the chemical immobilization of wild carnivores. High doses of such drug combinations produce a state of general anaesthesia in these species. Anaesthetised animals are more manageable and safer to handle and may even be transported over very long distances before they recover. (Young, 1966)[8].

RESULTS

Sex & Weight of Animal	*Drugs and Dosages*	*Response of Animal:*
	AFRICAN LION (Panthera leo)	
1 ♀182 lbs.	Sernylan: 2.8 Mg/Kg + Largactil: 3.6 mg/Kg Intramuscular.	Down in 7 minutse. Tractable in 20 minutes—second plane (medium) anaesthesia for more than 6 hours. Recovered completely in 24 hours.
	PUMA (Felis concolor)	
1 ♀50 lbs.	Flaxedil: 0.8 mg/Kg + Acetyl promazine: 1.6 mg/Kg Intramuscular.	Muscular tremors after 3½ minutes followed by posterior paresis. Tetraplegia after 5 mins. Paralysed and tranquilised for more than 3 hours. Recovered completed within 8 hours.
2 ♀50 lbs.	Sernylan: 1.2 mg/Kg. I/Muscular	Slight ataxia after 10 minutes.
3 ♀50 lbs.	Sernylan: 1.0 mg/Kg. Oral.	Ataxia after 40 minutes. Developed posterior paresis and hypersalivation. Ataxia lasted for more than 3 hours.
	LEOPARD (Panthera pardus).	
1. ♀75 lbs.	Sernylan: 5.2 mg/Kg + Largactil: 6.6 mg/Kg. Intramuscular.	Locomotor inco-ordination and paresis after 6 minutes. Gradual development of general anaesthesia—reached second plane anaesthesia in 25 minutes. Commenced recovery after another hour
2. ♂	Largactil: 150 mg. I/Muscular	These animals were very nervous and aggressive before tranquilization as they had been caught as adults. 20 minutes after the administration of Largactil, both animals were heavily tranquilized and they could be put together in the same cage without any possibility that they would fight. They became accustomed to each other and did not fight after the effects of Largactil had faded.
3. ♀	Largactil: 200 mg. I/Muscular	
	CHEETAH (Acinonyx jubatus)	
1. ♀17 lbs.	Sagatal: 3 gr (3 ml) Intravenous	Second plane (medium) anaesthesia: was suitably anaesthetized for dental surgery. Recovered from anaesthesia after 8 hours.
2. ♂90 lbs.	Sagatal: 12 gr (12 ml) Intravenous	Animal had been wounded and suffered from shock. Third plane (deep) anaesthesia lasted for 24 hours. X-ray photo's were taken, wounds were treated and a cast was fitted to one leg.
3. ♂90 lbs.	Sagatal: 16 gr (16 ml.) Intravenous	Third plane (deep) anaesthesia which lasted for 36 hours. X-ray photo's were taken and wounds were treated.
4. ♂90 lbs.	Sagatal: 12 gr (12 ml) Intravenous	Second plane (medium) anaesthesia which lasted for 8 hours. Animal received same treatment as above.
5. ♂52 lbs.	Sagatal: 6 gr (6 ml) followed by brevane: 75 mg (3 ml) Intravenous	Recovered from deep anaesthesia after 24 hours. No post narcotic excitement during recovery. Had been anaesthetised for treatment of wounds and removal of stitches.
6. ♂52 lbs.	Sagatal: 6 gr (6 ml), followed by brevane 25 mg (1 ml) Intravenous	Started to recover from anaesthesia after 15 minutes. Post narcotic excitement was absent during the recovery phase. Was suitably anaesthetized for amputation of mutilated tail.
7. ♂46 lbs.	Brevane: 100 mg (4 ml) Intravenous	Recovery commenced 5 minutes after the onset of anaesthesia. The recovery phase was characterized by convulsive movements of the legs.
8. ♂70 lbs.	Largactil: 100 mg Intramuscular	Deeply tranquillized from 30 minutes after injection. Effect of Largactil lasted for several hours and faded gradually.
9. ♂94 lbs.	Largactil: 100 mg Intramuscular.	Heavily tranquillized for more than 12 hours. Had previously damaged bandages and plaster cast but left it undisturbed during and after tranquillization.

BLACK-BACKED JACKAL (Canis mesomelas)

1. ♂	Fluothane. Inhalation.	Induction of anaesthesia took 1 minute and was accompanied by narcotic excitement. After administration of Fluothane was stopped the animal suddenly recovered after 5 minuts. The jackal was suitably anaesthetized for any clinical examinations or minor operations.
2. ♂13 lbs.	Brevane: 10 mg/Kg. Intravenous.	Recovery, accompanied by jerking movements of the legs, commenced after 5 minutes.
3. ♀7 lbs.	Flaxedil: 0.5 mg/Kg + Acetyl promazine 2 mg/Kg. Intramuscular.	Tetraplegia after 5 minutes. No dyspnoea. After another 3 minutes: Prostigmin injected as antidote for flaxedil.
	Prostigmin: 0.07 mg. I/venous.	Paralysis had disappeared but animal was still deeply sedated.
4. ♀8 lbs.	Flaxedil: 1.0 mg/Kg+Acetyl promazine: 2 mg/Kg. I/venous	Tetraplegia and sedation after 5 mins. No interference of respiration. After another 3 mins. intravenous administration of Prostigmin.
	Prostigmin: 0.08 mg I/venous.	Improvement of paralytic condition, paresis of limbs persisted. Complete recovery after 8 hours without additional administration of Prostigmin.
5. ♂14 lbs.	Sernylan: 10.5 mg.	No reaction (if the Sernylan is not carefully inserted into the centre of the meat, the jackal may refuse to take it or may regurgitate the meat within a few minutes after it has been eaten.)
6. ♂8 lbs.	R0.5–2807/B–21: 300 mg (3 ml) Intramuscular.	Ataxia and posterior paresis after 2 minutes. Animal very "tame". Vomition after 13 mins. General paresis and narcosis after 19 mins.
7. ♀8 lbs.	R0.5–2807/B–21: 100 mg (1 ml) Intramuscular.	Ataxia after 1 minute. Only slight sedation and vomition.

SILVER JACKAL (Vulpes chama)

1. ♀4 lbs.	Flaxedil: 1.0 mg/Kg. I/Muscular.	Tetraplegia and brachypnoea after 5 minutes. Antidote administered after another 2 minutes.
	Prostigmin: 0.04 mg. I/venous.	Complete clinical recovery after another 2 mins.

AARDWOLF (Proteles cristatus)

1. ♀5 lbs.	Largactil: 10 mg. I/muscular.	Had been very nervous and aggressive. Heavily tranquillized and manageable after 40 minutes. Animal, while under the influence of Largactil became used to the presence of human beings.

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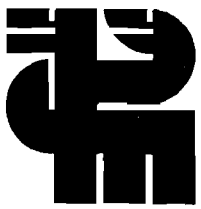

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NOTES ON THE IMMOBILISATION AND BIOLOGY OF ZEBRA (EQUUS BURCHELLI ANTIQUORUM) IN *ETOSHA GAME PARK, S.W.A.*

H. EBEDES.*

SUMMARY

To facilitate the study of the annual zebra migration in the Etosha Game Park, 19 zebra were successfully immobilised with M 99 and marked with neckbands. Concurrent with the marking, blood was collected for haematological and immunological studies, and other valuable information was obtained.

1. IMMOBILISING DRUGS:-

Drugs previously used for the immobilisation of zebra included:

i) Nicotine salicylate[1].
ii) Succinylchlorine chloride[1 2 3].
iii) Gallamine triethiodide[4 5].

The drugs used in Etosha were combinations of M 99 with:

i) Hyoscine hydrobromide and Acetylpromazine
ii) Acetylpromazine and Sernylan and
iii) Acetylpromazine.

a) M 99 (RECKITT & SONS, LTD.)

M 99 is 6 : 14 - endoetheno - 7 a (2 - Hydroxy - 2 Pentyl) Tetrahydro - Oripavine Hydrochloride - a synthetic morphine preparation with analgesic properties 5,000 - 10,000 times greater than morphine and was supplied to us by Mr. Colman Green of Reckitt & Sons, Hull, England. The advantage of M 99 is the small quantity necessary for immobilisation, the wide safety margin and the low toxicity. Furthermore the narcotic action can be reversed by morphine-antagonists. The M 99 was weighed out into 20 mg. doses and dissolved in 1 or 2 cc's of Acetylpromazine (Boots) giving a concentration of 2.00 or 1.00 milligrams per 0.1 cc.

b) HYOSCINE HYDROBROMIDE:

(B.W. & Co.) (Scopolamine). Hyoscine is closely related to atropine chemically, but unlike atropine depresses the central nervous system and produces general sedation. The mydriatic affect is also more powerful than atropine. When mixed with morphine, morphine derivatives and barbiturates, hyoscine potentiates the narcotic effect and in human medicine is used in a "cocktail" to produce "Twilight sleep". Hyoscine is incorporated in the immobilising mixtures for the following reasons:

i) Potentiation of M 99 and tranquillisers.
ii) Mydriasis.
iii) Counteraction of respiratory depression caused by morphine.
iv) Prevention of excessive salivary and bronchial secretions.

The hyoscine was weighed into 100 milligrams doses and dissolved in 1 cc. (10 mg.) of Acetylpromazine (Boots) giving a concentration of 10 milligrams per 0.10 cc.

c) "ACETYLPROMAZINE" (BOOTS.)

2 - Acetyl - 10 - (3 - dimethylaminopropyl) phenothiazine. Acetylpromazine (A.P.) is a derivative of promazine and is a powerful tranquilliser. It is commercially available at a strength of 10 milligrams per cc. Acetylpromazine acts synergistically with M 99 and small doses produce marked tranquillisation. Following Dr. S. Hirst's advice (personal communication) we routinely dissolve M 99 and Hyoscine powder in Acetylpromazine as the acidity of this preparation hastens the solubility of these drugs.

d) SERNYLAN. (PARKE, DAVIS & CO.)

1 - Cl - phenylcyclohexyl) piperidine hydrochloride (Phencyclidine hydrochloride.) Serny-

*S.W.A. Nature Conservation & Tourism, Etosha Game Park, Okaukuejo, S.W.A.

lan is recommended by the manufacturers as an immobilising and/or anaesthetic agent for primates and laboratory animals. However in the past few years Sernylan has been used for immobilising wild ungulates either on its own or in combinations with other drugs[5, 6]. Sernylan potentiates narcotics and tranquillisers and is rapidly absorbed by the body.

e) ANTIDOTES.

As the narcotic action of M 99 is reversed by certain antidotes, two of these preparations were used.

i) *Nalorphine hydrochloride.*

("Lethidrone" - (B.W. & Co.) Nalorphine reverses the narcotic effects of morphine and morphine-like drugs. It is effective parenterally but acts more rapidly when injected intravenously. The dosage of nalorphine is not dependant on the dose of narcotic, but on the size of the animal.

ii) M 285. (RECKITT & SONS.)

N - cyclopropylmethyl - 6 : 4 - endoetheno - 7 - (2 - hydroxy - 2 - propyl) tetrahydro - norovipavine hydrochloride, is a specific antidote M 99. It is available from Reckitt & Sons in powder form and is readily soluble in water. Very much smaller quantities of M 285 are necessary for antagonising the effect of M 99 than nalorphine.

Marked zebra recovers after antidote.

2. METHOD:

The Palmer Cap-Chur Powder-charge gun and gas-operated pistol were used with standard Palmer darts described by previous workers[7, 8]. We did not find the Powder gun dependable beyond 50 yards, on a stationary animal even on a calm day. This was probably due to the low charge of powder in the shells (± 240 mg.)

The gas-operated pistol was satisfactory from 15-35 feet.

On the wide open plains of Andoni, Grootvlakte and Leeubron — (see map) — the zebra could not be approached closer than approximately 60 yards before taking flight. The most practical method of darting them was to pursue them in a vehicle and "dart" a selected individual from a distance of 10-15 yards while travelling at a speed of 20-35 miles per hour. The most suitable vehicle for this work was a Land-Rover with the left door removed. The centre of gravity of the Land-Rover was excellent for excecuting dangerous turning manoeuvres without rolling or turning over. Although a short-wheel base vehicle would have been preferable for this work, we had to use a long-wheel base. Initially we were disappointed with this method because of several misses, due to bumpy conditions over uneven terrain. After some practice however the darter achieves a fair amount of accuracy and two out of three shots are direct hits.

SITE OF DARTING:

In a right-hand drive vehicle with the darter seated on the left-hand side, the majority of zebra were darted in the right hind limb.

Right hind limb	—	17
Right shoulder	—	3
Left gluteal	—	2
Left shoulder	—	1
Left flank	—	1
Right thorax	—	1

3. RESULTS:

The results are summarised in the table.

a) The *weights* of the animals were based on estimations.

b) *Ageing* was based on Dr. Klingel's[10] ageing criteria. (Klingel 1965.)

c) IMMOBILISATION TIME.

Immobilisation time was accurately timed on a stop-watch from the moment the dart struck the animal until it dropped and re-

mained down. Our results show disagreement with those of Harthoorn and Bligh[6], who found that 2 mg. M 99 completely immobilised adult zebra in about 3 minutes. This disparity is probably due to the nutritional, physiological, sub-species and climatic differences of our zebra.

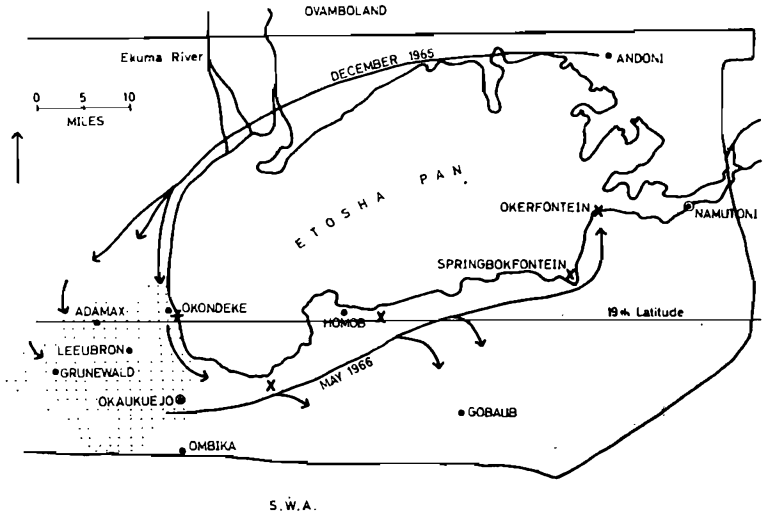
Zebra immobilised under 10 minutes 6.
Zebra immobilised under 15 minutes 11.
Zebra immobilised over 15 minutes 7.

d) RECOVERY TIME.

This was timed from the moment the antidote was injected until the animal regained it's balance and was mobile. Usually the zebra ran off soon after it had risen. N 1 did not require antidote as he was not fully immobilised.

Because of the smaller quantity necessary and the more rapid antagonism, M 285 appeared to be the antidote of choice.

Etosha Game Park.



Arrows indicate migration routes.
Stippled area indicates summer concentration.
Crosses indicate marked zebra sighted.

N 1 and A 5 were caught with a rope after 30 minutes. G.V. 4 was darted twice because we thought that the first dart missed. The substitution of small quantities of Sernylan for hyoscine (L 1, L 2, G.V. 8 & G.V. 9) resulted in more rapid immobilisation. Higher doses of Sernylan and hyoscine will probably result in still faster immobilisation and we will check this in our next immobilisation/marking project. We recommend hyoscine in the mixture although it was not included in 11 darts. Five zebra were not immobilised and this was most probably due to faulty firing mechanism of the darts.

Three of these zebra were followed for 30-45 minutes with no sign of narcosis. Two zebra were lost during a stampede in the thick Cactophractes alexanderi and Acacia nebrownii bush near Adamax.

e) MARKING.

With the exception of the first four zebra immobilised on Andoni, all the zebra were neckbanded. Neckbands similar to those used in the Kruger National Park were used. (Pienaar. Personal communications.) The neckbands consisted of coloured plastic strips ± 6″ wide strengthened by celluloid and canvas and identified as follows:-

Red on white — Adamax.
Red on yellow — Grootvlakte.
Yellow on blue — Leeubron.

The above regions fall in the summer rainfall concentration areas. Large numbers of zebra were found migrating from Andoni along the northern edge of the pan during December 1965. During January ± 3,000 were found in the mentioned areas. The winter dispersal

regions are south and east of the Etosha Pan and the Andoni plains. To-date (May 1966) three marked zebra have been found up to 100 miles south-east from the areas in which they were marked. From present observations it would appear that the zebra migrate around the pan in an anti-clockwise direction (see map.) We are not certain if this is the usual annual occurrence. Two neckbands, apparently fitted too losely, were recovered in the Grootvlakte area within three weeks of marking.

No. of Zebra	Antidote	Route	Mean recovery time.
8	"Lethidrone" 60-100mg.	I m.	7 min 4secs.
7	"Lethidrone" 50-120mg.	I v.	43 „
3	"M. 285" 10-123 mg.	I v.	37 „

The manes and tails of the last ten zebra immobilised were clipped to facilitate identifications. The zebra were all tagged with plastic ear-tags and branded with cold branding-fluid. The branding of zebra does not hold much promise for identification purposes because the brands are not clear among the stripes and shadow-stripes.

f) BLOOD SMEARS.

Fifteen blood smears were examined but no protozoal parasites were found.

g) HAEMATOLOGICAL TESTS:

Nineteen blood samples were sent on ice by air to the Blood Group Laboratory, Onderstepoort. The transferrin types were similar to horses and donkeys and the hemoglobin types similar to horses and mules. The haemoglobin, transferrin and albumin typing was studied by means of starch gel electrophoresis. (D. R. Osterhoff 1965. Pers. Com.)

h) SEROLOGICAL TESTS.

Eleven serum samples tested at Onderstepoort were negative for Trypanosoma equiperdum (Dourine) and Trypanosoma brucei (Nagana). (Prof. W. O. Neitz. 1966. Pers. Com.)

i) EXTERNAL PARASITES.

a) Tick-infestation varied from mild to absent. Ticks identified at Onderstepoort were:
Hyalomma rufipes.
Rhipicephalus evertsi mimeticus.
(Theiler. G. Pers. com.)

b) No lice, fleas or mites were found.

j) BODY TEMPERATURE.

The rectal temperatures of seven zebra were recorded prior to the injection of the antidote.

G.V. 1 — 104 F
G.V. 2 — 107 F
G.V. 3 — 103 F
G.V. 4 — 104.2 F
G.V. 5 — 107 F
A. 3 — 106 F
A. 5 — 106.4 F

Mean temperature of 7 zebra 105.4 F.

4. BEHAVIOUR AFTER DARTING:

Observations on the behaviour of zebra during our immobilisation project support Dr. Hans Klingel's[9] studies on the social structure of zebra.

a) When young animals were darted they ran with their mothers until the immobilising drug started taking effect. The mares became very agitated when the foals showed ataxia and moved away from the group in a bemused state and invariably neighed in an attempt to entice their young back to the fold. When we approached the immobilised foals, the mothers retired to a distance of 200-300 yards and watched us intently. On recovering from the narcosis, the young zebra were either joined by the mares or ran towards the family where they were immediately accepted.

b) When a mare was darted, the stallion usually ran with her until she was fully immobilised. On one occasion, a young mare on heat (L2) was closely followed by the stallion who reluctantly gave way when we approached. During the time that we worked on her, he stood around observing us inquisitively not more than 50 yards away. On recovery, the mare bounded off in an opposite direction and the stallion immediately ran after her neighing and calling and when pacified, they both joined up with the rest of their group.

c) The mares and foals were completely disinterested when the stallion — the pater-familia — was darted. They usually ran off and left him to his fate. (N, G.V. 1, G.V. 10, A. 3, and A. 5.) This coincides with Dr. Klingel's[9] observation:- "In five cases the stallion disappeared from his group, which was subse-

quently taken over *as a whole* by another stallion. This demonstrates that the family members are not held together by force by the stallion, but form a stable group even without him". It was pathetic to watch a recovered stallion attempting to join up with his family because he was severely kicked and bitten whenever he approached another family group, not his own. Family groups do not tolerate intruders.

5. CONCLUSIONS:

1) M 99 in combinations with hyoscine, acetylpromazine or sernylan proved effective in immobilising nineteen zebra for marking, haematological and other studies.
2) The antidotes, Nalorphine hydrobromide and M 285 were successful in reversing the narcosis.
3) Darting running zebra from a moving vehicle was practicable under the conditions in Etosha Game Park.
4) Marked zebra were found up to 100 miles away and observations indicate that they move/migrate in an anti-clockwise direction around Etosha Pan.
5) Zebra lead a family life.
6) Interesting haematological and immunological data were obtained concurrent with the marking project.
7) Under narcosis, seven zebra had a mean temperature of 105.4 F.

ACKNOWLEDGEMENTS:

The writer wishes to thank the Secretary for South West Africa for permission to publish this paper and the Chief Ranger of Etosha Game Park and his staff for assisting with the project. A special word of thanks to Joseph whose dexterity in handling the Land-Rover greatly facilitated our work.

We are indebted to Mr. Colman Green of Reckitt & Sons, Hull, England for experimental supplies of M 99 and M 285, and to Dr. U de V. Pienaar of Kruger National Park for his interest and advise.

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TABLE.—IMMOBILISATION OF ZEBRA IN ETOSHA GAME PARK S.W.A.

Date	Code No.	Area	Sex	Age yrs	Estimated weight lbs.	M99 mg.	Hyoscine mg.	A/P. Acetyl-promazine mg.	Sernylan mg.	I.M.M. time	Antidote mg.	Recovery time
5/11/65	N.1	Andoni	M	4	550	1.5	25	15		30 min.	—	—
	N.2	Andoni	M	1	320	1.5	25	15		3 min. 30 secs.	L.100 I.M.	16 min.
	N.3.	Andoni	F	¾	250	1.5	25	15		3 ,, 41 ,,	L. 50 I.V.	3 ,,
	N.4	Andoni	F	3	350	1.5	25	15		? ,,	L. 50 I.V.	44 secs.
8/1/66	GV. 1.	Grootvlakte	M	10	750	2.5	25	10		33 ,, 22 ,,	L. 60 I.M.	2 ,, 30 ,,
	GV. 2	Grootvlakte	F	3	400	2.5	25	10		25 ,,	L. 100 I.M.	6 ,, 30 ,,
	GV. 3	Grootvlakte	F	3	375	2.5	25	10		8 ,, 33 ,,	L. 80 I.M.	6 ,, 10 ,,
	GV. 4*	Grootvlakte	F	?	450	2.5	25	15		5 ,, 30 ,,	L. 100 I.M.	12 ,, 53 ,,
						2.5	25	15				
	GV. 5	Grootvlakte	F	4	475	2.5	25	15		20 ,,	L. 70 I.M.	30 ,,
1/3/66	A. 2	Adamax	F	3	400	2.5	12½	12		10 ,,	L. 100 I.M.	6 ,,
	A. 3	Adamax	M	5	550	2.5	12½	10		12 ,,	L. 100 I.M.	6 ,,
		,,	M	3	400	2.5	12½	12		—	—	
		,,	F	4	460	2.5	12½	12		—	—	
	E.O.	Grootvlakte	F	4	475	2.25	—	5	15	24 min.	L. 50 I.V.	20 secs.
23/3/66	L. 1	Leeubron	F	3	350	2.5	—	5	10	10½ ,,	L. 60 I.V.	15 ,,
	G.V. 8	Grootvlakte	F	2	350	2.5	—	5	10	7½ ,,	L. 60 I.V.	18 ,,
	GV. 9	,,	F	5	550	2.5	—	5	10	10 ,,	L. 60 I.V.	19 ,,
29/3/66	L. 2	Leeubron	F	2	360	2.5	—	5	10	10½ ,,	M. 10 I.V.	1 min. 2 ,,
	A. 4	Adamax	M	2	350	2.25	—	10	—	20 min.	M. 10 I.V.	5 ,,
	GV. 10	Grootvlakte	M	8	680	3	—	10		7½ ,,	M. 12½	45 ,,
		,,	M	5	?	3	—	10	—	?		
		,,	F	4	450	2.25	—	10	—	?		
		Adamax	M	4	500	2.25	—	—	—	?		
	A. 5	Adamax	M	7	650	2.25	—	—	—	30 min.	L. 120 I.V.	5 ,,

Abbreviations:
L. = "Lethidrone" (Burroughs Wellcome & Co.)
M. = M 285 (Reckitt & Sons.)
I.M.M. = Immobilization Time = Time between darting and capture
* = Darted twice.

A NOTE ON THE TOXICITY OF FERRIC CHLORIDE

T. F. ADELAAR, M. TERBLANCHE AND G. J. TRUTER.

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SUMMARY

The acute and chronic toxicity of ferric chloride in sheep and goats has been studied. The smallest single dose to kill a sheep was 2.5 g/kg.

Daily doses of 0.5 g/kg caused death after 22 days while 34 mg/kg/day (1.0g $FeCl_3$ total/day) was found to have caused accumulation of iron in the soft tissues after a year. The symptoms and lesions found are described.

INTRODUCTION

In 1964 Visser[1] reported on the prophylactive value against gousiekte of ferric chloride when added to the drinking water at a rate of 0.5 g $FeCl_3$ per gallon. In repeating these experiments we[2] could not demonstrate any such protection. Experiments on the toxic effects of ferric chloride at the level advocated by Visser and higher are reported.

TOXICITY TRIALS

Eleven 2-tooth to adult merino wethers and ewes and one adult ewe goat were dosed with varying amounts of either a 17% $FeCl_3.6H_2O$ (Merck's Ferrum sesquichloratum) or a 3% anhydrous $FeCl_3$ (BDH) solution. These animals were kept in individual pens and clinically examined daily. The temperature, pulse-rate, respiratory-rate and ruminal movements were recorded. The animals were bled once a week (or more often in acute cases) for chemico-pathological examination. The red blood cell sedimentation rate, packed cell volume, hemoglobin, serum glutamic oxaloacetic transaminase, serum alkaline phosphatase, zinc sulphate turbidity test, unconjugated and conjugated bilirubin, blood urea nitrogen, creatinine, glucose, total plasma proteins, cholesterol, calcium, magnesium, phosphates, chlorides, bicarbonates and often leucocyte and erythrocyte counts, were determined according to methods described previously[3].

Acute toxicity: (See table 1)

Chronic toxicity: (See table 2)

SYMPTOMS

Acute Toxicity: Death occurred within 24 hours or up to 5 days after administration. A green to black tarry diarrhoea appeared after 1-4 days. Dyspnoea, often accompanied by groaning appeared within the first day, usually associated with tachycardia (up to 142 beats/min.), ruminal atony or stasis and anorexia. One animal (No. 4) developed marked thirst and signs of kidney dysfunction a day prior to death. The blood urea nitrogen increased from 20 to 75 mg% and the serum creatinine concentration from 1.1 to 3.5 mg%. Inco-ordination of movements, reluctance and later inability to stand or walk due to weakness set in early or just prior to death.

Chronic poisoning: Sheep No. 10 showed intermittent symptoms of hyperpnoea (48-60 or 100 per min.), and ruminal atony from the 91st day, but symptoms did not progress further. Sheep No. 11 showed spells of listlessness, soft faeces, anorexia, poor condition and weight loss.

Sheep No. 12 showed a black diarrhoea on the 2nd day. From the third day onwards the faeces were black and pasty. From the seventh day the animal became listless, appeared thin but the faeces were normal. From the fourteenth day marked anorexia and ruminal atony set in. From the sixteenth day a watery diarrhoea again appeared. On the 21st day there was a tachycardia (114/min.), complete ruminal stasis, dehydration with marked weakness and the animal could hardly stand. Chemico-pathologically the dehydration was confirmed by a relative high concentration of total plasma proteins, haemoglobin and a high packed cell volume. There was also an increase in blood urea nitrogen (47 mg%) and creatinine (8.1 mg%) present.

Pathology: The post mortem findings in the acute toxicity group were as follows:- Marked congestion and oedema of the lungs. One case

also showed focal haemorrhages. Rumen:- stasis and mucous membranes usually thick and leathery with either a black or a red-brown rusty colour, depending on whether anhydrous or hydrous ferric chloride was dosed respectively. This leathery layer could easily be scraped off and only in one case (sheep No. 4) was there a hyperaemia in the underlying layers. This case also showed focal ulceration in the abomasum. Usually the intestinal contents were a dark green to black in colour. Histologically, slight fatty infiltration in the liver was seen while sections of the heart showed congestion, slight fatty infiltration and vacuolization around the nuclei in one case (No. 2). Another (No. 4) showed a fibrinous pericarditis and haemorrhages with leucocyte infiltration in the epicardium which was probably incidental. The kidneys were unfortunately too decomposed for satisfactory histological examination, except for those of No. 4 which showed nothing abnormal.

TABLE 1.—THE DETERMINATION OF THE ACUTE TOXICITY OF FERRIC CHLORIDE IN SHEEP.

Sheep No.	Weight in kg.	Dosage in mg/kg	Experimental Day	Result
1	58.6	5.0 increased intermittently by 5.0 up to 70.0	1 to 23	Occasionally dyspnoea, anorexia ataxia and reluctance to move for 1–2 days after dosing. Discharged on day 28*
2	38.6	150 increased intermittently by 30 up to 1000	1 to 57	Often soft black faeces for a day after dosing.
		1800	61	Soft black faeces for 2 days.
		3000	66	Dead the next day.
3	25.9	900	1	Diarrhoea for 2 days.
		1000	15	Diarrhoea on day 17.
		1250	20	Ruminal atony for 1 day. Discharged on day 46†
4	33.1	1500	1	Diarrhoea and anorexia for 7 days.
		1750	14	Ditto plus ruminal stasis for 3 days.
		2000	22	No symptoms.
		2500	35	Very ill for 5 days. Died on day 41.
5	43.0	2500	1	Very ill for 5 days. Died on day 5.

* Sheep No. 1 was heavily pregnant at this stage and was therefore discharged.
† Sheep No. 3 lambed on day 29 and then broke a leg on day 30. The leg was put in a plaster cast and the animal kept under observation until day 46.

TABLE 2.—THE CHRONIC TOXICITY OF $FeCl_3$ IN SHEEP AND A GOAT.

Experimental animal	Weight in Kg.	Dosage $FeCl_3$ in mg/Kg/day	No. of dosages.	Results
Sheep 6	25.0	12 (0.3 g total)	203 in 248 days	No symptoms. Slaughtered on 249th day.
Sheep 7	41.8	24 (1.02 g total)	68 in 80 days	Intermittent soft stool, increase in serum alkaline phosphatase concentration. Slaughtered on 81st day.
Sheep 8	25.4	24 (0.60 g total)	203 in 248 days	No symptoms. Slaughtered on 249th day.
Goat 9	30.0	34 (1.02 g total)	326 in 422 days	No symptoms. Slaughtered on 423rd day.
Sheep 10	30.0	50 (1.50 g total)	147 in 182 days	Intermittent slight symptoms from 91st day. Slaughtered on 183rd day.
Sheep 11	34.1	100 (3.42 g total)	147 in 182 days	Symptoms from the 14th day. Slaughtered on 182nd day.
Sheep 12	33.2	500 (16.59 g total)	15 in 20 days	Symptoms from the 2nd day. Died on the 22nd.

Chronic poisoning: On slaughter, sheep Nos. 6, 8 & 10 showed no lesions macroscopically or histologically. Sheep No. 7 showed slight degenerative changes in the liver macroscopically but these could not be confirmed histologically. The heart muscle showed vacuolisation around the nucleii and in parts the muscle bundles had a granulated appearance. The goat showed fatty infiltration and cloudy swelling of the liver histologically and a large amount of yellow brown pigment in the red pulp of the spleen. Sheep No. 11 showed a focal lymphocyte infiltration in the heart especially perivascularly and subendocardially. Sheep No. 12, which died, showed marked congestion and slight oedema of the lungs, marked ruminal stasis with black discolouration of the mucous membranes of the fore stomachs and the intestinal contents.

The Iron contents of the organs: (See table 3). This was determined as described previously(4).

TABLE 3.—THE IRON CONTENTS OF THE ORGANS OF THE EXPERIMENTAL ANIMALS.

Experimental Animal	Liver	Kidney	Spleen
Sheep No. 2	3,520 ppm	—	5,500 ppm
Sheep No. 3	3,400 "	500 ppm	—
Sheep No. 6	440 "	206 "	530 "
Sheep No. 7	270 "	340 "	650 "
Sheep No. 8	395 "	280 "	1,860 "
Goat No. 9	480 "	640 "	9,850 "
Sheep No. 10	460 "	445 "	3,750 "
Sheep No. 11	980 "	660 "	4,020 "
Sheep No. 12	2,740 "	920 "	8,750 "

DISCUSSION

The acute MLD of $FeCl_3$ for sheep therefore seems to be between 2.0 and 2.5 g/kg while 500 mg/kg/day caused death within 3 weeks.

A dosage of 100 mg/kg/day over 182 days caused pronounced symptoms and marked accumulation of Fe in the soft tissues.

The concentration of Fe in normal sheep liver is given as 450 p.p.m. (210-880 p.p.m.) by Gardiner(5), 430 p.p.m. by Underwood(6), 393, (240-815) by Beck, cited by Gardiner(5), 223 (98-448) by Hemingway(7) and 180 (89-457) by McNaught(8). The normal concentration in the spleen is given as 3,800 p.p.m. and in the kidney as 460 p.p.m. by Underwood(6).

Five normal goats and sheep slaughtered at Onderstepoort had the following mean concentrations of Fe in ppm. in their tissues.

	Liver	Kidney	Spleen
Goat....	459 (324— 620)	277 (200—420)	277 (200—420)
Sheep...	758 (532—1,020)	424 (176—780)	4,600 (928–11,000)

As little as 34 mg $FeCl_3$kg/day (a total of 1.0 g $FeCl_3$) therefore caused an accumulation of Fe in the soft tissues. It is therefore possible that even low dosages given over long periods might not be without danger.

ACKNOWLEDGEMENTS

The Chief of the Veterinary Research Institute, Onderstepoort, is thanked for permission to publish this paper and Prof. R. Clark for his assistance with its preparation. The assistance of the following technicians is acknowledged. Miss A. W. de Villiers, Messrs. B. P. Maartens and A. M. S. van Straten.

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EUPHORBIA MAURITANICA L. AS A POISONOUS PLANT IN SOUTH AFRICA

M. TERBLANCHE, T. F. ADELAAR AND A. M. S. VAN STRATEN.

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SUMMARY

Euphorbia mauritanica L. has been proved toxic to sheep. The symptoms and post-mortem lesions produced are described and their similarity to those of *Sarcostemma viminale* R.Br. poisoning emphasised. Attention is also drawn to the similarity between the post-mortem lesions produced by these two plants and those seen in enterotoxaemia.

INTRODUCTION

In 1822 Burchell[1] reported that the milky juice from *Euphorbia mauritanica* L. was a frequent ingredient in the poisonous composition which Bushmen applied to their arrows, probably purely for it's cohesive properties[2]. In 1924 Steenkamp[3] analysed the latex but made no reference to its toxicity. In 1932 Steyn[4] tested the plant, after it had been suspected of having caused mortality in sheep, on a rabbit with negative results. In 1935 Henrici[5] reported that this plant was eaten by wild animals during drought periods. Therefore, although it was commonly known that the latex of this plant is an irritant to human mucous membranes and in the eyes, it was not commonly regarded as toxic to stock.

During July 1963 an outbreak of suspected *Sarcostemma viminale* R.Br. poisoning occurred among cattle in the Kuruman-Vryburg area. The symptoms resembled those caused by this plant and included an unsteady gait, convulsions and death soon after drinking. On post-mortem examinations haemorrhages were found in the rumen and intestines and plant material taken to be *S. viminale* was found in the ruminal contents. On closer examination, however, this proved to be *Euphorbia mauritanica* L. Specimens of the plant were obtained for trial and proved toxic, the symptoms produced being similar to those of *S viminale* poisoning. The object of this paper is to report these findings.

PLANT DESCRIPTION

Family: Euphorbiaceae
Name: *Euphorbia mauritanica* L.

A spineless freely branching shrub varying between 2 and 4 ft. high; the branching is random and never truly opposite; the branches are yellowish-green, usually about pencil thickness and marked with alternate leaf-scars. *Leaves* are alternate, sessile, up to about ½ in. long and less than ¼ in. broad, they soon become dry and fall off, thus for the most part the plants appear leafless. *Cyathia,* so called 'flowers', are usually in cymes or clusters at the ends of young branches, with a central sessile male cyatheum surrounded by 3 to several stalked bisexual cyathia; the involucres usually have 5 glands, rarely only 4 glands round the rim; glands are suborbicular and average 1.5-2 mm broad, yellow in colour and exude nectar.

The seed-vessel is a capsule 5-6 mm in diameter, somewhat 3-angled, which explodes on maturity releasing 3 seeds 3-3.5 mm long, grey, mottled with black and with a small caruncle.

Distribution:

This species is widely distributed and often very common in the Cape Province where it is of fairly uniform habit. It extends into the Orange Free State and Natal and is common in Namaqualand and South West Africa. In the latter territory it varies considerably in habit in different localities, some forms being more and others less fleshy than the common form of the Cape.

TOXICITY TRIALS

The plant material used was collected in post flowering stage and dried. It was chopped and dosed per stomach tube to adult merino wethers, weighing from 25.4 to 37.2 kg., as follows:

Eight sheep were dosed at a rate of 8 g plant material per kg body weight. Symptoms appeared

Euphorbia mauritanica L.

in all these animals from 4 to 12 hours after dosing and six of the eight died from 12 to 92 hours after dosing. The remaining two recovered after having shown symptoms for 3 and 5 days respectively.

Two sheep were given 10 g of the plant per kg body weight. Of these one died the same day and the other recovered after showing symptoms for four days.

One sheep was dosed 6 g per kilo. It showed no symptoms the following day and was then given 12 g/kg. It developed symptoms and died the day after the second dosing.

Symptoms

Affected sheep showed marked hyperaemia of the conjunctiva, marked foaming at the mouth, excessive salivation, ruminal paresis or atony sometimes accompanied by bloat, tachycardia (up to 208 beats/min) hyperpnoea (up to 140 resp./min) often accompanied by groaning, cyanosis and occasionally an increase in body temperature of 1-2°F. The muscles showed increased tone and continuous twitching, shivering and tremor. The animals showed reluctance to stand or stood stiffly with arched back and limbs abducted for support. The gait was stiff and unsteady. However, true tetanic spasms did not occur as the extended limbs and neck could easily be flexed manually and spasms could not be elicited by external stimuli. Diarrhoea was frequently present.

The Blood Sugar

Routine blood tests showed a marked hyperglycaemia in affected sheep. Systematic determinations of the blood sugar levels were carried out on seven of the sheep dosed at the rate of 8 g plant material per kg body weight. Determinations were made by both the Folin-Wu[6] and Mohun[7] methods. The Mohun method gave slightly higher values but as there was no significant difference between the results using the two methods, only those obtained by that of Folin and Wu are depicted in Graph I. In order to eliminate any possible effects of the bleeding and handling on the blood sugar levels, seven control sheep were dosed with lucerne and bled with the experimental animals.

Blood Urea Nitrogen (B.U.N.)

In one sheep dosed at the rate of 10 g/kg body weight, the blood urea nitrogen was determined[8] daily after dosing. It rose steadily from an initial 22 mg% to 142 mg% on the 5th day. The animal recovered and the B.U.N. was again normal when tested on the 16th day after dosing.

Post-mortem Lesions

The characteristic post-mortem lesions were:- Subcutaneous haemorrhages over and behind the shoulders, probably due to trauma during spasms; tympany; oedema, hyperaemia and focal emphysema of the lungs; subepi- and endocardial petichiae or haemorrhages; often diffuse hyperaemia in the rumen, abomasum and small intestines. The kidneys usually appeared congested and showed more advanced post-mortal changes than the other organs, when the animals died while showing hyperglycaemia. Urine from the bladders of these

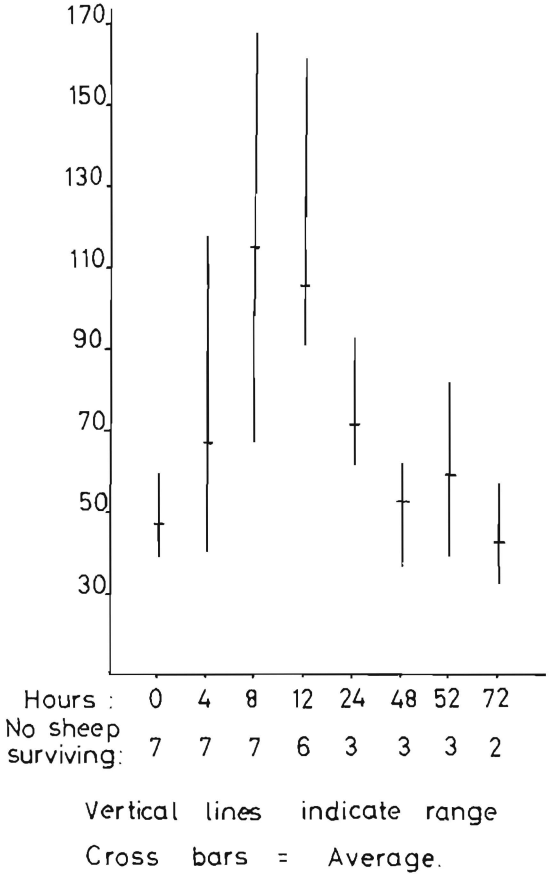
animals tested positive for glucose with "testape" indicating 0.25% and more. Histologically the kidneys often showed nephrosis while in one case the pancreas showed degeneration and necrobiosis of individual cells of the acini.

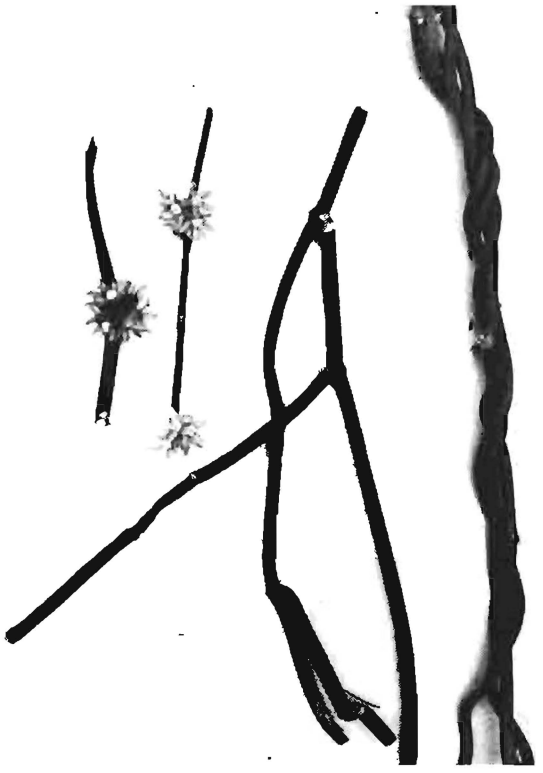
Discussion

E. mauritanica has been proved toxic to sheep. The symptoms produced closely resemble those seen in *S. viminale* poisoning[9] and portions of the two plants which might be found in the ruminal contents of animals at post-mortem might easily be mistaken for each other. Furthermore the plants themselves may be confused under certain circumstances. *E. mauritanica* is bushy whereas *S. viminale* is by habit a climber, the stems trailing, twining or scrambling over bushes and trees but

GRAPH I.

Blood Glucose Levels.





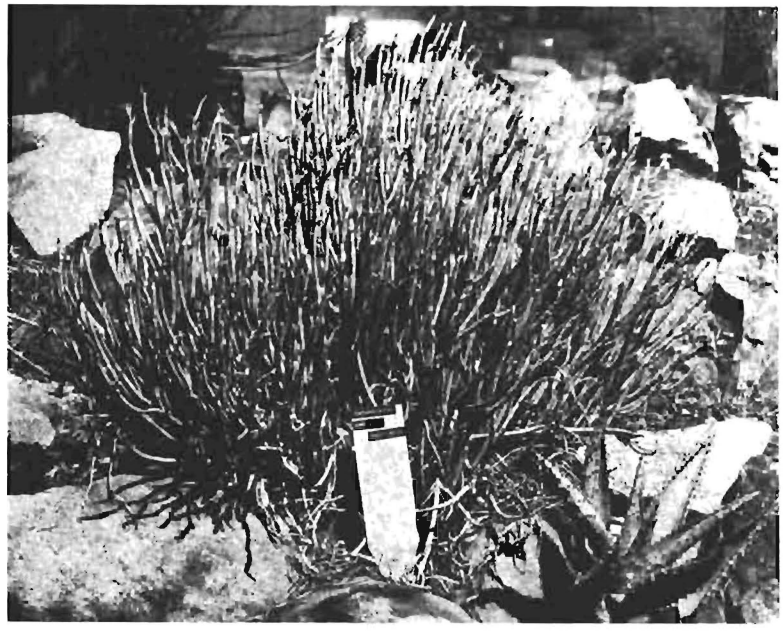
Sarcostemma viminale RBr.

when growing in the open it may assume a bush form. This may happen particularly in the Kuruman-Vryburg area where the natural distributions of the two plants overlap.

They can be distinguished by noting the following:- In *E. mauritanica* the branching is random but never strictly opposite nor are the leaf-scars ever strictly opposite. In *S. viminale* the branching is opposite but if only one branch arises from a node, it may give the false impression of random branching. It will be found on careful examination that the leaf-scars are invariably opposite each other on the branches.

The neuro-muscular symptoms caused by the two plants differ somewhat in that *S. viminale* causes true strychnine-like tetanic spasms whereas in *E. mauritanica* poisoning there is increased extensor tone accompanied by continuous tremors but the limbs can be flexed manually with comparative ease.

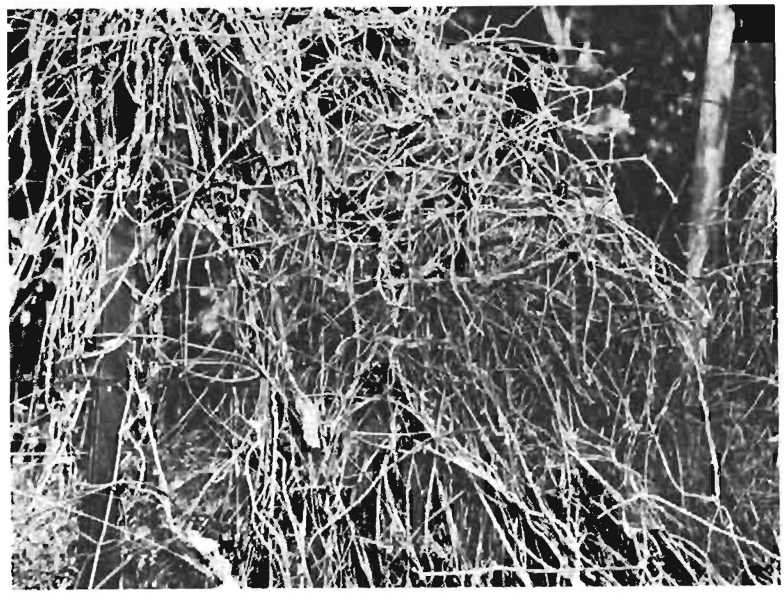
The polypnoea, foaming at the mouth and cyanosis on excercise were much more pronounced in *E. mauritanica* poisoning. There was also a



Euphorbia mauritanica L.

tendency to a diarrhoea in contrast to that of a tendency to a constipation in *S. viminale* poisoning[9]. However, in both instances an animal may be found lying on its side, the head drawn back, legs in extension or showing running movements, foaming at the mouth and showing tachycardia and polypnoea.

The post-mortem lesions in poisoning with both these plants closely resemble those of enterotoxaemia. The animals used in these trials were all immunized against enterotoxaemia and their serum epsilon antitoxin determined in order to eliminate enterotoxaemia as a possible complicating factor in the experiment[10].



Sarcostemma viminale RBr.

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The Chief of the Veterinary Research Institute is thanked for permission to publish this paper and Prof. R. Clark for his assistance in preparing it. The technical assistance of Miss. A. W. de Villiers and Mr. B. P. Maartens, is acknowledged. The plant identification was done by the Botanical Research Institute, Pretoria. The plant description was supplied by Dr. R. A. Dyer also from the latter Institute. The plants were sent in by Dr A. M. van Heerden, Vryburg.

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CASE REPORT

CYSTIC OVARIES IN A HAMADRYAS BABOON, *Papio hamadryas.*

E. YOUNG.

Veterinarian, Kruger National Park, South Africa.

A female hamadryas baboon of the Pretoria zoo manifested clinical symptoms of continuous oestrus. The vulva was always oedematous and hyperaemic and a sanguinous discharge from the vulva was sometimes observed. The perivulvar tissues threatened to become necrotic and it was decided to perform an ovariectomy on this animal.

Pentobarbitone sodium ("Sagatal") was administered intravenously to medium plane anaesthesia, while the animal was restrained in a squeeze cage. The required dose of pentobarbitone sodium was lgr./4.7lb. The operation was performed in the animal hospital of the National Zoological Gardens of South Africa. On examination after removal the ovaries showed multiple cysts and the uterus appeared to be hyperaemic. The baboon recovered without any complications and the signs of oestrus gradually disappeared after the operation.

Symptoms of oestrus were again provoked with the subsequent intramuscular administration of 10 mg. of diethylstilboestrol. That oestrogenic hormones cause external manifestations of oestrus in the ovariectomised hamadryas baboon and the therapeutic value of ovariectomy for a baboon with cystic ovaries, was clearly illustrated by this case.

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FURTHER STUDIES ON *SARCOSTEMMA VIMINALE R. Br.* POISONING.

M. TERBLANCHE AND A. M. S. VAN STRATEN.
Veterinary Research Institute, Onderstepoort.

SUMMARY

The occurrence of hyperglycaemia and glycosuria in *Sarcostemma viminale* R.Br. poisoning is reported. The symptoms and post-mortem findings are described as augmentation of previously published work. The resemblence of the post-mortem findings to those of enterotoxaemia are emphasised.

INTRODUCTION

Sarcostemma viminale R.Br. is used in Africa and Asia both medicinally and as a foodstuff[1]. In 1937 Steyn[2] first proved it toxic to animals and described the symptoms and lesions produced. Further toxicological studies were reported on by van der Walt and Steyn[3] and by Philip *et al*[4].

During recent experiments it has been observed that animals suffering from poisoning with this plant show a marked hyperglycaemia and glycosuria. This fact has not been reported previously.

In this paper the effects of the plant on the blood sugar level are described. In addition, further details of the symptoms and post-mortem lesions are given and the differential diagnosis discussed.

MATERIALS AND METHODS

Plant material derived from the Kuruman area and proved to cause symptoms at a dosage level of 1 g/kg and death at 2 g/kg was used. This was dosed to four 4-tooth merino wethers (Nos. 1 - 4) weighing between 23.1 and 33.6 kg each at a rate of 2 g/kg. The material used was dried and ground. It was suspended in about two litres of water and administered per stomach tube. Four similar animals were dosed with lucerne at the same rate to act as controls.

The blood sugar concentration was determined at intervals as indicated in Table 1. by the method of Folin and Wu as described by Hawk[5] and by that of Mohun and Cook[6].

RESULTS

There was a marked rise in blood sugar starting 4 to 8 hours after dosing and reaching a peak at from 8 to 12 hours. As will be seen from the table death occurred after the peak of hyperglycaemia had been reached in sheep 2 and 4.

It was also found that affected animals tended to show a 25 to 50% rise in serum glutamic oxaloacetic transaminase.

CLINICAL SYMPTOMS

The following descriptions of the symptoms and post-mortem lesions are based on observations made on a total of 18 sheep.

Symptoms appear from 4 to 8 hours after dosing.

Poisoned animals are hypersensitive and nervous and show a stiff gait followed by incoordination. They then go down and are reluctant or unable to stand when helped up, often falling repeatedly to the same side. There is an increase in muscle tone and muscular twitching. Animals may lie on their sides making paddling movements as in heartwater. Later tonic spasms occur. These last some ten seconds at intervals of 30 to 60 seconds during which time the animal appears paralysed or exhausted. The spasms affect all the muscles of the body with rigid extension of the limbs and rigidity of the thoracic and abdominal muscles. The head may be pulled backwards or towards the sternum. The animal may emit weak, anxious bleats. The spasms, as in strychnine poisoning, can be induced by handling or by tapping the animal e.g. on the head, but not by a noise such as clapping of the hands. One animal went into spasm while being chased. It leapt into the air with all four legs rigid and fell still in spasm. During spasms animals may die of respiratory arrest.

Animals showing severe symptoms may recover, while others showing much milder symptoms may die. Recovering animals show nervousness and paresis for days after the convulsions have ceased.

The above symptoms are accompanied by tachycardia (130-140, occasionally up to 200 beats per min.), polypnoea (40-80, occasionally up to 108

per min.) often accompanied by a groan on expiration.

Opisthotonus, foaming at the mouth, marked hyperaemia of the conjuctivae and elevation of body temperature were also noted.

In acute cases bloat following ruminal stasis may cause death.

Post-mortem Findings

A marked generalized congestion with subcutaneous haemorrhages especially behind the shoulders, congestion and oedema of the lungs and glycosuria were the most constant findings. Bloat, rumen-stasis, constipation, light subepi- and subendocardial haemorrhages and rare cases of focal congestion of the small intestine, were also seen. The kidney tended to decompose much quicker than the other organs and showed marked congestion. The urine tested ++ to ++++ for sugar with "Lilly Tes-tape".

Discussion

The cause of the hyperglycaemia has not been established but it may well be due to adrenaline secretion during the attacks probably followed by increased glucocorticoid secretion. The rise in serum glutamic oxaloacetic transaminase might be ascribed to rupture of muscle fibres.

The similarity of the post-mortem findings to those of enterotoxaemia prompted us to have the stored sera of the experimental animals tested for enterotoxaemia epsilon antitoxin, although they had all been immunised. In all four of the sheep used in the blood sugar experiment, as in most of the other cases, the level was above 0.15 I.U. According to Jansen[7] this excludes enterotoxaemia.

The symptoms and post-mortem lesion described here are very similar to those described by Gilruth and Murnane[8] and by Hall[9] in *Sarcostemma australe* R.Br. poisoning. According to a letter from O. A. Leistner of the Royal Botanic Gardens, Kew, the two plants are very closely related if not identical.

Table 1.—The Blood Glucose concentrations (mg %) in sheep nos. 1 to 4 after being dosed with *Sarcostemma Viminale* R. Br. compared with that of control sheep nos. 5 to 8 which were dosed with Lucerne.

Sheep No.	Method	0 hrs	4 hrs	8 hrs	12 hrs	24 hrs	28 hrs
1	Folin Wu	40	43.5	62.5	103.5	Dead	
	Mohun	32	35	60	140		
2	Folin Wu	41	42.5	97.5	51.0	Dead	
	Mohun	42	56	112	70		
3	Folin Wu	36	43	74.5	Dead		
	Mohun	28	32	100			
4	Folin Wu	38.5	43.5	87.5	92.5	57.5	Dead
	Mohun	32	35	92	116	66	
Mean Values	Folin Wu	38.5	43	93	82	57.5	
	Mohun	33.5	39.5	91	108.5	66	
5	Folin Wu	49	45.5	42	45.5	40.5	40
	Mohun	50	50	53	65	55	46
6	Folin Wu	43.5	43.5	46	52	40	40
	Mohun	32	56	60	56	32	46
7	Folin Wu	47.5	45	44.5	47.5	43.5	34
	Mohun	53	50	50	62	53	46
8	Folin Wu	51	49.5	42	45	35	30
	Mohun	56	35	60	56	24	26
Mean Values	Folin Wu	47.5	45.5	43.5	47	39.5	36
	Mohun	47.5	47.5	55.5	59.5	41	41

Acknowledgements

The Chief of the Veterinary Research Institute, Onderstepoort, is thanked for permission to publish this paper and Prof. R. Clark for his assistance in preparing it. The identification of the plants was done by the Botanical Research Institute at Pretoria and the plants submitted by Dr. A. M. van Heerden, State Veterinarian of Vryburg. For the serum enterotoxaemia epsilon antitoxin determinations performed by Mr. Visser of the Bacteriology Section and in the histological examinations by Prof. J. D. Smit of the Pathology Section of this Institute we extend our thanks.

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THE BRITISH VETERINARY CODEX

Pharmaceutical Press, London. 880 pp. 2nd edit. 1965 Price £5 5s.

The major advances of pharmacology in recent years have tended to rather outmode the 1953 edition and 1959 supplement of the British Veterinary Codex, and it is indeed gratifying to record the publication of the second edition of this useful reference manual.

The general presentation and format of the first edition have been retained but numerous alterations to the contents have been introduced.

Over 100 drugs have been deleted from Part I which deals with drugs, chemicals and related substances, and 57 monographs, consisting mainly of new chemotherapeutic agents, have been added.

In keeping with the development of modern biological products, Part II, the chapter relating to antisera and vaccines has been revised to include 18 new monographs while 9 monographs have been deleted.

Among the new preparations in Part III, a similarly revised section entitled The Formulary, are injections for the treatment of mineral deficiencies, cobalt "bullets" and some intramammary antibiotic preparations.

A few interesting appendices have been included in this edition, the most notable being an appendix devoted to pre-mixes and concentrates used for medicating animal feeds and one dealing with pharmaceutical adjuvants. A number of appendices included in the first Codex have been deleted.

An authoritative text of this nature which, however, retains both brevity and clarity, may be found lacking in some finer detail of drug action or toxicity but any such omission is of little importance when set against the tremendous value of this work.

There is no doubt that the British Veterinary Codex has established its rightful place on the bookshelves of those engaged in the practice of veterinary medicine and the 1965 edition should be well received.

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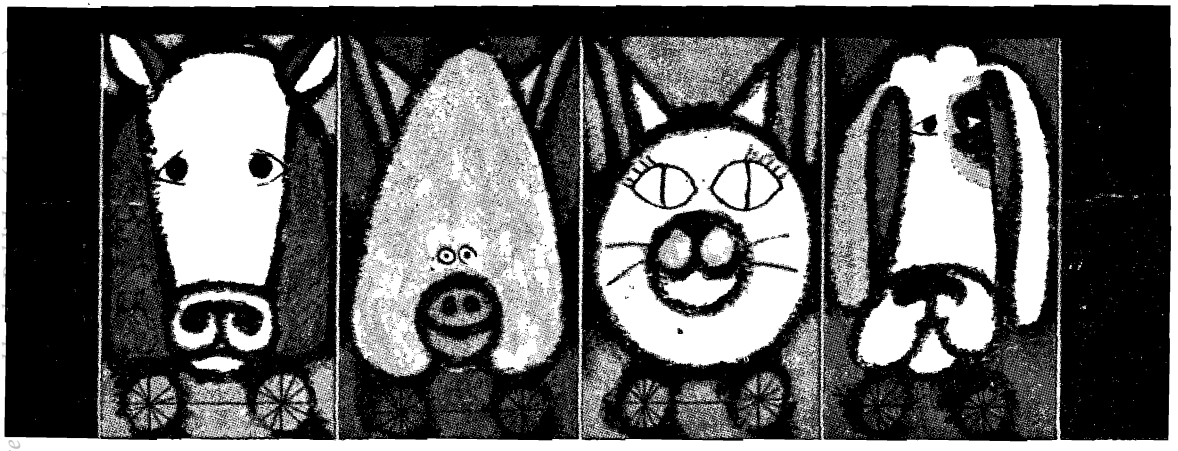

A MAJOR ADVANCE IN ANTIBIOTIC THERAPY

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ADVANCES IN GEELDIKKOP (TRIBULOSIS OVIS) RESEARCH. 9. THE EPIZOOTIOLOGY OF ENZOOTIC ICTERUS.

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SUMMARY

The history of enzootic icterus research in South Africa is reviewed. Some notes on the general incidence of the disease are given followed by a detailed description of the epizootiology with respect to geographical distribution, geological considerations, farming, botanical, seasonal and climatic conditions, and animals affected. The various factors which precipitate acute episodes of the syndrome are discussed and some indication is given of the tremendous annual losses which may be ascribed to the disease.

INTRODUCTION

In its typical form enzootic icterus is an acute haemolytic syndrome precipitated by various forms of stress. The acute episodes, which are often fatal, are characterised by intense icterus, severe haemolytic anaemia, severe renal pathology, severe gastrointestinal stasis, severe disturbances of the electrolyte balance and hypercupraemia and other biochemical disturbances of great interest[1 6]. The aetiology of the condition has not been finally elucidated although much is known in this regard. It is believed that geeldikkop and enzootic icterus actually represent different manifestations of a single disease entity, possibly a subclinical chronic selenium intoxication[2 5]. Enzootic icterus is the more violently acute and often fatal syndrome and acute episodes are precipitated by relatively mild forms of stress, whereas in the case of the "biochemically" milder geeldikkop, stress of a much more severe nature is required before the syndrome makes its appearance[2 4 7].

Enzootic icterus, like geeldikkop, is characterised by marked inactivation of certain "key" dehydrogenases which during the acute attacks of the disease results in catastrophic disturbances of metabolism[2 4 7]. Latent damage to various metabolic systems is evident before and between acute episodes. Such defects may possibly have been in existence much earlier, even from the time of birth and possibly persist for years in affected sheep[1 6 8 9]. Although mild photosensitivity is seen in most cases of the acute syndrome, the development of this disturbance is often masked or abruptly terminated by the explosive haemolytic crisis which is the dominant event in acute enzootic icterus[2 3]. Intravascular haemolysis has been shown to be due to inactivation of glyceraldehyde-phosphate dehydrogenase and resulting increased erythrocyte fragility[2 4, 6 7, 9]. Since the function of the methaemoglobin-reductase system is largely dependent on the activity of this enzyme, methaemoglobincythaemia is a frequently observed symptom just before or during the haemolytic crisis[3 4]. Haemoglobinuria is a common symptom in all acute cases.

Chronic forms of the disease occur in which renal lesions dominate the symptom complex and in which intravascular haemolysis still proceeds, but at a much lower level[4].

The symptomatology, histopathology and chemical pathology of this syndrome will be the subjects of following papers in this series.

HISTORY

Henceforth referred to in this paper as E.I. — enzootic icterus (and geeldikkop) almost certainly have been known from the earliest times of intensive farming in the Central and South-western areas of the Cape Province, under the name of "Geelsiekte" (literally, "Yellow disease"). Numerous aged inhabitants in the enzootic areas recount outbreaks of the disease covering three generations on their particular farms. Included in these reports are some of devastating outbreaks amongst wild antelope (see further). As in the case of geeldikkop there is a voluminous folklore surrounding this disease, but unlike the former condition there is no general incrimination by the farming community of any single factor in its aetiology. The very

multiplicity of alleged causes, both natural and super-natural, is a measure of the bewilderment of the farmers regarding the syndrome.

The first record of the disease in the scientific literature of South Africa is that of de Kock in 1928 in two papers on other topics[10 11]. Similar disease conditions are well known in Australia and many European countries, and much of the early research on E.I. in South Africa was based on those data. In this paper observations and references will be confined to the condition as it occurs in South Africa.

Although E.I. is well known to most veterinarians in this country and has formed the subject of numerous unpublished reports and of voluminous correspondence there is a remarkable void in our literature regarding the disease until 1959. Since this date various aspects of the disease have been touched upon in publications of the authors and their co-workers[1 9 12]. The dearth of published information during the period mentioned is in no way due to lack of research. Numerous studies had been conducted during this time, the results of which have served to narrow down the fields of investigation and have allowed formulation of our present thoughts on the aetiology of this syndrome. Much of the material has been drawn from reports and notes of previous workers, from the considerable filed correspondence at this Institute and from personal communications from colleagues in the field. Recognition of these sources is made in the appropriate places.

Until about twenty years ago the disease remained localised in a relatively remote corner of the Karoo, namely the Roggeveld and Nuweveld Mountain Ranges with only limited and sporadic outbreaks occurring elsewhere. Within recent years, however, the incidence of the disease, like that of geeldikkop, has increased alarmingly and it is now enzootic in vast areas of the Cape Province and Southern Free State.

The disease was first studied at Onderstepoort by de Kock from 1924 until his retirement in 1949. The following information regarding its incidence at this Institute has been drawn from his notes, correspondence and published work[10 11]. The syndrome was first noticed at Onderstepoort in July, 1924. From that time until December of 1926, 4000 sheep arrived at the Institute from Carnarvon, Philipstown, Colesberg and Middelburg (C.P.). In all 50 cases of E.I. occurred amongst these animals during the period mentioned, most of which were in a batch of 500 which arrived from Middelburg in July of 1924. In August of 1925 one case occurred in a batch of 830 sheep, and 11 cases one year later amongst a batch of 250 sheep from Philipstown. The majority of cases occurred shortly after arrival at Onderstepoort, viz. within 10 - 30 days, and fewer cases 31 - 40 days after arrival. The earliest case appeared 8 days after its reaching Onderstepoort and the longest intervals between arrival and appearance of the syndrome were given as 82 - 388 days. All these cases had a fatal termination. De Kock considered the condition to be some type of intoxication or autointoxication in which the following acted as predisposing factors: - fatigue from being herded and railed, exposure, insufficiency of food and water while in transit, and to being offered unaccustomed food on arrival at their destination.

In a note to one of us, J. W. Groenewald, then officer in charge of animal nutrition at this Institute, made the following points: In 1935 it was generally accepted that 10% of sheep which arrived at Onderstepoort every April from Beaufort West were lost from enzootic icterus. They were subjected to a train journey of three days and then placed on a ration of ½ lb of crushed maize per head per day and teff *ad libitum*.

From the next year onward mortality was decreased particularly by placing the sheep on roughage for 14 days before slow introduction to ¼ lb crushed oats and ¼ lb crushed maize, so that by 1949 losses from E.I. did not exceed 5%.

Since that date sporadic losses still occurred at this Institute amongst sheep obtained from areas where the disease is enzootic, but the incidence is less than 1%. Many sheep still show biochemical features of the disease[6] and acute haemolytic crises can be provoked in such animals by subjecting them to mild forms of stress.

The marked decline in the incidence of the disease at Onderstepoort is due to the fact that most of the animals now emanate from Laingsburg, Barkly East, Prieska and the Transvaal Highveld, areas in which the disease is not enzootic as yet.

A further point of interest is that all the sheep covered by de Kock's report and most of those seen by Groenewald were introduced to Onderstepoort for the purpose of bluetongue vaccine preparation and were assumed to have been fully susceptible to this disease. We will refer to the importance of this point shortly.

The first field investigations into E.I. by officers of this Institute took place in December of 1946 on the farm Witteklip at Murraysburg under the direction of one of us (H.P. de B.) assisted by C. W. A. Belonje, at the time State Veterinarian at Middelburg and other officers of the Dept. of

Agriculture. This was followed up by field work on the same farm and in de Aar and Aliwal North in 1947, in which Dr. M. Henrici of the Dept. of Botany played a prominent role. The disease has since been studied extensively in the field by the authors, their co-workers and officers of Grootfontein Agricultural College and by officers of the Veterinary Field Services. The results of these recent studies with regard to the epizootiology of E.I. are included in this paper. Some observations have already appeared elsewhere[1 9 13].

Bionomics.

The following facts must be appreciated in order to understand the epizootiology of E.I. In the first instance E.I. in its apparently asymptomatic state appears to be a far more advanced and severe form of chronic subclinical selenium intoxication than is geeldikkop. Tissue levels of this element are always consistently higher in E.I. than in the latter syndrome[2 5]. The biochemical lesions in apparently asymptomatic E.I. cases are far more advanced than in animals which are candidates for acute attacks of Geeldikkop. In the latter syndrome severe forms of non-specific stress are required to precipitate acute crises[2 5 7] E.I. by contrast requires comparatively mild forms of stress to precipitate acute attacks. Chiefly adult animals are liable to suffer exacerbations of the syndrome. Since the basic intoxication appears to be cumulative[2 5], they are apparently perpetually verging on the brink of a haemolytic crisis.

The incidence of E.I., unlike that of geeldikkop, is not confined strictly to a particular season. This is due to its biochemical nature and to the circumstances which precipitate exacerbations. A clear distinction must be drawn between E.I. as it occurs in the areas where it is enzootic and its sporadic occurrence elsewhere in the country amongst animals which emanate from the enzootic areas. Theoretically E.I. can occur all the year round in flocks in which exist the basic chronic intoxication and the presence of any of the various triggering factors. In the areas where the syndrome is enzootic, the incidence is largely seasonal with sporadic cases occurring throughout the year. The disease can be expected elsewhere in the country at any time of the year, whenever animals are moved out of their original environment and depending on their handling and management during and following the movement in question. Whenever such outbreaks occur, it is always possible to identify the farm of origin with an enzootic area. This point is extremely important to those who have to deal with outbreaks of the syndrome far from its natural home. Not only does their handling of the outbreak depend upon this knowledge but also the correctness of their standpoint in the frequent litigations between purchaser and seller of the animals concerned.

Geographical distribution.

The main area in which the syndrome is enzootic is still the Nuweveld and Roggeveld Mountain Ranges, where Fraserburg and Sutherland are the two main centres affected. The second most important enzootic area is a roughly triangular stretch of rugged mountainous country bounded by the towns of Richmond, Murraysburg, Aberdeen, Graaff Reinet and Middelburg. This area encloses the Winterhoek, Lower Sneeuberg, Kamdebo, Koueveld, Renosterberg, Agter Renosterberg and Sneeuberg Mountains. The disease is by no means as widespread in this area as it is in the Nuweveld Range. Its distribution is rather patchy and confined to regions in which marked deterioration of the veld has taken place. The farms mainly affected lie in the Winterhoek, Kamdebo and Koueveld Ranges. Elsewhere in this area the disease appears on isolated farms.

During the last twenty years the disease has spread slowly northwards and eastwards, whilst still remaining confined to regions which are either mountainous or consist of low broken sandstone ridges and hills with doleritic intrusions. North of Fraserburg it has become enzootic in the Harpuisberge and Taaibosberge, ranges southeast of Loxton, and is to be found on hilly farms north of this town and in the Steenkampsberge between Loxton and Beaufort West. We have also seen cases in the Boesmansberge between Loxton and Nelspoort and in the Komsberg Range south of Sutherland. The syndrome appears to have become established in the Hantamsberge immediately north of Calvinia and in the extreme western parts of the Roggeveld Range around Middelpos. Numerous cases have come to our notice within the last five years on farms around Stormberg, Cyphergat and Molteno in the Stormberg Range.

This area, in which geeldikkop is by no means unknown, lies far to the East of the centres mentioned above. From all accounts the disease appears to have become enzootic in these mountains.

Hitherto we had always regarded the disease as being one of mountainous regions in contrast to geeldikkop, which is essentially a disease of the plains. Within recent years E.I. appears to have become firmly established on numerous farms in the broken hilly country around Victoria West,

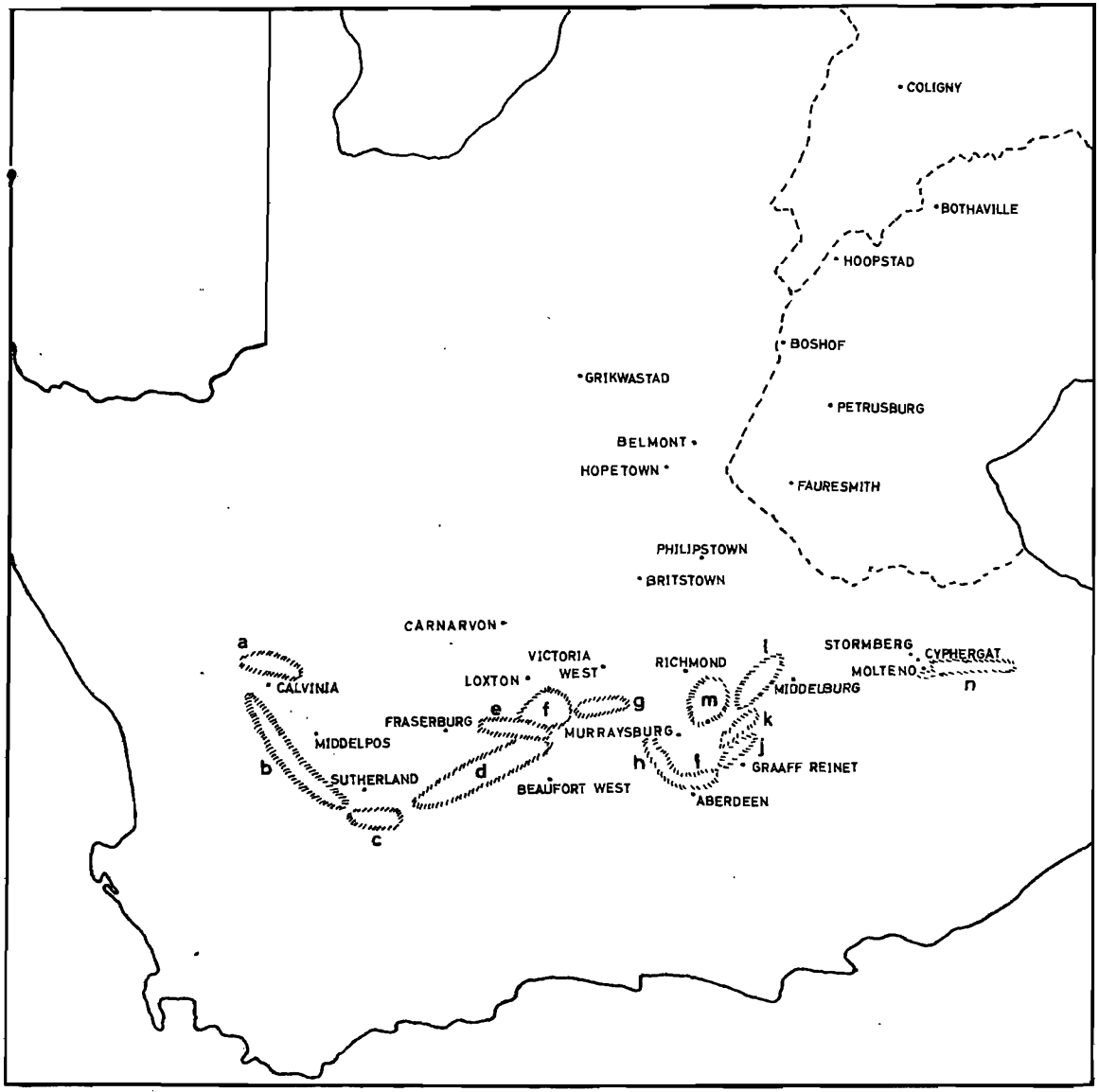
Britstown, Hanover, Carnarvon, Philipstown, Belmont, Heuningneskloof, Witput, Hopetown and Griquatown.

The syndrome has been known in the Southern Orange Free State since 1947 when one of us (H.P. de B.) had the opportunity of studying cases in the Petrusburg and Fauresmith areas. Reports have reached us during the last few weeks of cases in the Boshoff, Hoopstad and Bothaville districts. The recent severe drought has been attended by considerable movement of small stock between the Karoo, Griqualand West and the Free State; it is quite likely that most, if not all, of these latter cases are animals which have come from areas in which the disease is truly enzootic.

We know of only one outbreak which has taken place in the Transvaal in which the sheep concerned were bred and raised on the farm involved. This occurred in 1956 on the farm Palmietfontein, near Coligny in the South-western Transvaal, an area very similar in most respects to those mentioned immediately above.

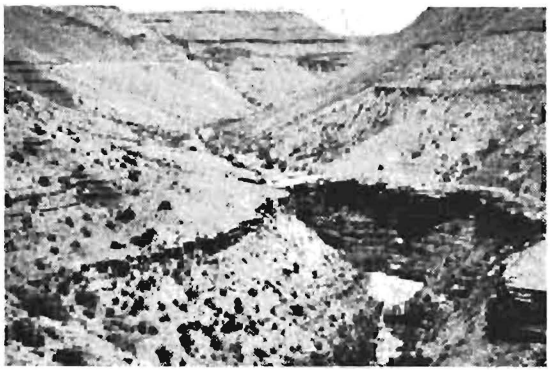
Geology and Topography.

Fraserburg and Sutherland lie in a plateau on top of the Nuweveld and Roggeveld Ranges which



varies in altitude from 4000 - 6500 feet above sea level. The geological formations of the area consist of shales and sandstone of the Beaufort series of the Karoo system which are extensively invaded by dykes and sills of Karoo dolerite. The copper content of this dolerite is constantly high, but abnormally so in only a few specimens which have been examined. It appears to be low in the sandstones and shales from which the soils of this region are derived. The mountainsides are covered in many areas with numerous large red-brown sandstone blocks which are indicative of severe temperature fluctuations and wind erosion. On numerous farms in the region, particularly towards Victoria West and Loxton, considerable glacial moraine is evident on the hillsides. Figure 1, Plate 1 is typical of the topography and geology of these regions.

Fig. 1 Plate 1



The farms on which the disease occurs in these districts are either situated entirely within the mountain ranges or lie on the edge of the plateau on the northwest, west and southwest of these ranges. These latter farms consist mainly of numerous broken sandstone ridges and low foothills with numerous dolerite intrusions. As in the mountain farms, evidence of severe wind and stormwater erosion is only too obvious. The disease is more prevalent on farms where sandstones and shales are the main rock formations and occurs to a lesser extent on those where dolerite predominates[13].

The topography and geology of the farms on which the disease occurs in the Murraysburg, Richmond, and Aberdeen areas is basically similar to that described above. Further north, where the disease has appeared on the Karoo plains e.g. Britstown, Carnarvon, Hopetown, Belmont etc., the affected farms are generally situated in broken hilly country with the same geological formation as described.

Farming Conditions

In Table 1 are presented some data collected from 30 farms during a severe outbreak of the disease in the Fraserburg district in 1957 and 1958. These data are fairly representative of the area with regard to farm and flock size and stocking rates.

In general the farms in all the affected areas vary in size from 1000 - 10,000 morgen. Some exceptionally large farms are encountered of up to 45,000 morgen in size. (See the two farms described in Appendix 1). Such farms are of two historical types: (a) Old "family" farms on which the descendants of the original families are still living together as a small community and work the farm on a joint basis. Such farms are generally progressive, lightly stocked, well cared for and have a very low incidence of E.I. Veld vegetational cover is excellent and consists of a wide variety of Karoo bush types and grass, usually with most plant-species being palatable and nutritious types. A typical farm of this nature is *Klawervlei*, described in Appendix 1. Large parts of the farm are given over to cultivation of irrigated artificial pastures for use in times of drought and the animals are maintained on a high plane of nutrition. Farms like this are rare in the areas where E.I. is enzootic. (b) Large farms in which the original "family" farm has been extended by acquisition of numerous small neighbouring properties. The latter are often retained in their original form as large camps of the major unit, with shepherds or managers living in the old homesteads. Since the owners of such farms are generally financially secure, management and nutrition are as good as in the first instance. The original "family" farm is generally in an excellent condition and the incidence of the disease is negligible. The "acquired" camps, however, in most cases show evidence of previous misuse which the farmer is endeavouring to eliminate by careful farm planning and pasture management systems. The incidence of the disease in these "camps" is somewhat higher than on the original homestead but nevertheless kept firmly in check by good management and supplementary feeding. A unit of this nature is the farm *Celeryfontein* described in Appendix 1.

The incidence of the disease is highest on the smaller farms of from 1000 - 4000 morgen and it is these which merit closer attention. In many instances such farms are portions of old "family" farms on which the descendants of the original

owners are carrying out farming on their own account, or have sold these portions as complete farms. There seems to be a tragic tendency amongst such farmers to try and maintain the same sized flocks on each of their properties that were once run on the original family farm. Mortgages and bonds are a heavy burden on such farmers and flocks disproportionately large for the small size of the farm are often maintained to meet financial demands.

Whatever the history of these small farms, the cycle of events remains the same. Flocks which are too large for the carrying capacity of the farm are maintained; the owner cannot afford proper supplementation in times of drought; the nutritional plane on the farm decreases alarmingly; mortality due to all causes rises sharply, culminating often in a crippling outbreak of E.I. To recoup his losses the farmer is forced to restock again. This he often does at a higher rate than before. More often than not he buys animals from a neighbour in similar circumstances and is ultimately faced with even bigger ravages from E.I. The cycle is a vicious one, to which the "wool booms" of previous years have contributed in no uncertain measure. The rising price of mohair at the present time is an added complication. Many of these farmers are now maintaining increasing numbers of Angora goats without significantly reducing their sheep flocks.

Due to paucity of water and poverty of soil very little can be grown in the way of supplementary feeding. Consequently the farm becomes a subeconomic unit and the owner financially unable to bring about the improvements required to check the cumulative processes of attrition.

The following information has been drawn from reports by officers of the Grootfontein College of Africulture[14]. The veld is in a state of constant overgrazing. This is evident from the virtually complete absence of grass (except isolated patches of unpalatable or pioneer types like *Danthonia, Aristida* and *Sporobolus* spp.), and the absence of nutritious and palatable shrub types like *Pentzia* and *Salsola* spp. and of succulents like *Mesembryanthemum* and *Aridaria* spp., purslane and *Psilocaulon* spp., whilst unpalatable and undesirable bushes like *Nestlera, prostrata, Chrysocoma tenuifolia, Eriocephalus spinescens, Eriocephalus glaber, Pteronia glomerata* and *Elytropappus rhinocerotis* dominate the picture. On some farms even these bushes have been grazed down extensively.

Wind erosion is severe, the topsoil is poor and shallow and the residual sandstone and shale soil types support the less palatable and inferior bushes

Fig. 2 Plate 1

mentioned above rather than the more valuable types. Such soils deteriorate rapidly if mismanaged. In a recent paper on the pasture management of these areas Skinner[13] predicted with confidence the areas in which E.I. was likely to establish itself. Events in the last five years have proved him correct in all essential details.

Previous botanical surveys conducted by Henrici[14] on farms in the Murraysburg, Fauresmith and Petrusburg areas agree in all details with the recent work. During the course of our own investigations we have made identical observations and have further found that the selenium content of the inferior and unpalatable types mentioned above is consistently higher than that of the more nutritious bushes[5]. Where the disease is severe, *Nestlera prostrata, Chrysocoma tenuifolia, Eriocephalus spinescens* and *Pteronia* spp. are constantly the dominant plants; selenium levels of up to 70 p.p.m. have been found in some of these species[5].

The condition of the veld in the affected areas has been aggravated by prolonged periods of intense drought and by the ravages of the karoo caterpillar. The difficulties in restoring many of these farms to the required standards have become enormous, if not insurmountable.

We have presented in Appendix 2, short case histories of 12 farms on which the disease has appeared in the form of severe outbreaks or on which it has been known for many years. They have been selected to be as representative as possible of the farms in all the areas where the disease is now considered to be enzootic and form an interesting comparison with those described in Appendix 1. Figure 2, plate 1 is representative of the small uneconomical farming units which suffer severely from the ravages of the disease and in figures 3 and 4, plate 1, a comparison is made between the veld cover on such farms and that on farms where management is excellent and where the incidence of the disease is low.

Climatic Conditions

Although E.I. can theoretically occur at any time throughout the year, in areas where it is established there is a definite seasonal incidence of major outbreaks of the disease. Heaviest losses are experienced in the late spring and early or mid-summer months, i.e. September to December.

There is general agreement amongst the farmers and the officers of the Department of Agriculture who have studied their farms[13, 14] that usually the incidence of the disease tapers off once the first heavy summer rains have fallen. We have found this to be so in general, but depending on the farms and state of the animals concerned it need not necessarily be so.

Bearing in mind the condition of the farms described earlier, the cycle of climatic and seasonal events which lead up to the appearance of an E.I. outbreak must be considered. The annual rainfall in most of the affected areas varies from 6″ - 12″ with an average precipitation of about 9″ throughout. This is roughly divided into a winter rainfall of 3″ and a summer rainfall of 6″, the former in the form of soft rains or showers and the latter mainly as heavy thunderstorms often associated with hail and followed by a day or two of bitterly cold wind. The rainfall is highest in the southern and eastern parts of the escarpment and decreases considerably as one goes further northward. In Table 2 we have reproduced rainfall data from the records of the owner of the farm Bastersberg, in the Sutherland district, where the disease is severe.

These data cover the winter months May to August and Spring to early summer. Winter in this part of the country is intensely cold and can be very long: severe frosts occur right up to November. Average monthly temperature minima recorded in Fraserburg during the winter of 1957 varied around 0.2°C. In Sutherland temperatures fell even lower and many farmers were obliged to trek with their stock to warmer parts.

Winter rains occur mainly towards the end of June and in July and good falls are followed by rapid growth of the natural vegetation. The rains are followed by an extremely dry period and rainfall during spring and early summer is generally low. (Table 2). During these seasons the nutritional level of the natural grazing is at its lowest[13]. Conditions obtain which are most conducive to severe digestive disturbances in ruminants, viz.

Soaking rains followed by growth of natural grazing and then a period of drought with rapid wilting and desiccation of fast growing plants. Many farmers have declared that good winter or spring rains are harbingers of severe E.I. outbreaks.

Many farmers, depending on seasonal conditions, start shearing from July to October, while lambing occurs from August onwards. Numerous factors now enter which can be regarded as physical or physiological stress, e.g. herding and handling which are necessary for shearing, the marked drain of a rapidly developing foetus on a sometimes very weak maternal animal, parturition and finally lactation. All of these play their own particular parts in precipitating the syndrome.

The summer months are very hot and drought conditions may be extremely severe. The average of the midsummer temperature maxima recorded at Fraserburg in 1957 is 31.5°C. Down in the flats around Loxton, Victoria West and Beaufort West, temperatures soar to 40-50°C. during very hot summers. During this time strong, hot north-westerly winds are common and have a further severe desiccating effect on the vegetation. The summer rains generally fall in December, January and February. They are associated with rapid and often luxuriant growth of fastgrowing annuals.

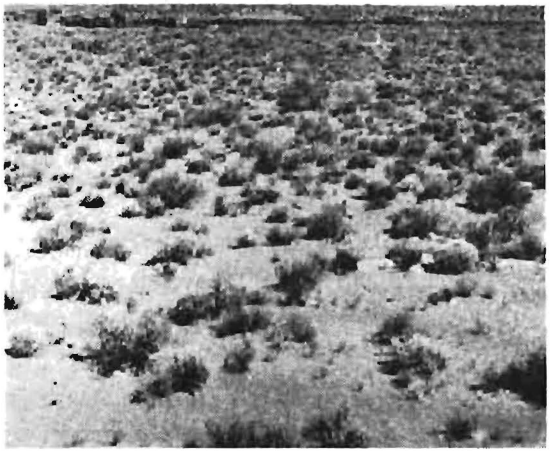
Here again the sudden super imposition of a lush plant growth on a rapidly falling nutritional plane predisposes to digestive disturbances. The period of rapid growth is again followed by one of intense heat and desiccation in which wilting and deterioration of the grazing is to be expected. This period of climatic and nutritional upheaval is generally associated with a second mortality peak. Wethers figure prominently in the lists of dead and dying at this time. Should the rains continue intermittently throughout the rest of the summer, as in good seasons, farms in excellent condition are assured of good grazing and mortality falls off sharply. On many farms sporadic cases continue to appear until April, when more settled weather conditions prevail once more.

From our studies in the Fraserburg and Sutherland areas it is apparent therefore that the total annual rainfall is not nearly as important as is its distribution over the drier part of the year. Very irregular rains during the early summer, with periods of intense drought especially after a fairly wet winter and early spring, play a major role in the incidence of the disease.

In tables 3 and 4 data obtained from the owner of Bastersberg (mentioned earlier) and from the Hondefontein meteorological post in the Nuweveld Mountains, show the monthly variations in rain-

fall over the period just considered for 1957-1958, when one of the severest outbreaks in recent times occurred.

Fig. 3 Plate 1



Studies on the relative humidity during the summer months add little to the pattern of the epizootiology so far constructed. Relative humidity measured at Fraserburg at 8 a.m. and 2 p.m. shows an appreciable decrease as the temperature rises. The humidity pattern for the summer of 1956 contained more low values (down to 11.8%) and more irregularities than that of the same period in 1957. Monthly variations were also greater in the summer of 1956 than in 1957.

The reader is referred once more to the case reports presented in Appendix 2 where details regarding seasonal and climatic factors in the epizootiology on some individual farms are presented.

Susceptibility

When present knowledge concerning the aetiology of E.I. is carefully considered, there is no obvious reason why the disease should not occur in any species of small ruminant. Bovine species may be excluded tentatively from this generalization, since glycolysis in the red cell of these species is presumably not so susceptible to disturbances of the nature which pertain in E.I. as are the erythrocytes of sheep and goats[9]. We have studied the syndrome in all breeds of sheep and goats which are normally maintained in the Karoo, viz. Merino, German Merino, Afrikander, Blackheaded Persian, Dorper and Karakul sheep and various crossbred animals, the common domestic goat ("boerbok"), Angoras and Saanen goats. Many older farmers in the district tell of severe mortality during very dry seasons amongst springbuck (*Antidorcas marsupialis*) and steenbuck (*Raphiceros campestris*) in which the carcasses of affected animals were stained intensely yellow. We have not been able to confirm such reports.

The syndrome is seen mainly in older animals, i.e. two years and older, and particularly in aged animals. This is consistent with the view that the disease is basically a cumulative intoxication[1,9]. During the last five years numerous cases have occurred in suckling lambs and hoggets. Cases of this nature, however, are seen infrequently and are confined to extremely severe outbreaks on farms where deterioration of the veld is in a most advanced condition, (see e.g. case report (f) in Appendix 2; the farm Hebron). It is noteworthy that we have found evidence of considerable placental transfer of selenium from maternal animals to rapidly developing foetuses[5]. It is thus quite conceivable that given proper conditions, the disease may appear in very young animals.

The syndrome is not confined to any particular sex, although its rate of incidence is definitely determined by sexual factors. During the spring and early summer months the incidence is undoubtedly highest amongst ewes, correlated with advanced gestation, parturition and lactation. During mid- and late summer the disease is often seen mainly amongst wethers. A number of management factors are operative in this case. In the first instance the ewes with suckling lambs are often brought down from the mountains into camps around the homesteads and are given better care than the wethers, particularly with regard to any supplementary food which is available. In other instances, the wethers may be receiving

Fig. 4 Plate 1

special care in order to fatten them for the markets of the Christmas season and are highly susceptible to ketosis following sudden changes of diet.

We are frequently informed by farmers that rams are seldom affected by the disease. This is certainly not the case (see again case f, Appendix 2) but there are a number of factors which must be taken into account to explain the apparently lower incidence in these animals. The most important of these is that there are considerably fewer rams than either ewes or wethers in a flock. The mortality amongst the latter is therefore always more spectacular. Secondly, on many farms where an attempt is being made to improve the quality of a flock, rams are expensive and highly prized animals and get just that additional care and feeding which may make all the difference in determining whether the animal will be a candidate for a fatal haemolytic crisis or not. The accent here is on *fatal,* since many animals develop mild attacks of the syndrome or become "chronic" cases and are not easily noticed by the owner. In such cases the diagnosis of the syndrome can be very difficult without the aid of many elegant laboratory tests.

The condition of the animal, whatever its age or sex may be, is one of the most important factors in determining the severity of a particular outbreak of E.I. Most cases and the highest mortality occur amongst flocks in which the nutritional plane is low and the animals are in a very poor condition. The incidence is in general lowest amongst those

TABLE I.—EXTENT OF THE ENZOOTIC ICTERUS OUTBREAK ON 30 FARMS IN THE FRASERBURG AND SUTHERLAND AREAS (DECEMBER 1957—JANUARY 1958) AT THE TIME OF FIELD INVESTIGATIONS.

Name of farm	Size of farm (Morgen)	Approximate Number of sheep in flock	Mortality	% of flock	Morgen per sheep
Bastersberg	11,000	2,500	300	12	4.4
Bloemfontein	7,000	1,800	17	0.9	3.9
Elandsberg	6,500	900	30	3.3	7.2
Onderste Brandwag	5,759	3,300	120	3.7	1.7
Toon se plaas	5,240	1,700	130	7.6	3.1
Weltevrede	5,200	1,350	60	4.4	3.9
Grootfontein	5,025	1,200	35	2.9	4.2
Palmietfontein	5,000	1,200	40	3.3	4.2
Draairivier	4,975	1,400	1	0.07	3.6
Eselsfontein	4,648	1,400	15	1.1	3.3
Sandgat	4,400	1,250	20	1.6	3.5
Louw se plaas	4,237	1,100	5	0.45	3.9
Hartebeesfontein	4,000	1,300	20	1.5	3.1
Fontein	4,000	1,250	31	2.5	3.2
Bontberg	4,000	1,100	30	2.7	3.6
Bo-vlei	4,000	1,200	55	4.5	3.3
Gunsfontein	4,000	1,450	120	8.2	2.8
Tierhoek	3,750	900	20	2.2	4.2
Grasleegte**	3,600	400	60	15.0	9.0
Rietvlei	3,042	850	152	17.8	3.6
Genegenheid	3,015	1,200	60	0.5	2.5
Spinnekopkraal	2,800	1,100	195	17.7	2.5
Bok se plaas	2,016	500	50	10.0	4.0
Wilgerboskloof	2,000	650	60	9.2	3.1
Tafelberg***	2,000	500	40	8.0	4.0
Achterste Land	1,980	500	70	14.0	4.0
Melk se plaas	1,500	400	4	1.0	4.0
Avondrus*	1,416	600	122	20.3	2.4
Geelhoek	1,400	400	70	17.5	3.5
Bakoondskraal	1,250	300	40	13.3	4.2
TOTAL	118,753	33,700	1,972	5.85	Average- 3.5

*During the two months following this survey the mortality figure rose to 170, i.e. 28.3%

**During a previous ownership, up to 5 years before this outbreak, the morgen: sheep ratio was 1:1 for short periods after good rains.

***Before we arrived on this farm the morgen: sheep ratio was 5:1. The owner had obviously attempted to recoup his losses by increasing his stock during the outbreak.

that are *consistently* and *regularly* well fed. Paradoxically, severe outbreaks are often seen amongst fat wethers and pregnant ewes. In these instances sudden change of diet or nutritional plane with resulting ketosis is one of the determining factors.

Precipitating Factors

Throughout this paper, we have used the words *mild* or *severe* stress as general terms to cover a host of factors or circumstances which trigger off acute haemolytic episodes of E.I. The words have been used in their original context as defined by Selye and the basic reactions provoked in the animals concerned follow the broad pattern of the General Adaptation Syndrome.

Studies on the blood of this sheep during this stage of settling down produce findings which are not at all unexpected in terms of the General Adaptation Syndrome. There is fleeting hyperglycaemia, less transient eosinopaenia and evidence from plasma electrolyte studies of alternating adrenal hyper- and hypocorticism. These are general findings in all sheep irrespective of their origin. However, in a large precentage of our Karoo sheep we note towards the end of the period of adaptation to the novel circumstances, the appearance of an interesting phenomenon which is best described as a mild subclinical intravascular haemolytic crisis. Within two or three days of putting the animal into the cage, the plasma assumes a distinct yellowish or reddish brown tint.

Table 3.— Monthly variations in rainfall at Bastersberg, Sutherland during the spring and summer of 1957—1958 (Given in millimetres.)

Month	September	October	November	December	January
Rainfall	21	3	0	54	11

Table 2.—Rainfall at Bastersberg, Sutherland during 1954—1957 (Given in millimetres.)

Year	1954	1955	1956	1957
Annual precipitation	242	323	189	298
Winter rainfall (May to August)	81	94	94	113
Early Summer rainfall (Sept.—Nov.)	30	98	35	24

The typical responses to mild stress of an apparently clinically healthy laboratory sheep, which has been brought some years previously from an area on the fringe of the E.I. zone but where Geeldikkop is rife, will serve to illustrate this point.

The animal has been taken from a group of sheep maintained in a small camp with water and green lucerne fed *ad libitum* from an environment in which it was presumably quite content, and placed in a metabolism cage where it still has free access to water and the same green lucerne. It is now in an unfamiliar and confined environment with steelmeshed floors; strapped to it is a harness required to support a faeces collection bag. Furthermore the animal is being bled once a day by jugular venipuncture for chemical analysis. The sheep is quite justifiably highly apprehensive and remains obviously restless for 2-3 days before "settling down" to its new routine. The disturbances to which the animal has been subjected may be broadly classified as psychological, since, apart from a small amount of daily exsanguination, it has not been subjected to any physical stress.

Spectroscopic examination has shown this to be due to free haemoglobin. This is rapidly replaced by unconjugated bilirubin in amounts of up to 3mgm % in frank cases[2,7]. The marked yellow colour in the plasma at this stage then slowly disappears during the course of the next three days, by which time the sheep appears to have settled down completely and values for the major blood constituents are once more well within the accepted normal ranges.

If such a sheep be subjected to more severe forms of stress, such as drastic changes in diet and infection with disease producing agents, the period of adaptation is more prolonged and the pigmentation of the plasma persists for much longer. Only in isolated instances does the sheep pass into a clinically obvious haemolytic crisis, (see the earlier remarks dealing with de Kock's observations on enzootic icterus at Onderstepoort). This often happens when one least expects it. The position, however, is very different in animals living in the areas where the disease is enzootic, or amongst those which have *recently been removed* from such areas.

We have during the course of our studies on E.I. been struck by the large percentage of cases encountered during the spring, and early and midsummer months in the enzootic areas, which have shown an extremely severe gastrointestinal atony. This was in most cases so severe that considerable atroply of the digestive tract had taken place and the contents of the forestomachs and caecum were in a very advanced state of desiccation. One is forced to conclude from the condition of the digestive tract that gastrointestinal stasis had preceeded the onset of acute intravascular haemolysis by quite some time. Meticulous autopsy examination of such animals and a careful study of the anamnesis of the outbreak concerned have excluded all other factors except severe digestive disturbance as the primary precipitating agent in these cases. The epizootiological factors leading up to such disturbances have already been discussed.

Lambing and lactation are two very potent physiological stress conditions which may be coupled to digestive disturbances consequent to the rapidly deteriorating vegetation in spring and early summer. In most of the investigated outbreaks lactating ewes have figured largely in the mortality at this time of the year. In many outbreaks reported to us mortality was confined to ewes in advanced pregnancy.

Large numbers of deaths often follow shearing operations particularly if these are followed by rains and periods of intense cold. The main factors concerned here are herding over long distances to the shearing sheds, in many cases a change of diet while the animals are confined near the shearing sheds, the physical and psychological stress of handling during the shearing operation and subsequent exposure if rain and cold spells occur. The reader is referred to case reports (a), (c) and (d) in Appendix 3 where cases of this nature are presented.

Many farmers in the affected areas are loath to institute regular dosing and inoculation programmes since the herding, handling and inherent toxicity of the remedies used often result in significant mortality. (See cases (b) and (e) in Appendix 3 and cases (d) and (g) in Appendix 2). The use of live vaccines which produce a mild febrile reaction is often attended with a small number of losses from acute E.I. attacks.

One of the most potent forms of stress remains movement of large numbers of animals over short or long distances or transport of animals over long distances in a confined space with limited food and water. Movement of flocks from camp to camp or from the mountains down into the plains often involves herding over distances of 3 to 15 miles and, if performed during the spring and summer months, is nearly always attended by significant mortality. The heaviest mortality, however, is encountered amongst large groups of animals which are moved long distances by bus, freight lorry or train. This involves loading large numbers of animals into confined spaces under the summer conditions mentioned and keeping them thus for 2-4 days on end with limited access to food and water. To this severe physical stress must be added the considerable psychological disturbances engendered. The combined stresses are generally so severe that numbers of animals apparently quite normal at the start of the journey, are either dead on arrival at their destination showing typical autopsy signs of acute E.I., or succumb to the disease shortly afterwards. In Appendix 4 we have presented details from 11 reports of mortality from E.I. following stock movements of various types. These are representative of the large number of cases of this nature which are on record. The position has become so serious with regard to this aspect of E.I. that butchers, stockdealers and agents for producers of meat products are refusing to buy sheep from farms in the affected areas, with consequent considerable financial losses to the farmers concerned.

Matters are in no way improved by the frequent lawsuits instituted against the unfortunate sellers. It is considerations like these which make it extremely difficult to obtain accurate mortality figures from farmers in these areas during large scale outbreaks of the disease.

We have presented in Appendix 5, data regarding two very large scale movements of sheep from areas in which the disease is not at present enzootic. These data form an interesting comparison to those presented in Appendix 4, particularly with regard to the numbers of animals involved. In the former Appendix we have noted the movement of 41,000 animals without a single case of E.I. being reported and with a total mortality rate of 1.5% due to various other causes. If one considers cases (b), (d), (g), (h) and (j) in Appendix 4, it can be seen that out of 2352 animals moved, 209 succumbed to E.I. — a mortality rate of 8.9%.

In a preceding paper on the symptomatology of geeldikkop we have stressed the probable rôle of an infectious agent similar to bluetongue in precipitating the acute syndrome. The symptoms of the infection precede those of geeldikkop by about two weeks. One of the outstanding

symptoms in early acute cases of geeldikkop is an extremely severe gastrointestinal stasis identical to that seen in these cases of E.I. The infectious condition is of a very mild nature and is not noticed by the farmer, but its presence is readily detected by chemical pathology and haematological studies[7]. We cannot rule out the possibility that this may be the case with E.I. as well. We have not had the opportunity of studying enough cases of E.I. at the time of appearance of the acute symptoms, as we have had in geeldikkop. Climatic, seasonal and circumstantial evidence all support the theory of an arthropod-borne precipitating agent as in the case of the latter syndrome. Should this be the case, it would explain many of the early spring and summer outbreaks of E.I. more satisfactorily than can be done on grounds of digestive disturbances. In this respect Belonje's description of a particularly virulent outbreak of Wesselsbron disease in the Middelburg District of the Cape Province is most significant. His subacute cases suffered, "clinically at least", from "a haemolytic crisis and a haematogenous jaundice"; autopsies bore the unmistakable imprint of E.I. Sudden outbreaks of infectious diseases like bluetongue and enterotoxaemia are often not recognised, because the dramatic symptoms of acute E.I. may often dominate the disease picture. Severe stress of this nature will undoubtedly precipitate the acute syndrome in asymptomatic cases of the basic intoxication.

The importance of intercurrent disease problems in a flock prone to E.I. cannot be emphasized too strongly. Any condition which lowers the resistance of an animal will increase not only the probability of an acute haemolytic attack but will also in most cases ensure a fatal termination. The most potent factors in this regard appear to be verminosis especially when bloodsucking worms are involved, bluetongue, enterotoxaemia and ophthalmia with all its sequelae. The latter disease is widespread throughout the Karoo areas.

Economic Importance

Annual losses amongst the sheep population due to E.I. have never been accurately computed. When one considers all the various aspects of the epozootiology of the disease such a task becomes formidable if not impossible. Suffice it to say that the losses are tremendous. The reader is referred to the data presented in Table 1, where a mortality figure on 30 farms only in the Fraserburg and Sutherland districts during the outbreak of the summer of 1957/1958 is indicated as 1972. Subsequent to this investigation we received a report from the stock-inspector at Sutherland of a further 560 deaths on 12 farms in this area up to the middle of January, 1958, and by then the outbreak was by no means over. In a letter to the Director of Soil Conservation, Department of Agriculture, Grootfontein Agricultural College, the Chairman of the Fraserburg Agricultural Union stated categorically that a round total of 15,000 sheep had succumbed to the disease during the summer of 1957/1958. We see no reason to doubt this figure.

We have in the various appendices attached to this paper attempted to convey some idea of the mortality due to E.I. following stock movements and various other normal activities on the farms in the affected areas. It is deaths of this nature which make it virtually impossible to assess the total annual losses caused by the syndrome. Furthermore, many sick or dead sheep are never noticed by their shepherds in the mountainous farms and fall prey to predators. There is a natural tendency on the part of farmers to ascribe deaths due to pregnancy toxaemia, enterotoxaemia and hydrocyanic acid poisoning, to E.I. when large scale outbreaks are present in any particular district. On the other hand, deaths from those instances of the disease where icterus is negligible, but where anaemia and renal lesions are prominent signs, are often passed off as cases of enterotoxaemia.

Infinitely more serious is the fact that a large sheep population estimated at 8 million, is subjected to a high degree of risk, how high no one knows as yet, and must be regarded as E.I. prone. The seemingly simple solution of the problem, namely proper pasture and sheep management, will involve economic and sociological measures of herculean magnitude.

Appendix 1:

SOME DETAILS OF FARMS IN WHICH THE INCIDENCE OF ENZOOTIC ICTERUS IS NEGLIGIBLE

(a) *Klawervlei, Beaufort West*: 54,000 morgen situated in Steenkampsberg Mountain Range. Altitude varies on different parts of the farm from 4000-6500 ft. above sea level. Rainfall 8-10" per annum. 200 morgen under irrigation from a large dam in the catchment area of the mountains. Artificial pastures include oats, cocksfoot, fescue, *Bromus* and *Phalaris* types. Chaffed maize stalks and *Sorghum* sp. are given with molasses as additional supplements in times of drought. 10,000 sheep

maintained. Stocking rate: 1 sheep per 4.5 morgen. Strict grazing rotation and pasture management practised. No mineral supplementation. Regular inoculation and dosing programmes. 10-15 cases of enzootic icterus occur yearly.

(b) *Celeryfontein, Fraserburg*: 16,000 morgen situated on the broken plains south west of Fraserburg. Sand flats broken by numerous sandstone ridges and doloritic intrusions. Divided into 23 camps each with their own water supply. Strict grazing rotation practised. Wide variety of karoo bushes present. Supplements during times of drought include dry and green lucerne, wheat or oats straw and groundnut hay. Straw is fed together with molasses and salt. Dosing, dipping and inoculations are not regular practices. Size of flock varies annually between 2000-4500. Owner raises sheep for slaughter and shearing purposes. Stocking rate: 1 sheep per 3.6-8 morgen. Few cases have occurred amongst sheep bred and raised on the farm. The only pregnant ewe from a group of sheep moved by rail to Onderstepoort (800 miles) developed E.I. A large number of cases have occurred amongst sheep purchased from other farms in the area.

APPENDIX 2:

SOME DETAILS OF FARMS ON WHICH THE DISEASE IS ESTABLISHED AND SOME RELEVANT CASE HISTORIES.

(a) *Klipfontein, Fraserburg*: 14,000 morgen of which 10 morgen are under irrigation from a dam in the mountain catchment areas of the farm. Lucerne and barley are grown in small quantities. Topography largely sandstone and dolerite ridges. Dominant bush types are *Nestlera, Euryops, Pteronia, Chrysocoma* and *Eriocephalus* spp. 7000 sheep and 35 small antelope kept. Stocking rate: 1 sheep per 2 morgen. Dicalcium phosphate, Sulphur and Molasses given as supplements. No rotational grazing or farm planning practised. Veld severely overgrazed. Post natal lamb mortality is about 10% mainly due to tapeworm infestation. Lambing is attended with a 20% dystokia rate, due mainly to oversized foetuses. Water is scarce and boreholes are deep (100-180 ft.). Enzootic icterus occurs annually from September to November. Losses are heavy but vary from season to season. In Sept. 1959 the farmer sent 350 sheep by train to Ladismith, Natal. 150 died within a week of arrival from E.I. Numerous deaths occur annually from Jaagsiekte and purulent panophthalmia. Total deaths in the flock from all causes amounted to 800 in 1959.

(b) *Grootfontein, Fraserburg*: 8,400 morgen consisting mainly of Sandstone hills and ridges, on which 2200 sheep run. The owner shears in July-October. Lambing occurs from August onwards. In 1960 E.I. started at the end of August amongst ewes with lambs. In November wethers were affected. Most cases were in adult sheep in weak condition. 25 animals were lost from Aug.-Nov. 1960. Veld was severely drought stricken.

(c) *Avondsrus, Fraserburg*: 1416 morgen, situated in the mountains 5000 ft. above sea level. Summer rainfall 6", Winter 3". The farm consists largely of sandstone and shales of the lower Beaufort Series, with numerous dolerite intrusions in the form of dykes and sills. The surface of the hillsides are covered with numerous red brown sandstone blocks characteristic of severe temperature fluctuations and wind erosion. Top soil is poor and scarce due to the latter factor. The farm was heavily overgrazed in 1958, obvious from the lack of annual self sowing weeds, the abundance of heavily grazed inferior and unpalatable types e.g. *Nestlera prostrata, Pteronia tricephala, Euryops spp.* etc. Grass was almost completely absent except for some *Danthonia purpurea, Aristida* and *Sporobolus* spp. Evidence of invasion by *Elytropappus rhinocerotis* was present. Lambing percentage is around 70%.

Mortality on this farm from E.I. has been very severe and it has been the focal point of many investigations. Sporadic cases were known before 1935. No cases occurred again until 1945 when the disease reappeared and the incidence climbed steadily. In 1958 306 animals were lost; in 1959, and 1960 80 sheep lost annually. In the autumn of 1960 the outbreak ended following 1.20" of rain. Further mortality commenced again in June of the same year, when 5 lactating ewes were lost. In November a group of fat wethers were moved to another camp over a distance of 3 miles. 15 died within the week following this movement. Conditions have improved following introduction of planned grazing systems and drastic reduction in the number of small stock.

(d) *Albertsgraf, Fraserburg*: 5709 morgen situated in the mountains, 5000 ft. above sea level. Veld conditions and topography much as for Avondrus. In 1960, 1422 sheep were running on the farm of which 150 succumbed to E.I. Deaths started in October ten days after inoculation with enterotoxaemia vaccine. In 1959, there were 235 deaths from E.I.

See also appendix 4, case (b).

(e) *Kleinplaats, Aberdeen*: 1245 morgen situated at 3000-4800 ft. above sea level on the north-northeastern and southernly slopes of the Kamdebo mountain range. 4½ morgen are usually planted with oats. Water is scarce and boreholes are deep (190-360 ft.). No system of veld management is practised at all. Rainfall varies from 10-12" mainly as heavy storms from October to March. The veld is in an extremely poor condition. 470 sheep and goats are maintained. Wind and water erosion is evident wherever one turns. Dominant plants include *Nestlera, Chrysocoma* and *Eriocephalus* spp. Less common are *Cadaba juncea, Euphorbia mauretanica, Zisyphus, Buscia* and *Mesembryanthemum* species. Grass cover is sadly lacking. Sporadic deaths due to E.I. occurred over the last 25 years. Severest mortality occurred from 1961-1963. During this period one of the authors (J.M.M.B.) has personally seen 44 cases and removed many of those for biochemical studies.

Bluetongue is also prevalent on the farm. The lambing percentage on this farm varies from 3% in bad years to 55% in good years. Kidding % in Angora goats is no more than 50%. Post natal lamb mortality is 5%.

(d) *Witteklip, Murraysburg*: 3056 morgen, 5,450 feet above sea level on mountain headlands. Rainfall varies from 8-20 inches annually. Good rains occur in January and February, from whence very dry conditions set in until June to October when more rains fall. The farm consists largely of yellow shale and sandstone ridges with dolerite intrusions. When first seen by one of the authors (H.P. de B.) the farm, and one camp in particular where E.I. was severe, was heavily overgrazed with *Nestlera prostrata* and *Pteronia glomerata* dominating the vegetation. E.I. has been known on the farm since 1921. Mortality was high in dry periods especially in spring and early summer and usually stopped 1-2 weeks after the first heavy rains. In 1947 the outbreak studied by one of us (H.P. de B.) was associated with an exceptionally dry season and very variable warm to cold weather. 60 animals succumbed to E.I. and only 4-6 tooth ewes were involved. Lambing time on this farm was during August and the lambing % varied from 15-50% with an average of 20%.

(e) *Middelwater, Hannover*: 2351 morgen situated on the karoo plains typical of this area. Divided into two camps one of which carried 2,250 sheep and the other 1600 sheep at the time of investigation. (H.P. de B.). As a result both camps were severely overgrazed with inferior bush types like *Chrysocoma* and *Eriocephalus* predominating. The disease has been known for a long time on this farm. It seems to have been handed down as a family farming tradition since the present owners claim that seventy years ago their father lost 2,500 sheep out of 3,000 from E.I. on a farm at *Willowmore*. (The size of this farm was fortunately not recorded!). Heavy mortality first appeared on Middelwater in about 1941 amongst rams. Since then losses appeared to be sporadic until 1948 when 18 cases occurred. This outbreak was preceded by a severe drought. Previous outbreaks generally stopped after heavy rains had fallen. Pregnancy toxaemia was a common occurrence in pregnant ewes.

(f) *Hebron, Loxton*: This farm was first visited by one of us (J.M.M.B.) in the summer of 1959 during the course of Geeldikkop investigations. The farm is 4,400 morgen in size and consists of broken veld and low sandstone hills and ridges covered with loose shale. The shallow red soil was at one time thought to be diamondiferous and numerous diggings are still to be seen. The farmer was considered to be one of the leading farmers in the district, but at the time of our visit was in desperate strains owing to two years of continuous and extremely severe drought. The veld was in an extremely poor condition; 1500 sheep were on the farm at that time. At least 80% of the plants in the main camp of the farm were *Nestlera prostrata*, the remainder included *Tribulus terrestris* and *Eriocephalus, Lycium, Chrysocoma* and *Pentzia* spp. December of 1959 was an extremely dry month on this farm and was intensely hot. 0.8 inches of rain fell in two showers around about the middle of the month. Large numbers of lactating ewes and lambs commenced dying about three days later. All the cases examined, even those in a number of three month old lambs, were classical acute cases of E.I. Despite all our

attempts and advice the disease continued throughout the rest of the month, about 100 sheep being lost. During the last week of December and the first week of January, the symptom pattern changed completely to that of Geeldikkop. This syndrome supplanted E.I. entirely for the rest of the latter month. We were unable to assess the ravages of these disease syndromes accurately during this season on the farm. The author (J.M.M.B.) conducted biochemical studies on twenty classical geeldikkop cases some of which were stud rams *in extremis*. The farmer lost most of his breeding stock and sold the farm shortly afterwards.

The main interest of this outbreak is the close association of the two syndromes. The sudden change of diet following germination of quick growing annual plants after the December rains and the marked fluctuations in temperature at this time undoubtedly precipitated enzootic icterus in a large number of sheep verging on a haemolytic crisis. Geeldikkop appeared about three weeks later and bluetongue-like lesions were a prominent feature of the symptomatology at this time[1 7].

(g) *Harmsfontein, Middelburg, C.P.*: This account is taken from a report by T. E. Skinner of Grootfontein College of Agriculture, dated 19/11/59. The outbreak occurred in October of 1959 amongst a batch of old ewes which had been dosed with phenothiazine in August and then moved to a camp consisting mainly of sandstone and dolerite ridges. Mortality commenced 3 weeks later and 35 sheep died of typical E.I. The farm had been heavily grazed but not overgrazed.

Appendix 3:

CASE REPORTS OF THE DISEASE PRECIPITATED BY VARIOUS FORMS OF STRESS.

(a) Report by Mr. T. E. Skinner, Grootfontein College of Agriculture, of deaths occurring on a farm in Richmond. Sept./Oct. 1958. Numerous wethers died after shearing in a flock of 500, run on 1500 morgen. The farm is mountainous with sandstone soils and was heavily overgrazed. Dominant plants were *Chrysocoma tenuifolia, Nestlera prostrata* and *Pteronia glomerata*. Hardly any grass was to be seen anywhere.

(b) *Wolwekraal, Britstown*: 50 sheep died from E.I. out of a flock of 210 which had been inoculated with enterotoxaemia vaccine. Deaths started 21 days after inoculation. E.I. confirmed.

(c) *Liebecksfontein, Richmond*: 506 wethers brought down from the mountains on the farm for shearing. 15 died within 16 days following this operation. E.I. confirmed.

(d) *Wolwefontein, Victoria West*: 23 wethers died from E.I. out of a flock of 150 whose grazing had suddenly been changed from lucerne pastures to Karoo veld. Shearing followed this change of diet. E.I. confirmed.

(e) *Farmer, B., P.O. van Wyk's Vlei*: Report received from Stock Inspector of large numbers of animals dying from E.I. one week after dosing Onderstepoort Nodular Worm Remedy.

Appendix 4:

SOME OUTBREAKS OF ENZOOTIC ICTERUS PRECIPITATED BY LARGE SCALE MOVEMENTS OF ANIMALS.

(a) *Case of Louw and Frick*: Litigation involving purchase of a group of animals out of a flock of 800 sheep in Sutherland. Purchased animals transported 75 miles by freight lorry to Matjesfontein and then 100 miles by rail to Worcester. Numerous sheep dead on arrival. Numerous carcases condemned at abattoirs. Confirmed by State Veterinarians.

(b) *Outbreak at Hillside, Aliwal North*: 352 Karakul ewes were purchased at Albertsgraf, Fraserburg. Transported 120 miles by railbus and then 350 miles by train to Aliwal North. Entire journey covered 4 days. No food was given on the train. The animals were then driven 25 miles by road. 42 deaths occurred from E.I. over a period of 6 weeks amongst these animals. Numerous flock movements took place on the farm during this time. These Karakuls were particularly nervous and unmanageable sheep. Only one of the ewes was pregnant.

(c) *Spes bona Outbreak, Aliwal North*: Forty animals, from amongst a large group purchased in Carnarvon died from E.I. shortly after arrival in Aliwal North. Confirmed E.I.

(d) *Vetspruit, Greytown case*: 30 sheep died shortly after arrival from E.I. amongst a group of 140 bought in Fraserburg and sent by rail to Greytown, Natal.

(e) *Outbreak at Platvlei, Wolseley, Nov.* 1958: 570 sheep were brought in by lorry from Sutherland on 15/11/58. Numerous deaths amongst adult sheep started on 4/12/58 and continued during December. E.I. confirmed.

(f) *Wexford, Kei road*: 100 sheep out of a large flock purchased in Colesberg died 3-6 months after arrival in Kei Road from E.I. Confirmed by investigations.

(g) *Outbreak at Nuwejaarsfontein, Britstown*: 30 pregnant ewes transported over a distance of 15 miles in a trailer. 5 died from E.I. during the following 3 days. Stock Inspector's report confirmed by histological examination of specimens.

(h) *Outbreaks at Golden Gate, Clarens, O.F.S.*: Oct./Nov. 1964. Part of a mass sheep movement from drought-stricken Calvinia district. 32 adult sheep out of a group of 1050 from Middelpos, Calvinia died from E.I. within a month of reaching Clarens. The entire journey involved 8 days on the train and herding for 3 days over a distance of 26 miles. Outbreak investigated by local veterinarians and confirmed by the authors.

(i) *Elandslaagte cases, Platberg, Natal*: Numerous deaths in 1958 amongst a group of adult sheep imported from Carnarvon. Investigated by local veterinarian. Confirmed by the authors.

(j) *Correspondence from State Veterinarian, Kroonstad, O.F.S.*: 100 sheep died out of a group of 800 purchased from Beaufort West and Koffiefontein. The cases were typical of E.I. Average age of affected sheep: 6-12 months. This is one of the rare reports of E.I. amongst young sheep.

(k) *Correspondence from a farmer, M., in Stutterheim*: 25 sheep lost from E.I. out of a group purchased in Prieska. This report was not confirmed. Prieska is a bad Geeldikkop area, but as yet we have not encountered E.I. there.

(l) *Correspondence from a farmer, V.R. in Pokwani, Cape Province*: Numerous deaths amongst sheep bought in Beaufort West and Britstown. Deaths started one week after arrival of animals at Pokwani. E.I. diagnosed in material submitted for histological examination.

APPENDIX 5:

LARGE SCALE MOVEMENTS OF SHEEP FROM KAROO AREAS IN WHICH THE DISEASE IS NOT ENZOOTIC WHICH HAVE BEEN INVESTIGATED OR FOLLOWED UP BY THE AUTHORS.

(a) 11,000 Karakuls were brought to a farm in Aliwal North adjoining that mentioned in case (b) Appendix 4, during the course of 1945-1947. All the animals were bought from farms in the Strydenburg and Prieska areas. All stock movements involved a four day train journey without food and water. No animals were lost from E.I.

(b) 30,000 sheep were moved from Pofadder (Upington district) to Namaqualand in 1959. They were herded by road over distances of 150-200 miles. The movement was watched closely by State Veterinarian, Calvinia, and his Stock Inspectors. 600 animals died of injuries, exhaustion and poisoning by *Cotyledon* species. 11 cases of Geeldikkop were noted. No animals showed signs of E.I. and none died from this disease.

TABLE 4.—MONTHLY VARIATIONS IN THE RAINFALL RECORDED AT HONDEFONTEIN METEOROLOGICAL POST. (LATITUDE 32° 13′, LONGITUDE. 21° 22′) DURING THE SPRING AND SUMMER OF 1957—1958 (GIVEN IN MILLIMETRES)

Month	July	August	September	October	November	December	January	February
Rainfall.....	26	0	29	0	0	33	0	8

ACKNOWLEDGEMENTS.

The, Chief, Veterinary Research Institute, Onderstepoort, is thanked for permission to publish this paper. We have in our references acknowledged the source of a good deal of the material taken from unpublished reports. We owe however a debt of gratitude to many State Veterianrians whose names do not appear there. In particular we are indebted to Drs. C. W. A. Belonje, D. E. Truter, C. J. Coetzee, F. de St. J. van der Riet, K. M. van Heerden, C. Wilkins, M. van Tonder, L. Stonier and J. A. Badenhorst. Practitioners L. G. Steel and D. J. Thornton have sent us valuable material and information. We would like to thank The Director, Karoo region, Dr. W. J. Hugo and his staff for their willing and considerable help with botanical surveys. In this regard we remember with affection the valuable work of Dr. M. G. A. Henrici in the early days of this research. We have drawn extensively upon notes and material made available to us by Drs. G. van de W. de Kock and K. C. A. Schulz and Messrs. G. J. Truter and G. C. Roets.

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CORRECTION

In the article by S. M. Hirst "Immobilisation of the Transvaal Giraffe using an oripavine derivative" vol. 37 No. 1 page 88:- The heading to the tenth column should read "Nalorphine reaction time, secs.".

EDITOR.

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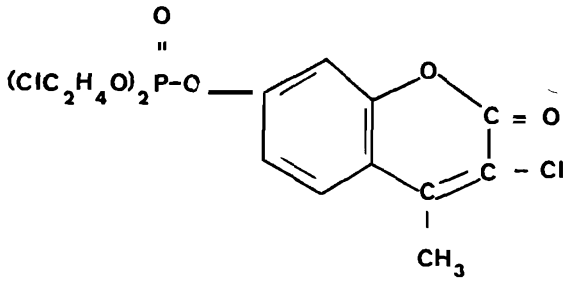

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THE USE OF AN AQUEOUS SOLUTION OF VOLATILE FATTY ACIDS AND AMMONIA AS A REPLACEMENT FOR THE DRINKING WATER OF FATTENING CATTLE IN A NON-PROTEIN NITROGEN FEEDING REGIME

D. K. SHONE AND K. M. BUCHANAN.
P.O. Box 7824. Johannesburg.

INTRODUCTION

The end stream of the Fisher-Tropsch process for the synthesis of petrol and other hydrocarbons from coal by Sasol (the South African oil from coal project) is an aqueous solution containing up to one per cent of short chain fatty acids — acetic, propionic, butyric and valeric. These acids are treated with sodium carbonate, concentrated to a 50 per cent slurry by evaporation and incinerated.

Shone and Buchanan (1965) investigated the use of the dried sodium salts of this material and found that the inclusion of these salts in the feed of sheep had a marked depressive effect upon the liveweight gain. This effect was considered to be due to the quantities of free sodium released in the body when the salts were metabolized.

The work reported here was undertaken to examine the possibility of using a combination of these fatty acids and ammonia as a replacement for the drinking water of fattening cattle in a non-protein nitrogen feeding regime.

MATERIALS AND METHODS

The volatile fatty acid and ammonia solution.

The aqueous solution of volatile fatty acids was treated at Sasol with gaseous ammonia to give 0.2 per cent nitrogen (N). The sodium content was determined and sufficient hydrochloric acid added to provide a similar quantity of chlorine calculated on a gm/mols per litre basis.

The pH of the solution was adjusted to between 5.5 and 6.0. A preliminary palatability trial established that this pH was necessary for optimal intake of the solution.

The treated solution was transported from Sasol to the Research Farm at Kempton Park by road tanker and piped into cement-asbestos tanks treated with an acid resistant paint. Each batch of solution was added to half the volume of the previous batch in the tanks to minimize variations between batches.

The proportions of the acids in the solution has been given by Shone and Buchanan (1965). The composition of the batches of solution used in this trial is presented in Table 1.

The solution was presented to the cattle in 20 gallon polythelene lined containers. The daily consumption of the solution and water was recorded.

Feed:

The composition of the two feeds is given in Table II. It will be noted that the only natural protein present in the feed of the group of cattle receiving the V.F.A./ammonia solution is that present in the maize.

All the feed ingredients were purchased as single consignments and the maize, cob and sheath meal was milled in a hammer mill fitted with a three-eighth inch screen. The urea was in the form of prills.

A weighed quantity of feed was added to the troughs daily and at the end of each seven-day period, the feed remaining in the trough was weighed back.

No feed, other than maize, cob and sheath meal with additives was available to the cattle.

Experimental Animals:

Eighteen Afrikander/Sussex cross-bred steers from a single herd aged between 12 and 14 months were used in the trial.

The steers were randomly allocated to pens on a liveweight basis and the pens randomly allocated to the two treatments.

Pen No. 1 V.F.A. and ammonia feeding regime 5 head
Pen No. 2 V.F.A. and ammonia feeding regime 4 head
Pen No. 3 Natural protein feeding regime 5 head
Pen No. 4 Natural protein feeding regime 4 head

Liveweight Records:

The liveweight of the steers at the start and at the end of the trial were taken as the mean of 3 weights taken at 24 hour intervals. The steers were not fasted. During the trial the liveweights were recorded at weekly intervals.

Trial Period:

The trial covered a period of 100 days including the period of adaptation. During the first 14 days the amount of feed available was restricted, after which the feed was available *ad lib* as was the V.F.A./ammonia solution and drinking water. At the end of the 100 day period all steers were slaughtered.

Results

The details of weight gains, feed, water and V.F.A./ammonia solution consumptions and the slaughter data are presented in Tables III, IV, V and VI.

In order to eliminate the differences in total liveweight gains associated with greater feed-intakes, an efficiency factor which is included in Table V has been calculated. The efficiency factor is obtained by dividing the total liveweight gain by the feed conversion factor (pounds feed per pound liveweight gain). The efficiency factors of 37.24 and 37.3 for the two groups showed no differences.

It will be noted from Table III that the 5 steers in Pen 1 were slower to adapt to the experimental feed than the cattle in the other pens. The average quantity of feed consumed per head per day by these cattle during the second week, was 10.6 lbs., while the steers in Pens 2, 3 and 4 consumed an average of 17.7, 16.9 and 16.9 pounds per head per day respectively. This delay in adaptation was reflected in the weight gains. The gains made by these steers never caught up with

Table II
The composition of the feeds

	Natural Protein Group feed	Volatile Fatty Acid/ammonia Group feed.
Maize plus cob sheath meal	86.5 per cent	95.5 per cent
Cotton seed cake	3.0 per cent	—
Fish meal	3.0 per cent	—
Blood meal	3.0 per cent	—
Urea	1.0 per cent	1.0 per cent
Mineral supplements	3.5 per cent	3.5 per cent
Vitamin A, international units per ton	6.5 million	6.5 million

Mineral supplements added per 100 lbs. feed.

	Natural Protein feed Group.	Volatile Fatty Acid and ammonia feed Group.
Monosodium phosphate	485 gm	485 gm
Potassium chloride	375 gm	375 gm
Sodium sulphate	170 gm	170 gm
Copper sulphate	1.25 gm	1.25 gm
Cobalt sulphate	1.25 gm	1.25 gm
Zinc carbonate	2 gm	2 gm
Sodium chloride	220 gm	110 gm
Limestone	135 gm	135 gm
Kaolin as filler	200 gm	310 gm

Table 1.—The composition of the volatile fatty acid solution.

Batch No.	Volume in gallons.	pH.	Na + gm. mols per litre.	Cl — gm mols per litre.	Fatty acids gm. mols per cent.	Nitrogen w/w per cent.
1	875	5.68	0.0209	0.0356	0.129	0.21
2	2360	5.75	0.0482	0.0496	0.119	0.18
3	1000	5.80	0.022	0.0420	0.155	0.2
4	2500	5.75	0.022	0.028	0.168	0.2
5	2100	5.75	0.0157	0.57	0.1445	0.2
6	1600	5.7	0.018	0.18	0.148	0.2

the steers in the other 3 pens. The reason for the delayed adaptation by this pen of steers could not be determined.

The amount of the V.F.A./ammonia solution drunk was consistently less than the amount of water drunk by the steers on the natural protein feed. The V.F.A./ammonia solution had a strong taste and smell from the valeric acid present and this may be the reason for the lower consumption of this solution. The difference in the volume of the V.F.A./ammonia solution drunk, to that of water drunk, was twice as great during the first 2 weeks of the trial as it was during the remaining period. At the start of the trial there was a complete replacement of the water in Pens 1 and 2 with the V.F.A./ammonia solution.

The cost of the feed and V.F.A./ammonia solution amounted to 11.909 cents per pound liveweight gained for Pens 1 and 2, while the cost of the natural protein feed was 13.721 cents per pound liveweight gained for Pens 3 and 4.

All the steers were graded as super at slaughter and sold at a price of R17.00 per 100 pounds cold dressed weight (C.D.W.) The guarantee floor price is R18.00 per 100 pounds C.D.W.

TABLE IV.—WEIGHTS OF STEERS AT START AND FINISH OF THE TRIAL AND TOTAL LIVEWEIGHT GAIN.

Pen No	Steer No.	Starting weight.	Finishing weight.	Gain in weight.
1	78*	673	961	288
1	86	576	815	239
V.F.A./ammonia	88	711	938	227
Group	89	588	768	179
	94	611	922	311
	80*	678	932	254
2	82	627	862	235
V.F.A./ammonia	85	674	957	283
Group	93	653	915	262
	77	729	1072	343
3	84	606	809	203
Natural protein	90	590	915	325
Group	91	676	957	281
	81	676	942	266
4	83	669	904	235
Natural	87	628	960	332
Protein	92*	570	709	138
Group	95	618	964	346

*These animals developed laminitis.

Seven per cent was added to the cost of the steers (10 cents per lb. liveweight) and the feed to cover other expenses, resulting in a nett loss of R5:52 per steer for the V.F.A./ammonia feeding regime and R8.20 for the natural protein feeding regime. At a price of R20.00 per 100 lbs. C.D.W. a profit of R3.60 per head would have been realized with the V.F.A./ammonia feeding regime. Basic feed costs in this trial were higher than would be the case if home grown feeds were used. It is estimated that feed costs were some 12% higher than those expected of commercial feeding units.

Three cases of laminitis occurred during the trial in steers 78, 80 and 92. In each case the laminitis developed 6 weeks after the commencement of the trial. The laminitis may have had an adverse effect upon the weight gains of steer 92, but steer 89 which did not suffer from laminitis was also a poor doer.

DISCUSSION

The contribution of the volatile fatty acids to the energy status of the feed as measured by liveweight gains, was negligible. The only value of these acids was in their role as carrier for the ammonia. The saving in costs achieved by the volatile fatty acid/ammonia solution over the natural protein feed would have been greater had it not been necessary to allocate a value to the sodium present and to incur further costs by the addition of the hydrochloric acid.

No significant differences resulted from the use of the volatile fatty acid and ammonia as compared to the natural protein feed with this high energy diet. The use of non-protein nitrogen in such a diet is therefore a practical proposition. It is probable that urea could successfully replace the volatile fatty acid and ammonia combination as a source of nitrogen and at no greater cost.

The feed conversion of 6.9 and 7.4 lbs. feed per pound of liveweight gained compares favourably with the range of 8.5 and 9.5 to 1 reported for California feedlots (Hopkin and Kramer, 1965). The average daily liveweight gains of 2.59 and 2.74 also compare favourably with the average of 2.44 for English breeds and crosses in California feedlots (Hopkin and Kramer, 1965).

The number of cattle used in this trial was small but the results are sufficiently encouraging to believe that a trial on a larger scale with a similar type of animal would give equally good results. Provided that reliable data of this type is available, it should be possible to plan a commercially successful feedlot in South Africa using feeds of the type used in this work. The costs of the basic ingredients (maize, urea, fishmeal) in South Africa are set well in advance and the only

variable factor is the price of the finished carcass, although a minimum price is guaranteed by the Meat Control Board. For the successful operation of such a feedlot, cattle can only be bought on a liveweight basis. Many farmers do not own cattle scales, and in such cases a shrinkage factor can be operated to allow for in transit weight losses. The minimum price paid will be geared to the minimum guaranteed floor price but an upward adjustment in the price paid to the farmer can be made if the price obtained is higher than the quaranteed floor price.

TABLE III.—AVERAGE DAILY QUANTITY OF FEED, WATER AND SOLUTION CONSUMED PER HEAD PER DAY AND PROGRESSIVE LIVEWEIGHT GAIN.

Week ending	Volatile Fatty Acid and Ammonia Group.						Natural protein Group.					
	Pen 1.			Pen 2.			Pen 3.			Pen 4.		
	Feed lbs.	Solution gallons	Weight gain lbs.	Feed lbs.	Solution gallons.	Weight gain lbs.	Feed lbs.	Solution gallons.	Weight gain lbs.	Feed lbs.	Solution gallons.	Weight gain lbs.
26.7.65.....	10.5	4.1	16.2	10.5	4.4	33.6	9.0	5.2	17.9	10.5	4.9	8.4
2.8.65.....	10.6	5.0	23.6	17.7	5.4	45.1	16.9	5.3	20.9	16.9	5.6	52.2
9.8.65.....	17.0	5.7	49.8	19.1	5.0	87.8	19.1	5.2	70.4	18.3	6.3	70.2
16.8.65.....	17.2	5.9	77.0	18.4	5.3	109.6	17.7	5.6	83.7	19.2	5.8	82.6
23.8.65.....	19.4	6.9	92.0	20.7	6.4	116.6	18.8	5.8	103.7	20.6	6.7	101.3
30.8.65.....	19.2	6.3	113.8	18.6	5.5	129.6	19.0	5.6	124.9	20.3	6.7	132.6
6.9.65.....	17.2	6.5	121.4	22.0	6.0	137.4	21.9	5.6	152.4	22.0	6.0	150.8
13.9.65.....	19.8	7.4	154.0	17.0	5.6	157.6	23.2	6.7	164.2	22.9	7.6	170.6
20.9.65.....	19.0	6.1	158.8	19.1	5.6	176.6	24.5	7.0	198.2	23.2	7.4	179.6
27.9.65.....	19.7	6.3	189.4	22.8	6.0	201.6	23.8	6.2	227.9	22.2	6.7	210.2
4.10.65.....	22.4	6.4	189.2	22.2	5.2	200.4	24.1	6.5	215.3	22.2	6.8	213.4
11.10.65.....	20.6	6.1	216.0	24.8	5.9	234.4	27.0	6.2	258.4	21.2	6.4	235.8
18.10.65.....	20.8	7.0	225.6	23.1	5.7	246.1	23.5	7.0	262.9	22.4	6.8	241.6
25.10.65.....	20.1	6.2	235.6	20.9	5.5	255.4	23.9	6.6	271.7	21.9	6.6	257.4
28.10.65.....			259.3			259.1			288.0			

TABLE V.—AVERAGE DAILY WEIGHT GAINS, AVERAGE DAILY FEED AND WATER CONSUMPTION, FEED CONVERSION AND EFFICIENCY FACTOR.

	V.F.A./Ammonia Group.			Natural Protein Group.		
	1.	2.	1 & 2.	3.	4.	3 & 4.
Average daily weight gain.....	2.59	2.59	2.59	2.88	2.63	2.74
Average daily feed eaten.....	17.8	19.62	18.61	20.75	20.11	20.4
Average daily water drunk.....	6.02	5.21	5.68	6.26	6.43	6.35
Feed conversion factor.....	6.8	7.1	6.9	7.2	7.6	7.4
Efficiency factor*.....	38.0	36.4	37.2	40.0	34.6	37.3

*Efficiency factor is obtained by dividing total weight gain by the feed conversion factor.

TABLE VI.—THE SLAUGHTER WEIGHTS, DRESSING PERCENTAGES, FAT AND MARBLING SCORES.

	V.F.A. plus Ammonia group.			Natural Protein group.		
Pen No.	1.	2.	1 & 2	3.	4.	3 & 4.
Average dressed weight.....	404	492	476	513	490	500
Average dressing percentage ...	52.6	53.7	53.0	54.6	54.7	54.6
Average fat score.....			6.77			6.66
Average marbling score.....			2.33			2.11
Iodine number of pooled brisket fat.....			55.5			55.9
Grading.....			All graded super			

ACKONWLEDGEMENT

We wish to express our appreciation to the Sasol Marketing Company Limited, for making available the volatile fatty acid solution used in this trial, and to Mr. P. Alderton for his able assistance.

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BOOK REVIEW

Wrights Veterinary Anaesthesia and Analgesia by L. W. Hall (M.A. Ph.D., B.Sc. M.R.C.V.S.) 1966 6th Edition 488 pp. 51 illustrations. Price in U.K. 50/-. Published by Baillière Tindall & Cassel Ltd.

Wrights book on anaesthesia has always been accepted as a standard textbook and Hall has maintained the same standard of contents.

The scope of the new edition has been widened by the inclusion of more pharmacological and physiological matter. This in turn has called for the necessity of a greater number of references and as the chapters on local, regional and spinal analgesia have been rewritten and brought up to date, and new drugs such as methohexitone sodium and methoxyflurane have received attention, the increase of some 100 pages over the previous edition is understandable.

The book now is not only a textbook for students, lecturers and practitioners but can be regarded as a book of reference for those veterinarians who wish to specialise in anaesthesia.

Hall quite correctly points out that anaesthesia is still an art; and although experience is a valuable asset in the mastering of this art it can be expensive in animal life and money to the individual. He therefore emphasizes the dangers and pitfalls likely to be encountered; and describes in detail the techniques which he has found to be the most efficient. For this reason most of the material relates to techniques of those drugs commonly used and not to the complete range of drugs available.

As the comfort, indeed at times the success of the operation, so often depends on the perfection of the anaesthesia, it is difficult to imagine any veterinarian not arming himself with the wealth of information and experience contained in this book.

— J. L. D.

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MELAMINE CRYSTALLURIA IN SHEEP

R. CLARK, Onderstepoort.

SUMMARY

Melamine was found capable of producing fatal uraemia due to crystalluria in sheep even when given in relatively small amounts (10g/day). For this reason it is not considered a safe non-protein nitrogen supplement.

INTRODUCTION

The value of melamine as a non-protein nitrogen supplement in rations for sheep has been tested by van der Merwe[1] and MacKenzie[2]. Both authors found the nitrogen could be utilized by the ruminal flora but MacKenzie reported five deaths among sheep which had been receiving melamine, but he had no way of establishing the cause of death.

Van der Merwe reported that a sheep dosed with 67 g melamine had shown "stress on the 3rd day and died on the 6th day" while another given 50 g had shown "stress on the 6th day and died on the 7th day". Autopsy of the second sheep had shown "inflammation and severe degeneration of the liver, kidneys, bladder and lungs. The kidneys were in the worst state and the bladder was full of blood". The cause of death was not stated. It was therefore decided to investigate the possible toxic effects of melamine.

METHODS

Merino wethers were used throughout. Those in Experiments 1 to 4 carried permanent ruminal fistulae which were used for dosing the melamine, the removal of ruminal contents for pH determinations and the recording of ruminal motility. Except in the case of Experiments 1 to 3 the experimental sheep were housed in metabolism cages and carried faeces bags. Twenty-four hour urine samples were collected.

Blood and urine examinations were carried out by standard methods as used in this laboratory.

RESULTS

Experiment 1.

A sheep weighing 46 kg was given 100 g melamine in a single dose.

The blood urea level rose progressively as shown in Table 1.

On the tenth day after dosing the animal stood with its back arched and showed complete anorexia and anuria. It was killed the next day. At autopsy the kidney tubules were found to be packed with crystals. Nephrosis and erosive abomasitis were also present.

Experiment 2.

A sheep weighing 37 kg was dosed with 50 g melamine on six consecutive days. On the fifth day it showed anorexia and a blood urea level of 340 mg %. The small amount of urine passed contained blood. The animal was found dead on the morning of the seventh day. Autopsy findings were crystals in the kidney tubules, nephrosis, haemorrhagic cystitis, abomasal ulcers and acute typhlitis.

Experiment 3.

A sheep weighing 49 kg was dosed with 25 g melamine on 18 consecutive days. No ill effects were observed until the 15th day when it went off its feed. The blood urea level was then only slightly elevated (70 mg %). On the 18th day the blood urea had risen to 260 mg % and the animal was found dead the following morning. Autopsy findings were as previously described, except that abomasal ulcers were not present.

Experiment 4.

Three sheep were each dosed with 10 g melamine per day. One died after 16 days and another after 31 days while the third was discharged apparently unaffected after 39 days. No ill effects, as judged by food and water intake and regular blood and urine examinations, were observed until a sudden onset of anorexia and anuria which appeared in both fatal cases three days before death.

The blood urea and creatinine levels then rose sharply, the terminal figures being 122 and 111 mg % for urea and 4.6 and 2.6 mg % for creati-

nine respectively. Autopsies on both sheep revealed crystals in the kidneys and severe oedema of the lungs.

TABLE 1.

Days after dosing	0	1	2	5	8	10	11
Blood Urea mg %	28	50	54	89	215	272	315

Experiment 5.

As it was now apparent that deaths from melamine were due to crystalluria, it was decided to test the effects of inducing greater urine concentration by reducing the water intake. In order to simulate natural conditions more closely, the melamine (7g/sheep/day) was offered mixed in 50 g of maize meal, and the daily intake recorded. Three groups of three sheep each were used. All groups received teff hay *ad lib*. Further treatments were as follows:- Group 1 received water *ad lib*. The sheep in groups 2 and 3 were offered an unlimited amount of water but only between 2 and 3 p.m. on alternate days. Group 3 was given maize meal but no melamine. The experiment ran for six weeks. The treatment for the animals in Group 1 (water *ad lib*) was maintained throughout but the sheep in groups 2 and 3 were reversed after three weeks. The figures in Table 2 are the daily averages throughout the experiment for each treatment.

All the sheep survived the experiment and at no time did any of them show excessively high blood urea figures.

Experiment 6.

In this experiment the water intake was limited to 600 ml per sheep per day and teff hay was offered *ad lib*. Three sheep were also offered a mixture of 7 g melamine mixed into 50 g maize meal daily. Three control sheep were given the maize meal alone. The experiment ran for seven days.

The control sheep took all the maize meal and consumed an average of 730 g teff hay each a day. The other group refused much of the maize meal melamine mixture. Calculated from the consumption of the mixture the average daily intake of melamine was 0.6, 2.2 and 6.3 g while the average daily consumption of teff per sheep was 640 g.

None of the sheep showed any ill effect from the treatment.

Other Observations:

The urine of sheep receiving melamine showed a heavy white deposit on the addition of picric acid. This reaction is given by dilute solutions of melamine and is a good presumptive test for melamine.

At most times the urines also showed a marked deposit of white crystals on cooling. Aggregates of crystals were seen hanging from the prepuce of sheep which were receiving higher doses of melamine. Crystals were collected from urine samples, washed and dissolved in 2 N.HCl. This solution gave an absorption peak at 235 mμ which corresponded to a reference solution and is characteristic of melamine.

Urine samples were tested periodically for S.G., pH and the presence of albumin (boiling test), sugar and blood. Except in one terminal case where blood was present, no abnormalities were found. The pH tended to be somewhat high (8.5-9.0). This might have been due to presence of melamine.

Periodic blood examinations also revealed no abnormalities other than terminal very marked rises in urea and creatinine in the fatal cases. There were no signs of liver damage at any stage as judged by levels of plasma bilirubin, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase. The bromsulphthalein clearance test applied to one sheep just prior to death showed complete clearance in 30 minutes.

The dosing of melamine also had no effect on the pH of the ruminal contents nor on ruminal motility.

TABLE 2

Gr	Water	Melamine Intake g.	Tell Intake g.	Water Intake l.	Urine Vol. ml.
1	*Ad lib*.....	6.3	800	1.81	613
2	Alternate Days.....	5.3	690	1.19	355
3	Alternate Days.....	nil	770	1.09	—

Discussion

The above results show that death following the administration of melamine is due to blockage of the kidney tubules by crystals with anuria and uraemia. This would appear to occur in an "all or none" manner. The excretion of melamine in the urine in those animals which did not develop anuria, appeared to have little effect on kidney function as judged by clinical urine examinations and blood urea levels. Crystalluric anuria could also explain the deaths reported by other authors. The autopsy findings reported by van der Merwe are compatible with such an assumption. The deaths reported by MacKenzie occurred over a period of 31 days after the termination of the experiment. One of our cases was killed for humane reasons 10 days after a single massive dose of melamine. Unfortunately, in this case, the animal was not in a metabolism cage and it is unknown when exactly anuria set in. Survival of up to 31 days as found by MacKenzie is unlikely if anuria were present at the end of melamine feeding but the earlier deaths may well have been from this cause.

The question arises as to whether the danger of crystalluria is of importance in the practical use of melamine as a nitrogen supplement. Van der Merwe had no ill effects from feeding 7 g per day for 8 weeks and considers it safe. On the other hand I had two deaths out of three when dosing 10 g per day. I failed to produce cases when 7 g per day was offered but the animals refused to take the full amount. MacKenzie also found that sheep were reluctant to take melamine containing supplements. This reaction would reduce the value of melamine as a feed additive even if it were entirely safe.

Gray and Clark[3] showed that biuret is also excreted as such in the urine when fed to sheep, but single doses of 275 g and 250 g to sheep have failed to produce kidney tubule blockage[4 5]. As stated above single doses of melamine as low as 50 g have proved fatal[1]. The danger of kidney blockage with biuret if present, would appear to be much less than with melamine. Despite the relatively large scale use of biuret over two years in South Africa, no cases of death from this cause have been reported.

Conclusion

In view of the danger of crystalluria, melamine would not appear to be a promising supplement to rations for sheep.

ACKNOWLEDGEMENTS

The melamine was kindly supplied by African Explosives and Chemical Industries Ltd. The Chief, Onderstepoort Veterinary Institute is thanked for permission to publish in this journal and the Section of Pathology for the autopsy reports.

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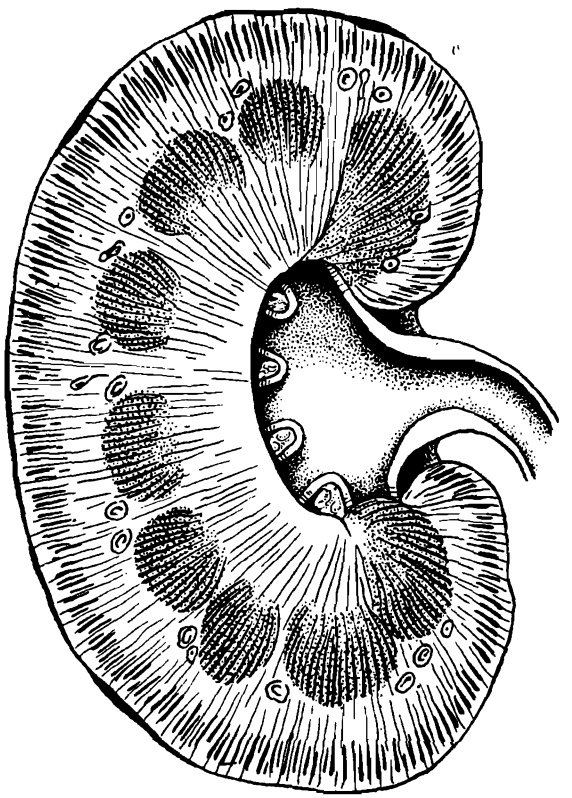

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DIE PIOMETRA-KOMPLEKS VAN TEWE: 'N KLINIESE OORSIG

A. P. SCHUTTE*.

SUMMARY

Pyometra in the true sense of the word refers to a condition of pus accumulation in the uterus. In the bitch, however, this condition constitutes only a facet of a more complex entity, manifested either a) during the post oestral phase of the breeding cycle or
b) to a limited extent as a complication of the puerperium.

With our present knowledge of the post oestrum pyometra complex it can be readily assumed that the etiology consists of two components. Firstly a predisposing hormonal entity which may manifest itself clinically only after a protracted period, and in which the ovaries are the primary seat of origin. Secondly a bacterial invasion with true pyometra as result. Due to the hormonal abberations these cases very seldom respond to treatment, and the only effective cure is a panhystorectomy.

Conversely the etiology of the post partum complex which does not include a predisposing hormonal component, only manifests itself after a bacterial invasion folowing on parturition, abortions or dystocias. These cases do respond to treatment and the bitch may be bred successfully during subsequent cycles.

The different phases which may be found in pyometra cases are discussed and photographically illustrated. The various methods available to facilitate the diagnosis, especially during the earlier phases of the complex (such as the formogel test, haematological studies, vaginal cytology and radiography) are outlined.

INLEIDING.

Alhoewel piometra etteraansameling in die baarmoeder aandui, word hierdie toestand in tewe in die ouer literatuur deur verskeie begrippe soos piometritis, endometritis, chroniese sistiese endometritis, hiperplastiese endometritis ens., beskrywe. Die redes hiervoor mag wees dat die etiologie van hierdie toestand in die teef ten eerste tot 'n baie groot mate verskil van die wat aanleiding gee tot die ontstaan van piometra in ander spesies. Ten tweede is verskeie fasette gedurende die patogenese van die toestand tot so 'n mate afgebaken, dat slegs 'n gedeelte van die kompleks raakgesien word; dan word die toestand as geheel onjuis aangegee en slegs in terme van die enkele waargenome faset.

Aangesien baie van die piometragevalle deur hiperplastiese veranderings van die endometrium gekenmerk word, het Low[41] en De Vita[21] die toestand as hiperplastiese endometritis bestempel. Dow[23] kon homself nie hiermee vereenselwig nie en wys daarop dat hierdie hiperplastiese veranderings nie noodwendig met enige besmetlike toestand geassosieer hoef te wees nie.

Na 'n baie uitgebreide en uiters volledige studie herken Dow[22 23 24] piometra in die teef slegs as 'n faset in die postestrum-sindroom van volwasse tewe, geassosieer met uiteenlopende kliniese en patologiese manifestasies. Die saamgestelde kompleks word dan omskrywe as 'n sistiese hiperplasiepiometrakompleks. Dit ly geen twyfel dat dit wel uiters raadsaam is om hierdie kompleks as sodanig te kan herken, want deur die vroeër stadia, die sogenaamde potensiele piometragevalle, te behandel, kan uitgesproke piometra-toestande voorkom word. Die probleem is egter dat hierdie kompleks soos deur Dow[22] beskrywe, slegs 'n gedeelte van die toestande behels wat gedurende die teef se geslagsiklus mag voorkom. Aandoenings van die baarmoeder wat gedurende *partus* of selfs *post partum* mag ontstaan en wat wel aanleiding tot die ontstaan van piometra kan gee word dus buite rekening gelaat. Omrede die etiologie van die twee groepe uiteenlopend van aard is, die behandeling wat toegepas kan word uit die aard van die saak ook verskil, en dit vir die klinikus uiters raadsaam is om tussen die twee te kan onderskei, word die volgende begrippe deurgaans gebesig:

1. Die Postestrum-kompleks.
2. Die Postpartum-kompleks.

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ETIOLOGIE

1. *Die Postestrum-Kompleks.*

Theunissen[61 62] was een van die eerstes wat bewys gelewer het dat die etiologie van piometra in die teef nie uitsluitlik aan bakteriese indringing toegeskrywe kan word nie. Hy het ook bewys dat 'n verhoogde estrogene-afskeiding op sigself ook nie die setel van oorsprong kan wees nie en huldig dus die standpunt dat daar predisponerende sowel as direkte oorsake moet wees. Deur estrogene in baie hoë dosisse toe te dien kon hy in enkele gevalle slegs 'n ligte hiperplasie van die endometrium verwek. Meer uitgesproke vorms kon verwek word deur estrogene en progesteroon afwisselend toe te dien. Hy beskrywe ook endometriale veranderings wat as gevolg van sekondêre bakteriese indringing teweeggebring word. Indien die progesteroon-toediening onttrek word, verdwyn hierdie reaksies tot 'n mate, terwyl die organismes nog steeds geïsoleer kan word. Met daaropvolgende progesteroon-behandeling word soortgelyke letsels weereens verwek.

De Vita[21] is ook van mening dat, alhoewel dit baie moeilik is om die ovarium en spesifiek progesteroon-afskeiding as die predisponerende faktor te inkrimineer, die setel van oorsprong tog wel hier mag wees. Hy wys ook daarop dat bakteriese isolasies vanuit die baarmoederinhoud nooit konstant is nie en dat geen spesifieke organisme verantwoordelik gehou kan word nie. Hierdie etiologiese uitgangspunt word ook deur ander skrywers gehuldig[11 41 60].

TABEL I

TABEL I.—SAAMGESTELDE GEGEWENS OM OMVANG VAN BAARMOEDERGROOTTE IN PIOMETRA-GEVALLE AAN TE DUI.

Outeur	Teef se Gewig	Baarmoedergewig of Volume van etteraansameling
*Spaulding[32]	Pekingese (6.4 Kg)	2.2 liter
Theunissen;[6]	Dwerg Kees (3 Kg)	0.47 Kg
Morris[2]	10 Kg	3 liter
*Engle[5]	7.3 Kg	1.8 Kg
Dow[25]	Serie gevalle (15—20 Kg)	3 — 4 Kg
Resultate alhier	Boxer (20 Kg)	1.2 liter

*Gegewens tot metrieke stelsel verwerk.

Dow[22 23 24] se werk, wat uitsluitlik oor die postestrum sistiese hiperplasie-piometra-kompleks handel, is die volledigste tot dusver. In sy reeks van 172 gevalle was in 96% daarvan *corpora lutea* teenwoordig. Kenmerkend van hierdie gevalle was dat al die *corpora lutea* nog histologies aktief was, ten spyte van die feit dat sommige van die gevalle alreeds in 'n gevorderde anestrumstadium van die siklus verkeer het. Die *corpora lutea* het dus nie degeneratiewe veranderings, soos normaalweg verwag word, ondergaan nie. Net soos Theunissen[62], wys Dow[22] ook daarop dat met langdurige progesteroon-toediening sistiese hiperplasie van die endometrium verwek kan word. Indien estrogene afwisselend met progesteroon toegedien word kan dieselfde endometriale veranderings teweeggebring word, maar met baie kleiner hoeveelhede progesteroon in verhouding tot dié gevalle waar uitsluitlik progesteroon gebruik was. Uit 89 persent van sy kliniese gevalle kon hy nie-spesifieke bakterieë isoleer.

Bloom[13] is van mening dat 'n verhoogde estrogeenafskeiding die werklike predisponerende oorsaak moet wees. Sy stellings is direk teenstrydig met die van Dow[22]. Bykans al die gevalle deur laasgenoemde ondersoek het histologies aktiewe *corpora lutea* hevat; hy kon geen korrelasie met die toestand en sistiese ovaria aantoon nie en wys ook daarop dat die endometriale klierafskeiding identies met die van normale gevalle is.

'n Kenmerkende eienskap van hierdie postestrum-kompleks is die kliniese manifestasies van abnormale estrumsiklusse, lae fekunditeit en selfs steriliteit, en veral die hoëre ouderdom van die pasiënte. Agt en sewentig persent van Dow[21] se gevalle het nog nooit gewelp nie, alhoewel hulle verskeie siklusse ondergaan het. Die gemiddelde ouderdom van hierdie groep was 8.5 ± 2.8 jr. Met enkele uitsonderings blyk dit baie duidelik dat die grootste persentasie van gevalle aan die uitgesproke vorme van die kompleks ly eers nadat 'n ouderdom van vyf jaar bereik is[21 25 33 41 60 61].

Met ons huidige kennis aangaande hierdie postestrum-kompleks kan met 'n redelike mate van sekerheid aanvaar word dat die etiologie basies uit twee komponente bestaan. Ten eerste 'n predisponerende hormonale oorsaak, wat oor 'n aantal siklusse strek alvorens die kliniese manifestasies sigbaar word en waar die ovaria heelwaarskynlik die setel van die hormonale afwyking is. Tweedens vind daar, as gevolg van hierdie hormonale invloed op die endometrium, makliker nie-spesifieke bakteriële indringing plaas om sodoende die algemeen erkende beeld van piometra teweeg te bring.

2. *Die Postpartum-kompleks.*

Inteenstelling met die postestrum-kompleks, is die etiologie van hierdie groep baie duideliker afgebaken. Die oorsaak is 'n direkte bakteriese indringing wat plaasvind wanneer die baarmoeder gepredisponeer word gedurende dragtigheid, gedurende die verskillende fases van *partus* en selfs gedurende die *puerperium.* Hier, weereens, kan verskeie bakterieë 'n rol speel[13 61]. Terwyl die baarmoeder onder progesteroonprikkeling verkeer, is diè baie meer vatbaar vir bakteriese indringing wat dan aanleiding tot piometra kan gee. Gewoonlik is die indringing stygend vanaf die vagina. Die organismes kan ook iatrogenies, byvoorbeeld gedurende 'n tangverlossing, ingedra word.

Algemene predisponerende oorsake is: *retentio secundinarium;* besmetlike fetusreste; trouma van die geslagskanaal gedurende *partus;* onvolledige aborsies en onsteriele binne-baarmoederlike manipulasies.

Alhoewel daar geen korrelasie met hierdie kompleks en ouderdom gevind kan word nie, blyk dit tog dat ouer tewe wat vir die eerste keer baar, meer geneig is om baarmoederinfeksies op te doen[61].

PATOLOGIE:

1. *Postestrum-Kompleks.*

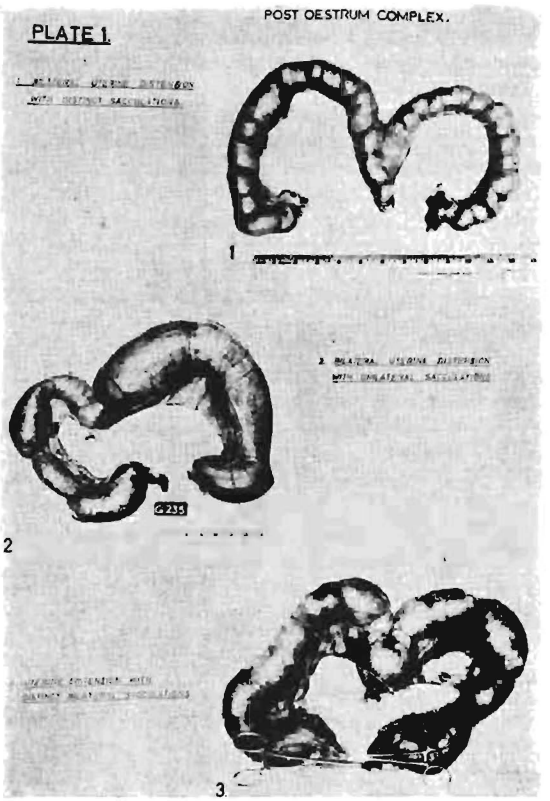
A. *Patologiese Anatomie.*

Volledige beskrywingspunte aangaande die patologiesanatomies sowel as histopatologiese veranderings is in die literatuur te vinde[11 13 18 21 25 27 30 35 42 47 48 50 54 56 61 62].

Soos reeds aangedui, is die primêre letsels wat aangetref mag word hoofsaaklik toe te skrywe aan hormonale aberrasies met daaropvolgende indringing van bakteriese organismes, wat dan aanleiding gee tot die uitgesproke piometra, oftewel die gevalle met massale etteraansameling. Dus is die patologiese afwykings wat die geval mag vertoon afhanklik van die stadium van ontwikkeling waarop die geval ondersoek word.

Die vroeë gevalle, oftewel die potensiële piometra-gevalle, wys slegs 'n geringe toename in die deursnee van die baarmoederhorings. Die konsistens is gewoonlik vermeerder en die omvang is meer rond in vergelyking met die normale afgeplatte voorkoms. Variërende hoeveelhede duidelik waarneembare siste lê verspreid dwarsdeur die endometrium. Hierdie siste mag soms een tot meer sentimeters in deursnee wees. Geen inflammatoriese reaksies is makroskopies sigbaar nie en geen etteraansameling vind plaas nie. Plaat No. 4 (fotos 10 en 12) toon hierdie fase baie duidelik.

Plaat 1.



Piometra-gevalle waar die onegalige sakagtige uitsetting van die horings weerspieël word.

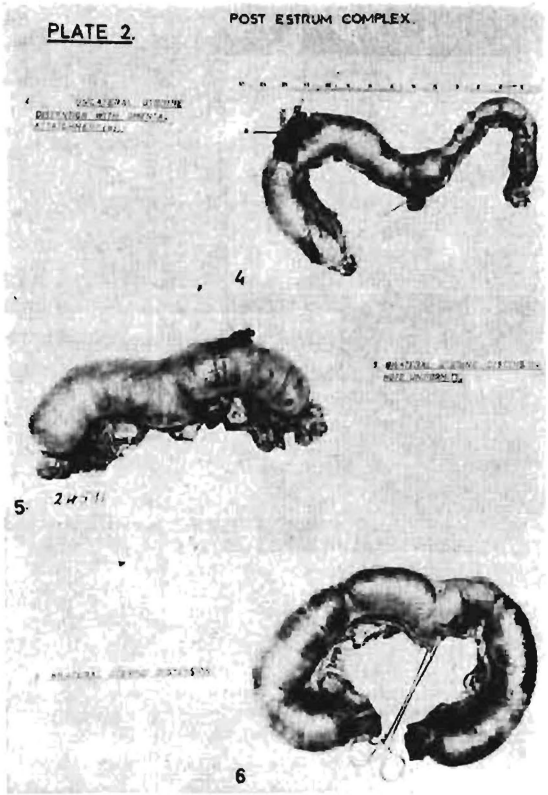
Na gelang die toestand vorder, dit wil sê, in die gevalle waar bakteriese indringing alreeds plaasgevind het en ook afhangend tot watter mate die baarmoederhals oop is, is die patologies-anatomiese voorkoms baie uiteenlopend van aard. Plate 1 en 2, (fotos 1-6) dui aan tot watter mate baarmoederuitsetting as gevolg van etteraansameling mag voorkom. Fotos 4 en 5 wys ook areas waar serosaverklewings plaasgevind het. Aangesien in beide gevalle die areas gelokaliseer was en ook beide groot hoeveelhede etter in die buikholte gehad het, word hierdie plekke beskou as moontlike punte waar etteruitsypeling op een of ander tydstip plaasgevind het.

B. *Histopatologie.*

Dow[22 24], wat voldoende bewys lewer vir die daarstelling van 'n duidelike korrelasie tussen die kliniese manifestasies en die patologiese verand-

erings, verdeel die gevalle van postestrum-kompleks bloot histologies in vier hoofgroepe. Gevalle met slegs hiperplastiese veranderings sonder enige ontsteking word in een groep gesorteer, terwyl die gevalle met uitgesproke inflammatoriese reaksies, dit wil sê, die meer gevorderde gevalle met eteraansameling onder aparte groepe bespreek word.

Plaat 2.



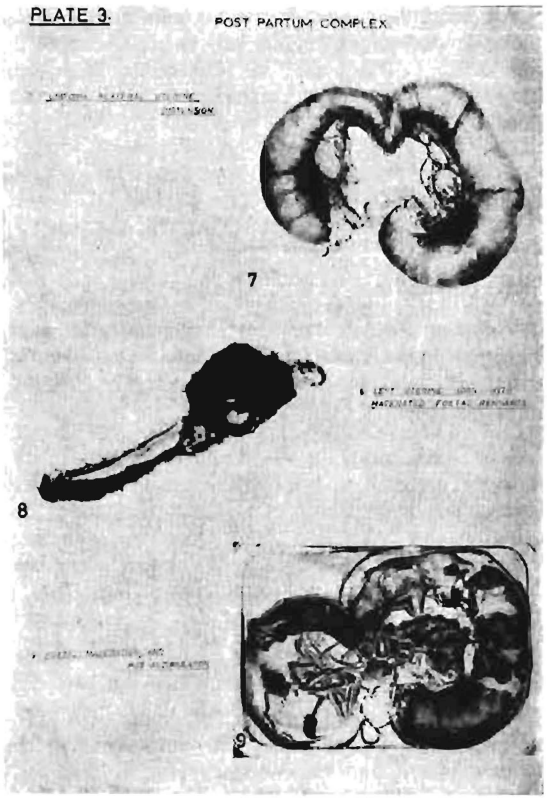
Piometra-gevalle waar die horings 'n meer egalige buisvormige uitsetting vertoon. Fotos 4 en 5 vertoon ook omentale verklewings.

Bloom[13], wat nie sistiese hiperplasie as 'n faset van die postestrum-kompleks erken nie, beskrywe die veranderings wat plaasvind slegs as akute, subakute, of chroniese metritis. Hy maak egter wel melding van die feit dat 'n groot persentasie van die subakute gevalle ook sistiese hiperplasie van die endometrium ondergaan.

Om die histopatologiese veranderings as eenheid te omskrywe verkies Theunissen[61] die term "endometritis". Alhoewel hy erken dat in sommige gevalle die ontstekingsprosesse tot die diepere lae van die baarmoederwand mag deurdring, is hy nogtans van mening dat hierdie term wel geregverdig word aangesien die belangrikste veranderings in die endometrium voorkom. Verder maak hy ook 'n onderskeid tussen die endometritis wat *post partum* mag voorkom en die van die postestrum-kompleks.

Plaat 5, fotos 1 tot 7, dui aan tot watter mate die histologiese beeld mag wissel. Afhangende van die stadium van ontwikkeling, kan sistiese hiperplasie voorkom sonder of met inflammatoriese reaksies as 'n samehangende verskynsel. Hierdie ontstekingsprosesse kan akuut of chronies wees. In die meer uitgesproke vorms kan daar tot so 'n mate vernietiging van die endometrium plaasgevind het dat soms geen klierweefsel meer opgemerk word nie. Alhoewel nie hier geïllustreer nie, kan chroniese sowel as akute letsels soms in dieselfde sneë aangetref word.

Plaat 3.



Fotos 7 en 9 dui postpartum-gevalle aan waar fetale retensie die predisponerende oorsaak was met daaropvolgende etteraansameling. Foto 8 toon retensie van fetalereste met lankstaande chroniese endometriale reaksie.

2. *Postpartum-Kompleks.*

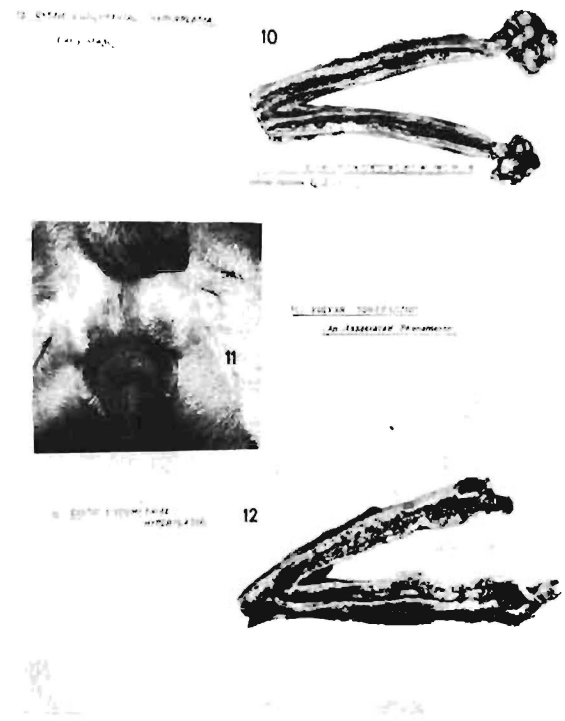
Aangesien die baarmoederhals gedurende die postpartumfase normaalweg redelik oop is, word baie selde massale etteraansameling aangetref. Waar daar wel meganiese sluiting van die hals plaasvind, kan dit wel gebeur: sulke gevalle word deur fotos 7 en 9 (Plaat 3) geïllustreer. Foto 8 toon weer 'n geval waar gedeeltelike fetale retensie in een horing plaasgevind het met chroniese patologiese afwykings van die endometrium as gevolg. Dié besondere geval het vir afwisselende periodes oor 'n tydbestek van drie maande *post partum*, 'n etterige skedeuitvloeisel getoon.

Die histopatologiese letsels wat in hierdie kompleks voorkom is hoofsaaklik akuut, alhoewel sommige gevalle meer chroniese letsels mag toon[13 61].

PATOLOGIESE LETSELS IN ANDER ORGANE.

Polidipsie en poliurie wat dikwels as 'n komponent van die postestrum-simptoomkompleks

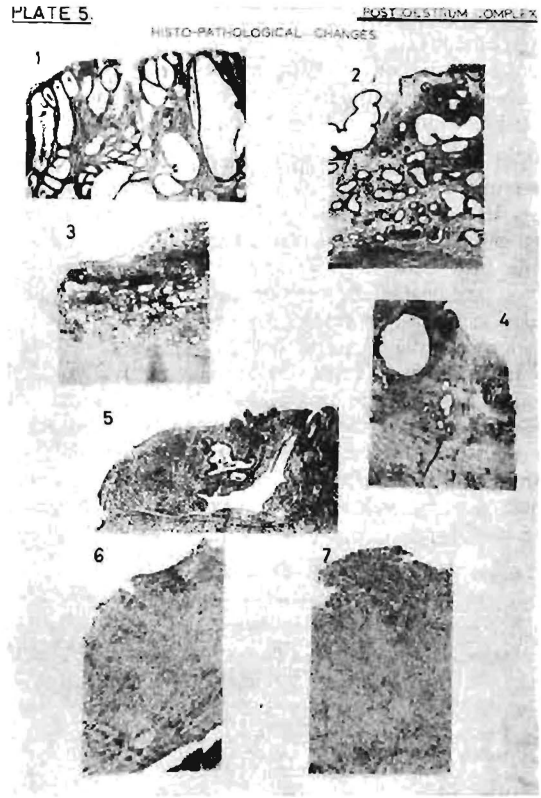
Plaat 4.



Vroeë gevalle waar daar slegs sistiese hiperplasie van die endometrium teenwoordig is. Foto 11 verwys na die vulva aanswelling as verwante verskynsel.

voorkom, word deur Talanti[60] aan hipofiseale letsels toegeskrywe. Sy bewering is dat nie genoegsame antidiuretiese hormoon gevorm word nie en dus vind daar geen urinekonsentrasie plaas nie. Gylstorf[32] beskrywe ook hipofiseale letsels en Landau[40] wys daarop dat progesteroon as 'n aldosteroon-antagonis kan optree. Asheim[1 10] lewer onteenseglike bewys dat daar wel voldoende ADH

Plaat 5.



Histopatologiese veranderings wat gedurende die verloop van die postestrum-kompleks aangetref kan word.

afgeskei word en bewys ook dat die poliurie met samehangende ontwaterings simptome uitsluitlik as gevolg van nierbeskadiging tot stand kom. Sy standpunt is dat as gevolg van bakteriese toksienabsorbsie die buisepiteel van die nier beskadig word. Elektronmikroskopiese studies van hierdie letsels is ook beskrywe[45].

Naas degeneratiewe veranderings in die nier word ook beenmurg- en bynierletsels deur Bloom[14 15] beskrywe. Hy is van mening dat die mees prominente ekstra-genitale letsel miëloïede metaplasie is, veral in die lewer, milt, byniere en niere aangetref.

BAKTERIOLOGIE

Uitgebreide studies[13 14 21 24 34 40 55 61 62 63] aanaangaande die bakteriese flora van die geslagskanaal dui daarop dat bakterieë uitsluitlik 'n sekondêre, maar nogtans belangrike rol speel in die ontstaan van hierdie piometra-kompleks.

Dat koïtus 'n rol speel met die oordraging en totstandkoming van die besmetlike komponent word sterk betwyfel. Baie van die gevalle ontwikkel uitgesproke piometra-letsels sonder dat dekking ooit plaasgevind het[61]. Die besmetting is hoofsaaklik stygend van aard, dit wil sê, organismes van buite of saprofitiese organismes wat in die vagina voorkom mag patogeen word en die minder weerstandbiedende baarmoeder binnedring[61].

Met enkele uitsonderings word die organismes gewoonlik in suiwer kweking afgesonder. Dit is egter belangrik om daarop te let dat die organisme wat geïsoleer word nie noodwendig die veroorsakende organisme hoef te wees nie: organismes kan afsterf gedurende die verloop van die kompleks en ander kan weer posvat[61]. In een geval, waar die verloop van die toestand oor 18 maande nagevolg is, is drie verskillende patogene organismes afsonderlik gedurende verskillende fases geïsoleer.

Soos in Tabel II saamgestel, is die voorkoms van *E. coli, Staphylococcus-* en *Streptococcus*-stamme die mees algemene organismes wat gevind word.

TABEL II.—DIE VOORKOMS VAN BAKTERIEE IN PIOMETRA-GEVALLE:

	Outeur	Mees algemene organismes geïsoleer
1	Theunissen'.	(i) *Colibacillus* (meer as helfte van gevalle) (ii) *Streptococcus* (10% van gevalle)
2	De Vita.,	*E. coli*, Hemolitiese *streptococcus*, *Staphylococcus areus.*
3	Bloom.,	*E. coli*, *staphylococcus*, *Streptococcus.*
4	Dow..	*E. coli*, *Staphylococcus aureus*, Hemolitiese *Streptococcus.*
5	Resultate al hier verkry	Hemolitiese *streptococcus* (60% van gevalle) *E. coli*, *Staphylococcus aureus*

DIAGNOSE

1. *Postestrum-Kompleks.*

Aangesien die etiologie saamgestel is uit 'n predisponerende hormonale komponent en uit 'n sekondêre besmetlike komponent, kan die kliniese waarneembare simptome soms heelwat varieer. Veral met die oog op die diagnose van die potensiële piometrageval, (wat wel klinies moontlik is,) is dit nie genoegsaam om slegs 'n kliniese ondersoek uit te voer nie. Die bestudering van 'n volledige anamnese, en deur gebruik te maak van laboratoriumdiagnostiese hulpmiddels, kan die taak baie vergemaklik word.

(a) *Anamnese*

Dit is nie alleen wenslik nie maar soms absoluut essensieel om 'n gedetailleerde geskiedenis in te win. Ten eerste moet gepoog word om die verband van die huidige toestand met vorige partus-data of met voorafgaande estrumperiodes te bepaal. Deur eers te probeer vasstel of dit 'n faset van die postestrum-kompleks is, en of die geval 'n gekompliseerde *puerperium* verteenwoordig, kan die simptoom-kompleks gewoonlik beter beoordeel word.

In die vroeë vorms van hierdie kompleks, die potensiële piometra-gevalle, dui die geskiedenis meestal slegs op hormonale aberrasies: dus hoofsaaklik abnormale siklusse met geen sistemiese simptomatologie nie. Hierdie gevalle het gewoonlik al twee of drie of selfs meer siklusse deurgemaak; in sommige is dekking wel toegelaat sonder enige sukses. Die estrumsiklusse self mag abnormaal verloop het sover dit die psigiese gedrag en intensiteit en duur van pro-estrum en estrum betref. Die teef mag selfs reuns aanlok weke na die werklike *estrumfase verby is. Die siklusse kan met* gereelde of selfs met kort tussenposes mekaar opvolg.

Mits 'n gedetailleerde anamnese beskikbaar is, verg die meer gevorderde gevalle, die werklike piometra-geval met samehangende sistemiese simptomatologie, gewoonlik nie veel moeite in die daarstelling van 'n akkurate diagnose nie. Die geskiedenis dui ten eerste op hormonale afwykings wat deur vorige estrumperiodes weerspieël is. Dit word opgevolg deur akute agteruitgang twee tot agt weke na die laaste estrumperiode: die stadium van bakteriese opvlamming met samehangende fenomene. Met enkele uitsonderings is die ouderdomsgroep van hierdie gevalle gewoonlik van vier tot agt jaar.

(b) *Simptomatologie*

(i) *Aanswelling van die Vulva*: Samehangend met 'n variërende mate van skedeuitvloeiing is die hipertrofie van die vulva 'n baie algemene simptoom[11 21 25 33 36 38 41 42 43 54 61]. Hierdie vergroting word gewoonlik vir die eerste keer opgemerk 'n paar weke na die voorafgaande loopsheid; geen atrofie het plaasgevind nadat die siklus verby is nie. Die vulva kan soms onreëlmatige groot afmetings aanneem met die gevolg dat trouma maklik kan plaasvind[21]. Die konsistens en tekstuur wissel van 'n sagte tot 'n meer sklerotiese geaardheid.

(ii) *Skedeuitvloeiing*: In die meer gevorderde gevalle kan 'n wisselende mate van etteruitvloeiing bespeur word. Die intensiteit van die vloeiing is

natuurlik afhanklik van die hoeveelheid etteraansameling in die baarmoederhorings, die viskositeit van die etter en tot watter mate die baarmoederhals oop is. Alhoewel groot hoeveelhede etter teenwoordig mag wees, is dit dus nogtans moontlik dat geen uitloopsel waargeneem word nie. Aangesien die teef soms aanhoudend die uitvloeisel weglek, is dit ook moontlik dat aanvanklik geen uitloopsel gesien word nie. In teenstelling hiermee kan die uitvloeisel sulke afmetings aanneem dat die hele perineale area, die stert en agterbene besoedel is.

Die kleur mag wissel van grys-wit tot vuil rooibruin en die viskositeit van 'n baie dun vloeibare tot meer taai slymerige vorm. Theunissen[61] is van mening dat 'n meer rooibruinerige uitloopsel gewoonlik 'n meer akute ontstekingsproses aandui, terwyl 'n geel, slymerige uitvloeisel vaginale besmetting as komplikasie mag aandui.

(iii) *Buikuitsetting*: As gevolg van groot hoeveelhede etteraansameling in die baarmoeder, en veral waar daar afsluiting van die baarmoederhals plaasgevind het, kan daar klinies waarneembare uitsetting van die buikholte plaasvind[11 21 25 38 41 61]. Die uitsetting kan selfs normale dragtigheid simuleer.

(iv) *Polidipsie, Poliurie, Braking en Ontwatering*: Hierdie verskynsels, wat 'n abnormale vloeistofbalans aandui, word uitsluitlik in die meer gevorderde stadia aangetref. Braking, wat geensins 'n konstante simptoom is nie, is hoofsaaklik aan 'n bygaande toksemie toe te skrywe[25 57 58 61]. Theunissen[61] stel dat dit slegs in vyf persent van gevalle opgemerk is, terwyl Low[41] drie en dertig persent aangee.

Polidipsie kan tot in vyf en twintig persent van gevalle voorkom en die hoeveelheid vloeistof wat per dag gedrink word kan groot volumes aanneem[61].

(v) *Temperatuur*: Nieteenstaande die feit dat by die meer gevorderde gevalle, ook dié wat toksiese simptome wys, gewoonlik subnormale temperature geregistreer word, is die temperatuurveranderings oor die algemeen so wisselend dat daar geensins op peil getrek kan word nie.

(vi) *Algemene Gedrag*: In die vroeë gevalle, waar slegs die hormonale komponent teenwoordig is, is die gedrag hoofsaaklik beperk tot psigiese afwykings wat assosieer kan word met abnormale estrumsiklusse. In die meer gevorderde stadia is daar gewoonlik verlies van eetlus, polidipsie en selfs 'n uitgesproke apatiese houding.

(vii) *Rassevoorkoms*: Die voorkoms van piometra is nie tot spesifieke rasse beperk nie. Alhoewel in ons reeks, Boxers agt en twintig persent van die gevalle uitgemaak het, kon Theunissen[61] geen spesifieke ras uit die 37 rasse wat hy ondersoek het, afsonder nie. Irwin[30] is weer van mening dat piometra hoofsaaklik in die kleiner rassoorte voorkom.

(c) *Kliniese ondersoekprosedures en Laboratoriumdiagnostiek.*

Sekere van die postestrumgevalle kan soms die klinikus se vernuf tot die uiterste beproef, ten spyte van 'n volledige anamnese. Veral in dié gevalle waar die simptomatologie so vervaag of gedemp voorkom, kan die diagnose deur laboratoriumdiagnostiese hulpmiddels gefinaliseer word.

(i) *Hemogram*: Van al die toeste word die hemogram baie algemeen gebruik.

Morris[43] maak melding van die uitgesproke leukositose wat mag voorkom. Hy beskryf ook spesifieke neutrofiele wat hy uitsluitlik met hierdie kompleks assosieer.

Khuen, Park en Adler[37] beklemtoon weer die waarde wat 'n totale witbloedseltelling, die persentasie onvolwasse neutrofiele en die persentasie limfosiete inhou vir die finalisering van die diagnose. Hoe hoër die aanvanklike witbloedseltelling hoe swakker die prognose.

Rehfeld[48] se uitgangspunt is nie so seer die bevestiging van 'n diagnose nie maar hy meen dat totale witbloedseltelling, besinkingspoed en hemoglobienkonsentrasie aangewend kan word vir die daarstelling van die prognose.

Die werk van Haighler en Hawkins[33] vermeld ook verhoogde witbloedseltellings in die meeste van gevalle. Hulle beskrywe 'n spesifieke neutrofiel wat homogeen kleur, ietwat groter as normaal, groot duidelik afgebakende kern en met toksiese stippeling in die sitoplasma. Die voorkoms van hierdie sel in smere is volgens laasgenoemde baie kenmerkend van piometra-gevalle. Soortgelyke afwykings in die ontwikkelingstadia van die neutrofiel word ook deur Bloom[15] beskrywe.

In die onlangse werk van Fowler[28] word die waarde van die hemogram verder beklemtoon. Hy verwys na die verspreiding van witbloedselle in die smeer wat as diagnostiese hulpmiddel aangewend kan word.

(ii) *Bloed-Ureumstikstof*: Volgens von Russe[51] lê die waarde van hierdie bepaling nie soseer in daarstelling van 'n diagnose nie maar is baie waar-

devol vir die stel van die prognose. Sy bevindings dui daarop dat hoe laer die waardes pre-operatief, hoe beter is die prognose. Met uitgesproke hoë peilwaardes is die prognose ongunstig, aangesien onomkeerbare nierparenkiembeskadiging weerspieël word.

(iii) *Die „Formogel"-toets*: Schalm[52] beskou hierdie maklik uitvoerbare toets as 'n uiters handige diagnostiese hulpmiddel. Hy beweer dat alhoewel die hemogram en veral die leukositose wel van waarde is, dit in gedagte gehou moet word dat verskeie toestande, en nie noodwendig net piometra nie, die witbloedseltelling kan verhoog. Cole en Christensen[19] huldig 'n soortgelyke standpunt.

Fox[29] gee baie duidelik die kliniese waarde van hierdie toets weer. Hy beweer dat 'n positiewe reaksie afhanklik is van die albumin: globulien-verhouding. 'n Positiewe reaksie dui op 'n verhoging van die gammaglobulien vlak. Hy beweer verder dat 'n negatiewe lesing postoperatief op 'n gunstige prognose dui.

(iv) *Radiografie*: Alhoewel hierdie aspek die diagnose kan finaliseer, is die praktiese hindernisse daaraan verbonde hoofsaaklik een van ekonomie. Slegs indien gebruik gemaak word van die groter en duurder Roentgenapparaat kan behoorlike resultate verkry word[28]. Daar is nogtans voldoende bewys gelewer dat radiografiese studies wel waarde inhou[11 17 20 25 31 53].

(v) *Vaginale Ondersoek*: Voordat die sitologie van die slymhuid deur diepere ondersoek van die skede versteur word, is dit raadsaam om ten eerste skraapselsmere daarvan te neem. Nuttige inligting met betrekking tot die hormonale milieu kan hieruit verkry word. Informasie kan ook ingewin word tot watter mate bakteriese indringing in die skede al plaasgevind het. Dit is ook wenslik om 'n tamponmonster van die baarmoederhals vir bakteriese afsondering en vir die samestelling van 'n antibiogram te neem. Met behulp van 'n spekulum kan dan vasgestel word tot watter mate die baarmoederhals oop is, tot watter mate etteruitvloeiing plaasvind en tot watter mate die slymhuid van die skede aangetas is.

Terselfdertyd is dit ook raadsaam om die uretra te ondersoek, en, indien moontlik, 'n urienemonster vir analise te versamel.

(vi) *Buikaftasting*: 'n Redelike algemene simptoom is die peervormige uitsetting van die buikholte. Aangesien 'n soortgelyke uitsetting van die buikholte mag plaasvind met dragtigheid, pseudo-dragtigheid, buikgewasse en selfs as gevolg van abnormale buikvloeistofaansameling, is dit wenslik om deur aftasting die werklike oorsaak te probeer bepaal.

Veral in die gevorderde gevalle, waar die baarmoederhorings worsvormig uitgeset is en die wand dun is, is dit soms uiters moeilik om deur die buikwand die werklike omvang van die baarmoeder te palpeer. Sulke baarmoeders word deur Plaat 2, fotos 5 en 6 in beeld gebring. Groot vet tewe en 'n gespanne buikwand kan die taak nog verder bemoeilik.

In gevalle waar daar slegs 'n verdikking van die baarmoederwand teenwoordig is, asook in dié gevalle waar uitsetting plaasgevind het maar waar die tonus nog goed is, kan die baarmoeder gewoonlik as 'n string gevoel word in die ventrale en mediale epi- en mesogastrium en ook in die dorsale hipograstrium tot voor die bekkenkanaal[61]. Hierdie gevalle word deur fotos 1, 10 en 12 geïllustreer.

Gevalle waar die baarmoederwand ook baie dun mag wees maar waar die horings nie 'n eenvormige uitsetting maar meer onreelmatige, afgebakende uitsettings vertoon, word deur fotos 2, 3 en 4 weerspieël. Hierdie gevalle is gewoonlik redelik maklik om te betas, mits berustingsmiddels toegedien is.

2. *Postpartum-Kompleks.*

Indien 'n sorgvuldige anamnese ingewin word en die verband met 'n voorafgaande *partus* getref kan word, lewer die diagnose van hierdie kompleks gewoonlik baie min praktiese probleme. Aangesien die baarmoederhals vir 'n geruime tyd na *partus* oop is vind daar nie maklik etteraansameling plaas nie. Dat dit wel kan gebeur is reeds bespreek. Desnieteenstaande is dit nogtans belangrik om die verskeie fasette in die ontstaan van die kompleks te kan diagnoseer. Uit die aard van die saak is dit ooglopend dat as gevolg van die verskillende predisponerende oorsake en met daaropvolgende bakteriese indringing, die kliniese tekens in intensiteit kan wissel.

Die meeste gevalle waar *partus* onvolledig verloop het met retensie van een of meer fetusse as gevolg, word gewoonlik 36-72 uur *post partum* vir ondersoek ingebring met lusteloosheid, apatiese houding, agalaktie en soms gevorderde toksiese simptome[34]. Hierdie gevalle het gewoonlik 'n verhoogte temperatuur, 'n slegriekende skedeuitvloeisel, ontwateringsimptome en die buikwand kan styf gespan wees. Indien gepoog word om die baarmoeder te palpeer kan hewige pyn getoon word.

Die kleur van die vaginale uitvloeisel kan wissel na gelang van die predisponerende oorsaak. Indien daar retensie van fetusse of plasenta plaasgevind het, is die uitvloeisel groen tot vuil donkergroen van kleur, terwyl andersins die kleur van vuil rooi-bruin tot grys-wit na gelang van die akuutheid van die geval kan wissel.

Dit gebeur soms dat 'n geval weke of selfs maande na *partus* vir ondersoek ingebring word met die klagte dat daar 'n aanhoudende etteruitvloeiing teenwoordig is. Geen sistemiese reaksies word opgemerk nie. Hierdie gevalle kan beide 'n chroniese puerperale metritis sonder of met retensie van fetus dele verteenwoordig. Bo en behalwe deeglike buikbetasting en vaginale ondersoeke is dit soms nogtans nodig om 'n laporotomie uit te voer alvorens die diagnose bevestig kan word.

In die gevalle waar die predisponerende oorsaak soos byvoorbeeld fetale retensie ontbreek, hang die simptomatologie hoofsaaklik af van die liggaamsreaksie wat deur die bakteriese indringing uitgelok word. Indien daar slegs 'n ligte graad van besmetting ontstaan het, is daar geen sistemiese reaksies te bespeur nie. Slegs 'n klein hoeveelheid etterige skede-uitvloeiing word gewoonlik opgemerk. In die meer akute gevalle, die akute puerperale metritisgevalle soos deur Bloom[13] beskrywe, vloei daar groter hoeveelhede etter uit. Selfs uitgesproke toksiese simptome, verhoogde witbloedseltellings, koorsreaksies en anoreksie kan verwag word.

BEHANDELING

1. *Postestrum-Kompleks.*

Waar die klassieke piometra-gevalle vir behandeling voorgelê word is daar geen sprake meer van enige teelvermoë wat die dier mag inhou nie. Inteendeel, daar moet gewoonlik gepoog word om die dier se lewe te red. Dus hoe gouer hierdie kondisie gediagnoseer kan word, verkieslik terwyl 'n mens nog net met die hormonale komponent te kampe het, hoe beter.

In die ouer literatuur[16 26 61] was die behandeling hoofsaaklik daarop toegespits om die baarmoeder met behulp van hormonale preparate of andersins[64] te dreineer. Die hormonale benadering berus hoofsaaklik daarop om die baarmoederwand te sensitiseer met behulp van estrogene en dan baarmoedersaamtrek middels toe te dien. Alhoewel die estrogene wel die bloedtoevloei na die baarmoeder stimuleer, bestaan die gevaar dat dit vir 'n verhoogde toksienabsorpsie verantwoordelik kan wees[59]. Die geval deur Fethers[26] aangeteken is 'n moontlike voorbeeld van bogenoemde reaksie. Brancher[16] se werk is die enigste wat aanduiding gee dat estrogene, alleen of met oksitosien gekombineer, in sommige gevalle wel bevredigende resultate kan lewer.

Die meeste skrywers is dit vandag eens dat 'n panhistorektomie die enigste effektiewe behandeling is, [1 11 25 44 42 54 56 57 59]. Benesch[11] en Stephenson[57] wys tereg daarop dat, alhoewel sommige van die gevalle wat vir behandeling op 'n vroeë stadium voorgelê word wel tot 'n mate op hormonale en/of antibiotiese terapie sal reageer, die meeste egter weer op 'n latere stadium, gewoonlik 'n paar weke na afloop van estrum met klassieke piometrasimptome terugkom. 'n Panhistorektomie is op laas tog noodsaaklik. Die prognose is dan heelwat swakker en die operatiewe risiko soveel groter.

Veral met die oog op die aangewese verdowingsmiddels[46] is dit belangrik om die moontlike ekstragenetale letsels in gedagte te hou. Ingrypende preoperatiewe behandeling is absoluut essensieel. Bild[12] beveel aan dat indien die hemoglobienvlak onder 12 mgm % val, bloedtransfusies toegedien behoort te word. In hierdie Departement word hoofsaaklik Ringer-laktaat en hoë dosisse vitamien-B-kompleks binneaars toegedien. Uitstekende resultate word hiermee verkry. Bild[12] beveel 'n soortgelyke benadering aan maar bykomstig skryf hy ook vitamien C en kalsiumglukonaat voor. Algemeen gesproke, is die toediening van hoë dosisse antibiotika pre- en post-operatief essensieel. Ondersteunende terapie met analeptika, antihistamiene en kortikoïede word na gelang van die toestand van die geval toegedien.

2. *Postpartum-Kompleks.*

Afhangende van die predisponerende oorsaak kan die behandeling toegespits word op die behoud van die teelvermoë van die dier. In teenstelling met die voorafgaande kompleks, het ons hier net met 'n predisponerende oorsaak en 'n sekondêre bakteriese indringing te doen. Indien die predisponerende oorsaak verwyder word en die besmetlike toestand bekamp word, is daar geen rede waarom die gevalle nie weer vir verdere teeldoeleindes gebruik kan word nie.

Die algemene terapie wat hier aangewend word, moet na verwydering van die predisponerende oorsaak daarop toegespits wees om die verspreiding van die besmetlike toestand aan bande te lê en die liggaamreserwes aan te vul. Hier, net soos in die vorige kompleks, word ondersteunende terapie na gelang van die geval toegedien.

Die uitsondering tot hierdie benadering is egter waar mens met die uitgesproke piometra-gevalle gekonfronteer word: waar daar fetale retensie, afsluiting van die baarmoederhals en etteraansameling plaasgevind het. Panhistorektomie is dan hier ook die enigste praktiese uitweg. Dieselfde pre- en post-operatiewe behandeling wat by die postestrum-gevalle bespreek is, is hier ook van toepassing.

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BOOK REVIEW

Haematological Techniques for Use on Animals by R. K. Archer. Blackwell Scientific Publications, Oxford. 135 pages. Publ. price 20s.

This book is of handy pocket format and designed for ready reference. Its nine chapters with appendices run to 135 pages and cover, broadly, apparatus and methods for obtaining blood samples, the examination of blood samples, and a section on aspiration biopsy and blood transfusion.

The author rightly points out that the clinical haematology of animals is still in its infancy but is "a healthy child which is growing rapidly". In general the techniques were originally borrowed from those current in human haematology and modified and adapted for use in the different animals. It is thus not surprising that one finds oneself in disagreement with quite a few statements on the one hand, and on the other finds quite a number of suggestions well worth trying out and worth adopting. The subject matter is certainly dynamic and lends itself to a variety of different preferences. For a veterinarian or clinical laboratory worker embarking on haematological determinations, a good basis on which to build up his own preferred techniques, will be found in this book.

A critic is to some extent disarmed by the author's statement that the techniques described are not necessarily the best but it is claimed that they work. There are, however, a few points of criticism taken at random which may possibly be remedied in a future edition.

Bleeding needles for various purposes and various animals are designated by length and diameter in millimetres. While they are usually and familiarly known and sold by gauge numbers and length in inches, equivalents for the no doubt scientifically acceptable metric system might have been given as a guide. On page 20 Fig. 10 is indicated as being on page 14 while it is found in a small series of excellent photographs following page 22. Lower down on the same page is the rather surprising statement that the tibial vein should be punctured "just above the *stifle* (*knee*) joint" (italics those of the reviewer). The word Giemsa in the well known staining method is consistently misspelt as Geimsa, while on page 47 a strange word "pledgelet" has crept in.

It was also felt that in a book of this type more could have been made of the factors likely to produce haemolysis during the taking and handling of blood. Methods of defibrination of blood are described in some detail but since haemolysis is such a frequent hazard in the domestic animal it is very little used. It is also not quite clear why such procedures as bilirubin determination and the little used estimation of total plasma protein by the copper sulphate specific gravity method have been brought into a book on haematology.

Concerning ESR it has been the practice for a number of years at Onderstepoort to take the reading at 15 minutes for equine blood and to stand the tubes for bovine and ovine blood at a 50° slope for an hour to overcome the difficulties mentioned by the author and to provide clinically useful determinations.

Blood transfusion is dealt with briefly. This could perhaps have been omitted in a book dealing with essentially diagnostic matters or otherwise treated in more practical detail.

These small criticisms are not intended to detract from the undoubted value of this book and from the many items of information made readily available, which otherwise would entail an extensive search. They are offered as suggestions for improvements to be considered when a new edition is contemplated.

— W. D. M.

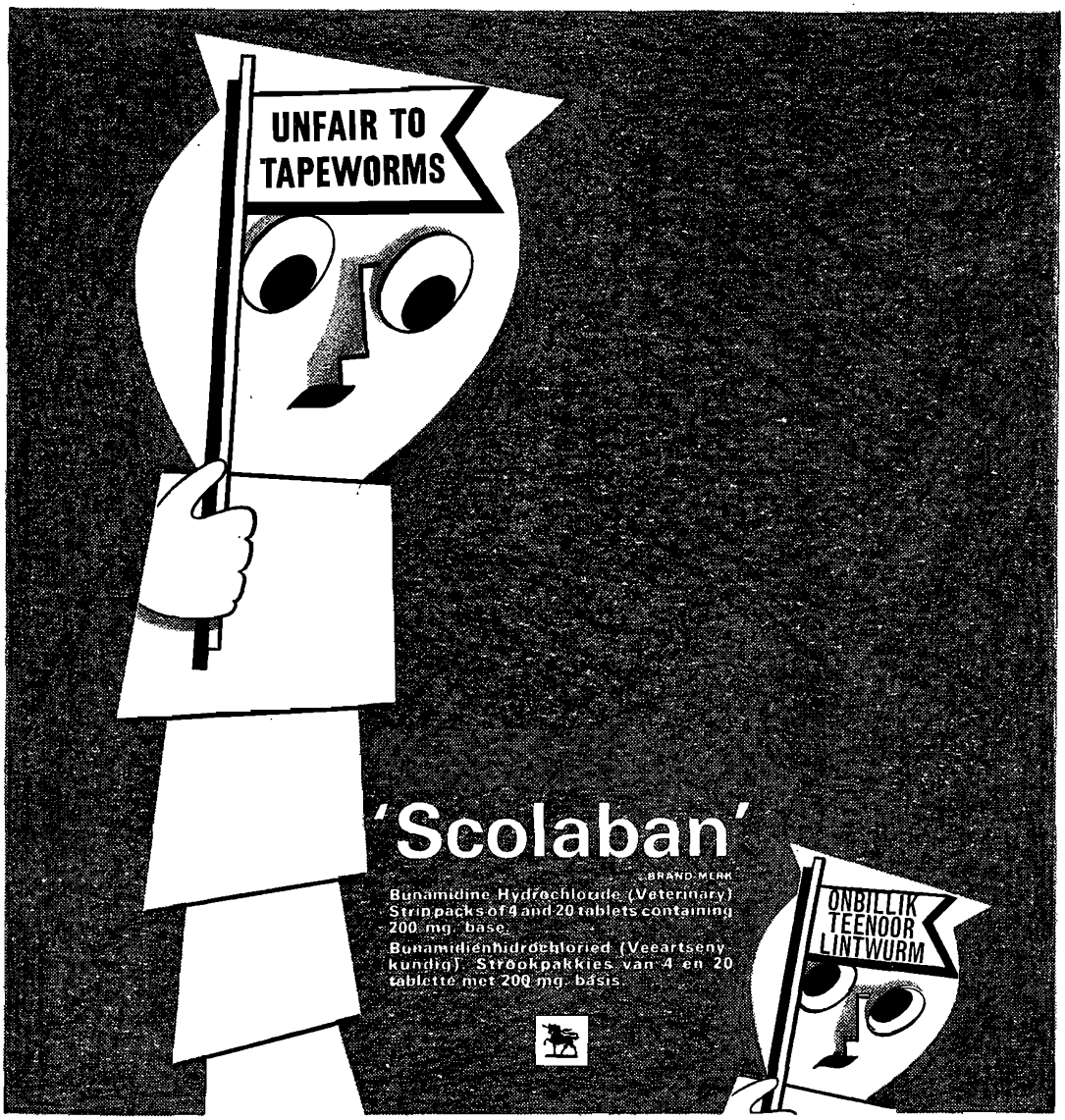
'Scolaban' BRAND MERK TABLETS TABLETTE

THE tapeworm treatment for dogs and cats

• High efficiency against Dipylidium and Echinococcus as well as Taenia. • Destroys and disintegrates the entire tapeworm. • Rapid, safe, gentle. Free from distressing side-effects. • Easy administration, small doses, no purging.

DIE lintwurmbehandeling vir honde en katte

• Hoë doeltreffendheid teen Lintwurms, Dipylidium en Echinococcus. • Vernietig die hele lintwurm. • Vinnig, veilig, sag. Vry van enige nadelige newe-effekte. • Maklike toediening, klein dosisse, geen laksering nie.



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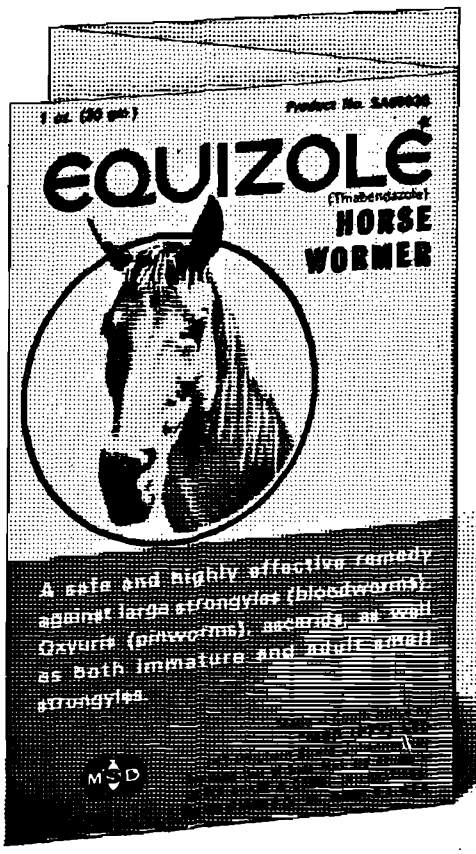

TRADEMARK

EQUIZOLE

(EQUINE THIABENDAZOLE)

HIGHLY EFFECTIVE

Strongyles:	Strongylus vulgaris 100%	50 mg./Kg.
	Strongylus equinis 100%	
	Strongylus edentatus 90%	
	Small strongyles 100%	
Pinworm:	Oxyuris equi 100%	
Ascarids:	Parascaris equorum 100%—100 mg./Kg.	

NO SIDE EFFECTS

"In the toxicity trials, doses of 600 mg./Kg. and below did not produce untoward clinical effects."

References:

(1) *Drudge, J. H., Szanto, J., Wyant, Z. N., and Elam, G.:* Critical tests on thiabendazole against parasites of the horse, *J. Parasitol. 48 (Suppl.): 28, April 1962 (In Soc. proc.)*

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SUPONA* (CHLORFENVINPHOS) FOR CATTLE TICK CONTROL PART I. HANDSPRAYING TRIALS

J. A. F. BAKER and G. E. THOMPSON
Cooper & Nephews S.Af. (Pty.) Ltd. East London.

SUMMARY

Supona at concentrations of 0.01, 0.02 and 0.05% is compared with Delnav (Dioxathion)** 0.05% and/or Toxaphene (Chlorinated camphene)*** 0.25% as an ixodicide.

These ixodicides were applied every seven days to cattle grazing on naturally infested pastures on farms in the Eastern Cape Coastal Belt of South Africa.

Heavy infestations of Blue (*Boophilus decoloratus*), Red legged (*Rhipicephalus evertsi*), Brown Ear Tick (*Rhipicephalus appendiculatus*) and Bont (*Amblyoma hebraeum*) ticks were encountered.

Supona achieved excellent results against these tick species both in the adult and immature stages, and proved to be safe at the concentrations used.

The methods of ixodicide application and the tick counting technique are described together with the method of assessing results.

INTRODUCTION

Useful prediction of developments in tick/ixodicide relationships throughout Africa have been made possible by studying developments in the Eastern Cape Coastal Belt of Southern Africa. Here ideal environmental conditions for tick life exist and changes in parasite/ixodicide relations occur more rapidly than elsewhere on the continent. Whitnall et al[1], Whitehead[2], Whitehead & Baker[3], and Baker & Shaw[4], have respectively described the development of resistance in Blue (*B. decoloratus,*) Red legged, (*R. evertsi*) and Brown Ear Tick (*R. appendiculatus*) to the chlorinated hydrocarbon group of insecticides most commonly used for tick control. In each instance the resistance was first recorded in the Eastern Cape Coastal Belt. Shaw[5] later found resistant Red legged tick strains in other parts of Southern Africa as well as in Central and East Africa.

The significance of these developments is important in areas where tick populations are naturally heavy and could be serious in endemic East Coast Fever areas. An answer is required and thoughts turn naturally to that vast family of insecticides, the organo-phosphates. Several of these, notably Delnav, Asuntal and Diazinan have been used. In general, they have been efficient against the single host blue tick but have weaknesses against one or more of the multi-host tick species. Drummond[6] and Shaw & Baker[7] reported that Supona was an excellent killer of cattle ticks in '*in vitro*' tests. Palmer[8] and Pickering[9] reported favourably on the lack of toxicity of Supona to cattle at effective concentrations.

The purpose of this paper is to describe controlled field tests made with Supona against a number of naturally occurring tick species and to compare its activity with that of the established ixodicides Delnav and Toxaphene.

EXPERIMENTAL METHODS

The three ixodicides used in these experiments were all formulated as Water Miscible Concentrates. Supona and Delnav as 30% wt/vol and toxaphene as a 75% wt/vol concentrate. The established ixodicides Delnav and Toxaphene were utilised at the concentrations recommended for field tick control 0.05% Delnav and 0.25% Toxaphene. Supona was used at concentrations within the range of 0.01% — 0.05%.

The animals to be treated were firmly secured in a suitable cattle race and the appropriate wash

* Supona is a SHELL trademark.
** Delnav and Toxaphene*** Registered Trade Markes of Hercules Powder Company, Wilmington, U.S.A.
** Delnav Cattle Dip (Cooper & Nephews S.Af. (Pty.) Ltd.,
*** Coopertox Cattle Dip (Cooper & Nephews S.Af. (Pty.) Ltd.

applied through an engine/pump unit having a delivery pressure of 20-25 lbs. p.s.i.

Spraywashes were mixed immediately prior to application, three gallons being prepared for each animal. The spray was applied so that the whole body area was completely saturated, particular attention being paid to the inner surface of the ear, the most difficult treatment site.

The animals were treated at seven-day intervals and tick counts and assessments were made on the animals prior to each treatment. Adult Red legged, Brown Ear and Bont ticks were counted *in toto* whilst the immature stages of these species were recorded as light (+), moderate (++) or heavy (+++).

At Gusha Mouth and Caprice, Brown Ear, Red legged and Bont tick adults on the untreated control animals were chloroformed, and/or manually removed at certain inspections. (Tables 3 and 4). Subsequent counts yielded a reliable guide to the daily attachment rates of these tick species. Blue tick counts and assessments were made according to the method of Whitnall et alia[1]. The accurate counting of Bont tick adults and immatures was only possible when the animal was cast and the whole underline exposed. Casting of each animal was standard procedure when Bont tick counts were made.

To test the efficiency of the insecticide against severe challenges of several tick species, it was necessary to utilise several farms. Riverdale for

FIG. 1.

BLUE TICK SCRAPINGS RESULTS - RIVERDALE - LEVEL OF INFESTATIONS OVER 39 WEEKS AVERAGE FROM GROUP OF TWO ANIMALS

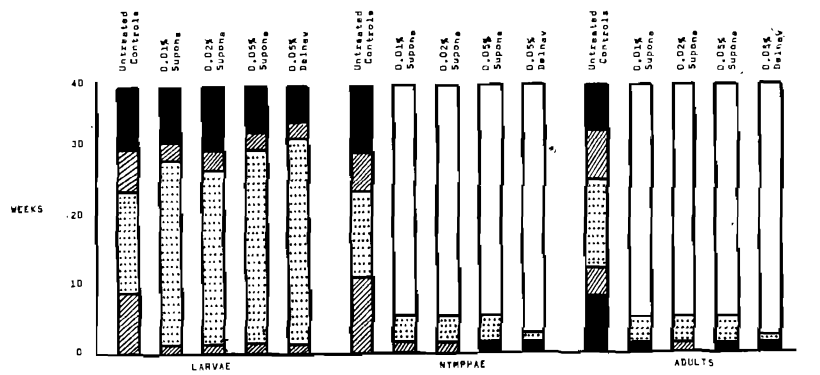
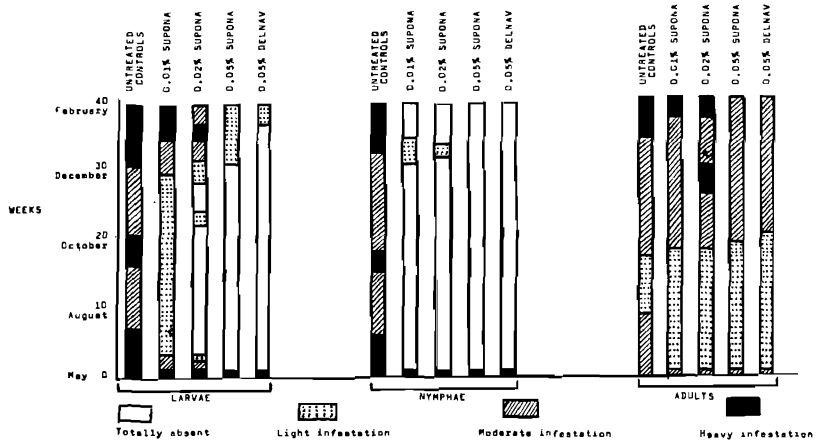


FIG. 2.

RED LEGGED TICK RESULTS - RIVERDALE. ASSESSMENTS OVER 39 WEEKS. AVERAGE FROM GROUP OF TWO ANIMALS



Blue and Red legged ticks, Caprice for Brown Ear Tick, and to a lesser extent, Bont ticks, Gusha Mouth for Bont and Brown Ear Ticks and Begha Mouth for Bont ticks. Two animals per group were used at Riverdale and Caprice, and four at Gusha Mouth and Begha Mouth.

At Riverdale, Whole Blood Cholinesterase determinations were made on treated and control animals at each visit according to the method described by Jolly and Ratcliffe[10].

Results

At Riverdale, excellent results were achieved by Supona against a steady and, at times, heavy Blue and Red legged tick infestations over a long period.

Table 3.—Total Bont and Brown ear tick counts and assessments—"Caprice" two animals per group.

Tick Species	Day	Untreated Controls	0.05% Delnav	0.25% Toxaphene	0.05% Supona
Bont Tick Adults (*A. hebraeum*).....	0_2	*131 ½f	156 F	151 ½f	152 ½f
	1	* 11 f	29 ½f	29 ½f	10 f
	2	* 5 f	10 ½f	14 ½f	4 f
	4	9 f	17 ½f	18 F	10 f
	6	14 f	23 f	26 ½f	37 f
Bont Tick Nymphs.....	0z	†† F	†† F	†† F	†† F
	1	†† F	0	0	0
	2	†† F	0	0	0
	4	†† F	†† f	0	†† f
	6	†† F	†† ½f	† f	†† ½f
Brown Ear Tick Adults (*R. appendiculatus*)..	0z	*976 F	918 F	644 F	1391 F
	1	*301 f	125 F	372 F	41 f
	2	*312 f	135 F	302 F	91 f
	4	575 ½f	449 F	503 F	444 f
	6	1077 F	958 F	1029 F	1118 ½f

Key. * Light infestation.
** Moderate infestation
*** Heavy infestation
f — No engorged specimens seen
½f — Partially engorged females present
F — Fully engorged females present
* Adult ticks killed with chloroform and/or manually removed from control animals at these visits.
z Day of treatment.

Table 4.—Total Bont, Brown ear and red-legged tick counts—'Gusha Mouth' four animals per group.

Tick Species	Day	Untreated Controls	0.05% Delnav	0.25% Toxaphene	0.05% Supona
Red-Legged Tick Adults (*R. evertsi*).	0	52 F	47 F	33 F	60 F
	2	Ticks removed. Not counted	4 f	12 F	3 f
	3	Not counted.	5 f	21 F	5 f
	4	8 F	9 f	31 ½f	15 f
	5	Ticks removed. Not counted.	10 f	33 ½f	17 f
	6	6 F	10 f	42 F	25 f
Bont Tick Adults (*A. hebraeum*)	0	160 ½f	186 ½f	179 F	175 ½f
	2	Ticks removed. Not counted	16 ½f	21 ½f	16 f
	3	Not Counted.	25 ½f	17 F	20 f
	4	21 f	22 ½f	18 ½f	23 f
	5	Ticks removed. Not counted.	17 ½f	15 ½f	22 f
	6	13 f	24 ½f	22 ½f	32 ½f
Brown Ear Tick Adults (*R. appendiculatus*)	0	1062 F	904 F	1045 F	1115 F
	2	Ticks removed. Not counted.	53 F	386 F	29 f
	3	Not counted.	62 ½f	225 F	36 f
	4	383 F	66 ½f	283 F	64 f
	5	Ticks removed. Not counted.	113 ½f	279 F	167 f
	6	327 F	218 ½f	480 F	203 ½f

f—Non engorged ticks only present. ½f—Partially engorged ticks present. F—Fully engorged ticks present.

Although none of the treatments applied prevented the attachment of Blue tick larvas over the seven day interval between treatments, nymphal emergence was prevented after the fourth treatment and, consequently, no adults were seen on any but the control group thereafter.

Red legged adult ticks (Fig. 2) were not completely controlled but were numerically much reduced by 0.05% Supona, and Delnav, and to a lesser but detectable degree by 0.01% and 0.02% Supona. At Gusha Mouth the initial kill and subsequent control of Red legged adults (Table 4) by

FIG. 5. BROWN EAR TICK RESULTS - BEGHA MOUTH. FOUR ANIMALS PER GROUP

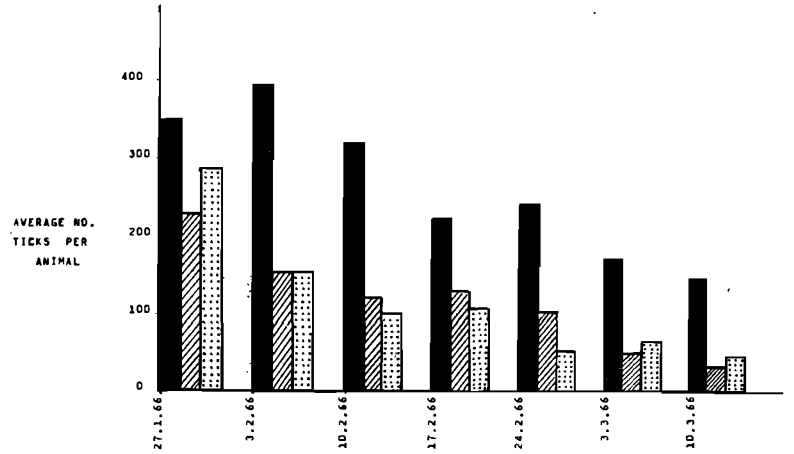
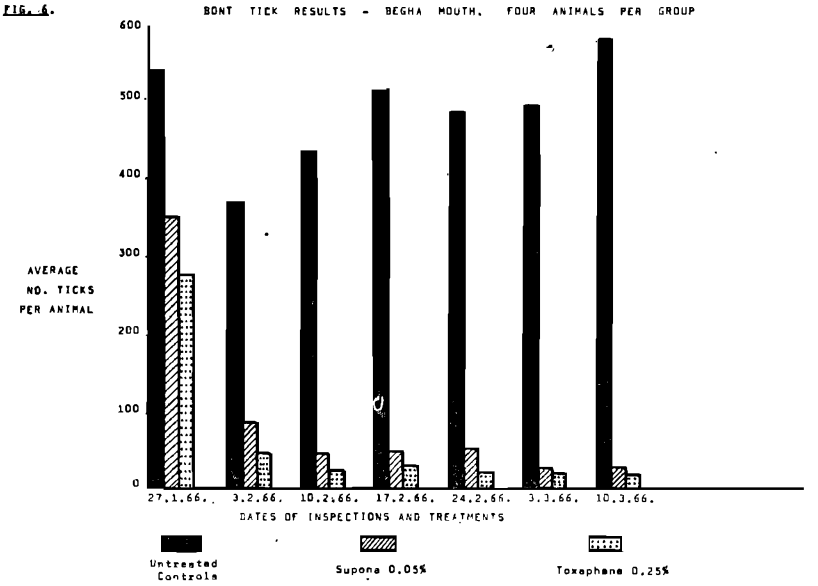


FIG. 6. BONT TICK RESULTS - BEGHA MOUTH. FOUR ANIMALS PER GROUP



Similarly, with Red legged tick immatures, fresh attachment of larvae was reduced but not prevented by the treatments; although 0.05% Supona and 0.05% Delnav were notably superior in this respect. Nymphal emergence was eradicated in these two groups and reduced to low incidence at times of severe challenge in the 0.01% and 0.02% Supona groups.

Supona 0.05% and Delnav 0.05% was markedly superior to that obtained with 0.25% Toxaphene.

Brown Ear Tick adults at Caprice and Gusha Mouth were sufficiently numerous to afford an excellent picture.

Supona 0.05%, achieved spectacular initial kill and good subsequent protection in the face of a

severe challenge. Delnav 0.05% gave good numerical reduction but failed to eradicate all attached ticks as evidenced by the specimens which continued to engorge after treatment. Toxaphene 0.25% was frankly disappointing, failing to clear the ticks at either Gusha Mouth or Caprice. In the latter case, Toxaphene reduced the tick infestations by less than 50% after 48 hours, and tick engorgement continued unabated. At Begha Mouth, Supona 0.05% again gave good results as did 0.25% Toxaphene.

Bont tick adults were well controlled by Supona 0.05% and Toxaphene 0.25% at Gusha Mouth (Table 4), and Begha Mouth (Fig. 6). At Caprice (Table 3) Supona 0.05% was clearly superior to Toxaphene 0.25% and Delnav 0.05% in rapidity of kill, and also effectively prevented female engorgement, whereas both Toxaphene and Delnav permitted continued engorgement by female *A. hebraeum*. Begha Mouth cattle were subjected to a severe Bont tick infestation maintained over a long period, and here both Toxaphene 0.25% and Supona 0.05% effected excellent protection of exposed animals.

As regards immature bont ticks, a steady infestation of Bont nymphs was well controlled by Toxaphene 0.25%, which was superior to the good results obtained by Delnav 0.05% and Supona 0.05%.

Weekly whole blood cholinesterase determinations (Fig. 7) on treated animals revealed a demonstrable but non significant depression of circulating blood cholinesterase of animals treated with up to 0.05% Supona.

Discussion

The outstanding general impression gained in these trials was the rapid kill of ticks attained by Supona. Clear evidence of this is given in Tables 3 and 4 and especially Table 3 (Caprice) where a heavy Brown Ear Tick infestation was reduced to a negligible number within 24 hours, and at 48 hours remained very low despite a field reinfestation rate, as demonstrated by the controls, of about 300 ticks per day. In sharp contrast, neither Delnav nor Toxaphene could match this numerical reduction, and both the latter compounds were not completely effective against engorging ticks, and engorged or partially engorged specimens were observed at each post treatment inspection. Supona exerted its rapid lethal effect regardless of the state of engorgement of the parasite. These field observations complement the findings of Baker & Shaw[4] and Shaw Baker[7] in '*in vitro*' experiments with engorged female ticks. The inference is that Supona will be more efficient than other materials at reducing farm tick burdens, as it is able to cut off the tick life cycle at almost any stage. Only moulting larvae and moulting nymphs seem to have any protection (Fig. 1 and 2). This avails them little, for after the fourth spraying at Riverdale, no further adult or nymphal blue ticks were seen, nor did nymphal red ticks reappear.

Reference to Table 3 and Figure 6 reveal that the behaviour of both Bont and Brown Ear Ticks to 0.25% Toxaphene differed on the two farms, Caprice and Begha Mouth. Baker & Shaw[4] established that the Brown Ear Ticks at Caprice are toxaphene resistant but, unfortunately, were not able to study the status of the Caprice Bont ticks. The history of dipping at Begha Mouth shows that toxaphene has never been used on the farm and the probability is that tick species on this farm are, as yet, completely susceptible to Toxaphene. In support of this theory Toxaphene achieved excellent control over heavy Bont tick and moderate Brown Ear Tick infestations at Begha Mouth and showed that against susceptible species of multi-host ticks it is of great value. Furthermore it demonstrated the prolonged residual action which has made toxaphene such a valuable field ixodicide over the past fifteen years. Supona has a more rapid action but at the same time does not possess the same persistency. This trend was also detected at Caprice.

Extended weekly sprayings at Riverdale followed by Whole Blood Cholinesterase determinations seven days after treatments (Fig. 7) endorsed the findings of Pickering[9] and Palmer[8] as to the safety of this compound when applied topically to bovines.

The results indicate that 0.05% Supona and 0.05% Delnav have similar long term effects on cholinesterase levels; Delnav has been widely and safely used for treating cattle for several years.

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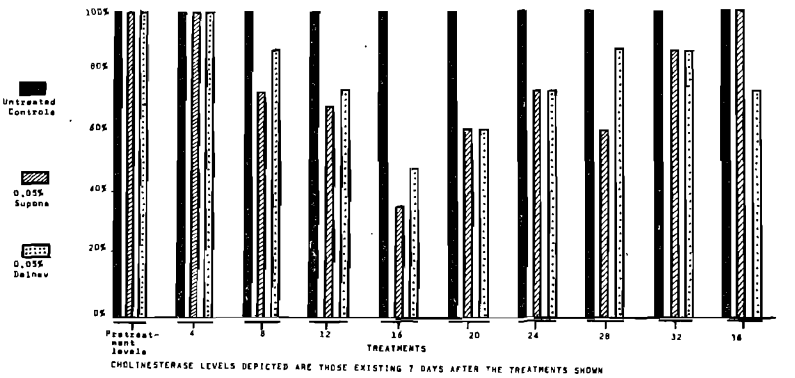
FIG. 1. WHOLE BLOOD CHOLINESTERASE DETERMINATIONS - RIVERDALE.
39 CONSECUTIVE WEEKLY TESTS. EVERY FOURTH TEST SHOWN



CHOLINESTERASE LEVELS DEPICTED ARE THOSE EXISTING 7 DAYS AFTER THE TREATMENTS SHOWN

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BOOK NEWS

South Africa's greatest revenue earner amongst the livestock is the sheep, and as such is receiving increasing attention from the veterinary profession. A thorough knowledge of its anatomy is therefore essential. A valuable aid for such a study is THE ANATOMY OF THE SHEEP by N. D. S. May, which is an excellent guide to the dissection of the sheep. Its 369 pages include comparative tables of the organs of domestic animals. R6.75.

A new book which will prove to be of great assistance in canine and feline orthopaedic surgery is AN ATLAS OF SURGICAL APPROACHES TO THE BONES OF THE DOG AND CAT by Piermattei & Greely. It is an atlas planned to show the veterinary student and clinician how to expose specific skeletal structures in the dog and cat for further surgery. 132 pp. Profusely illustrated by line drawings; R6.90.

Another new publication designed for the student and practitioner is CLINICAL DIAGNOSIS OF DISEASES OF LARGE ANIMALS by W. J. Gibbons. This incorporates the principles acquired by the author during 40 years' practice and teaching of veterinary medicine. It includes material on the physical examination of the eye, genital examination of the male and female, pregnancy diagnosis, examination for infertility, and clinical laboratory procedures that can be done by the practitioner in the field or at his laboratory. 257 pp.; 78 figs.; R8.35.

Up to the present there has been no comprehensive book on horses in South Africa. This void has now been filled by Pamela Struben in collaboration with people from every section of the riding community. They have produced HORSES AND RIDING IN SOUTHERN AFRICA. This is printed on high quality paper, well bound and has numerous excellent photographs covering every facet of horses and riding in this country. 287 pp.; R8.50.

The present day practising veterinarian cannot possibly subscribe to all the scientific journals containing articles that may be of interest to him.

To provide for his requirements an international journal, CHIRURGIK VETERINARIA, has been founded with the approval of the World Veterinary Association. This is published in three languages, namely German, English and French, and contains abstracts of articles that may be of value and have appeared in journals throughout the world. These cover all aspects of veterinary surgery, including general surgery, operative surgery, special surgery, ophthalmology, anaesthesiology and roentgenology. It is published quarterly and the subscription, including postage from Germany, is R21 per year. We shall be pleased to send a specimen copy and further information to anyone who may be interested.

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REVIEW

"Muscles of the Ox". BUTTERFIELD, R. M. AND MAY, M. D. S.:
University of Queensland Press, St. Lucia, Queensland, 1966. 164 pages.
11 Plates in Colour: 24 Text Figures: A.$8.50.

In the preface the authors state "This work, in which a description of the muscles of the commercial beef carcase has been compiled, will make possible uniform identification and description of these structures in future research". It is primarily aimed at the "great many workers in the field of meat and animal production research" who "do not have a basic training in Veterinary Anatomy . . ." "It should also prove a useful addition to the limited range of books available to the student of veterinary anatomy". These statements sum up the character of this work.

The muscles of the hindquarter are described in the first part, together with those that extend into the forequarter, thus obviating repetition. The order of description is that in which the muscles are met with during normal dissection procedure, thus making the work very handy for the practical worker. Those wishing to compile a direction guide could find this aspect useful. Origins and insertions of the muscles are briefly but adequately covered — more adequately than in most current textbooks. The structure of each muscle is described in detail, clearly and succinctly, with particular reference to its visual appearance. This is augmented by illustrations in coloured plates, which, although somewhat on the small side (to combat cost of production) allow one to obtain a good visual image.

The 24 black and white drawings are neat, simple and similarly make for easy identification of the muscle in the carcase.

Also by means of clear coloured plates the exact areas of origin and insertion of each muscle on the bones of the appendicular skeleton are given. This feature will particularly appeal to students of veterinary anatomy; it will also prove useful as a quick reference to the veterinary anatomist, who will find here, as well as in the description of the structure, more information than can be gleaned from most textbooks.

The recording of the average weight of each muscle and its approximate percentage of total side muscle weight, provides a valuable basis for studies not only on carcase composition and yield, but also on conformation and growth of cattle.

The following appendices evaluate themselves:

i Comparative myology of the subgenera of the genus Bos (4½ pages).

ii Correlation coefficients and regression equations of weights of seventeen muscles and seven groups of muscles on total side weight.

iii Composition of United Kingdom commercial cuts (in terms of percentage of total muscle of cut represented by each muscle).

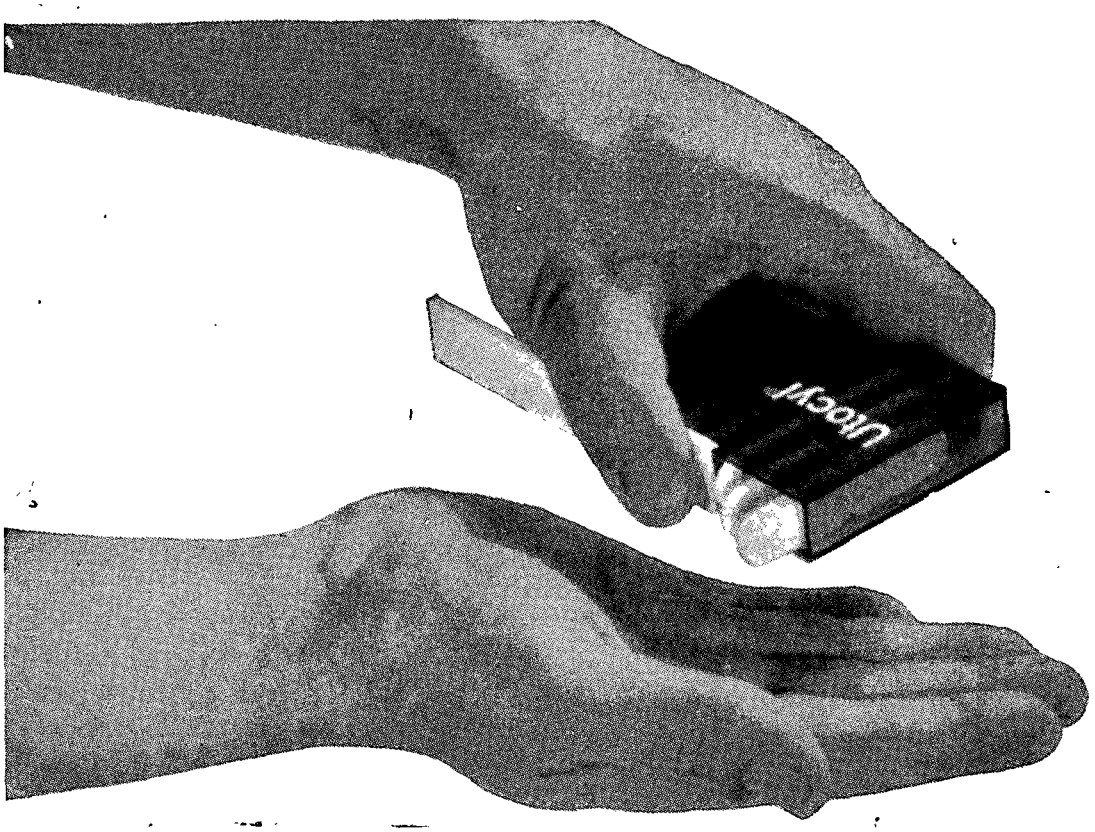
iv Percentage of each muscle in United Kingdom cuts.

v Weights of individual muscles in a typical carcase.

vi Revision of nomenclature (to make good the nomenclature used in the book, written before the revision of the *N.A.P. et B.N.A.* became available).

With its neat and handy format (14 x 22 cm) this work is a *must* for all workers in the field of meat production and a useful adjunct to veterinary anatomists, students of veterinary anatomy and to those concerned with meat hygiene.

— H. P. A. de Boom.



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WESTERN AUSTRALIA STATE PUBLIC SERVICE

DEPARTMENT OF AGRICULTURE — ANIMAL DIVISION

ANIMAL HEALTH LABORATORY VETERINARY PATHOLOGIST

(Permanent)

Salary: $A8,820 (gross) per annum.

Qualifications: Basic veterinary qualification registerable in Australia. Considerable graduate training required in veterinary pathology in the broadest sense including parasitology, biochemistry, microbiology and serology. Written proof of ability in research highly desirable.

Duties: Directly responsible to the Chief of the Animal Division for the administration and work of the Animal Health Laboratory. General supervision and responsibility for diagnostic and research activities in all aspects of animal health and disease in Western Australia.

Transport: Reasonable amount allowed for transport of appointee and dependent family to Western Australia, provided bond entered into to serve the State for period of three years.

Conditions of Service: Superannuation benefits, three months' long service leave after seven years' continuous service, cumulative sick leave entitlements and other general conditions applicable to permanent public servants.

Applications stating age, qualifications and experience accompanied with the names of two references, should be addressed by 12th November, 1966, to —

Public Service Commissioner,
184 St. George's Terrace,
Perth,
WESTERN AUSTRALIA.