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BLINDNESS AND ENCEPHALOPATHY CAUSED BY *HELICHRYSUM ARGYROSPHAERUM* DC. (COMPOSITAE) IN SHEEP AND CATTLE

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Abstract

BASSON, P. A., KELLERMAN, T. S., ALBL, P., VON MALTITZ, L. J. F., MILLER, E. S. & WELMAN, WILHELMINA G., 1975. Blindness and encephalopathy caused by *Helichrysum argyrosphaerum* DC. (Compositae) in sheep and cattle. *Onderstepoort J. vet. Res.*, 42, (4), 135–148 (1975).

An outbreak of amaurosis and paresis was observed amongst sheep, and occasionally cattle, which had been grazing on pastures consisting mainly of *Helichrysum argyrosphaerum* DC. A similar syndrome was produced by feeding the suspect plant to sheep, thereby providing proof of its toxicity. Although none of the sheep became blind and only one developed paralysis, typical spongy lesions were detected in the brains and optic fasciculi of all the experimental animals. The lesion had specific predilection sites, such as the white matter around the lateral ventricles, the optic tracts plus chiasm, the pyramidal tracts and the *brachium pontis*. Enlargement of the optic fasciculi furthermore gave rise to malacia, papilloedema and retinal changes.

Some aged sheep developed cataracts approximately 2–3 months after the initial outbreaks of amaurosis had occurred. Circumstantial and histopathological evidence suggests that the cataracts may be due to chronic *Helichrysum* poisoning, but this could not be confirmed in the present investigation.

Résumé

BASSON, P. A., KELLERMAN, T. S., ALBL, P., VON MALTITZ, L. J. F., MILLER, E. S. & WELMAN, WILHELMINA G., 1975. *Cécité et encéphalopathie dues au* Helichrysum argyrosphaerum *DC (Compositae) chez le mouton et le bovin.* Onderstepoort J. vet. Res, 42, (4), 135–148 (1975).

Les auteurs rapportent l'apparition d'une amaurose et d'une parésie chez et parfois bovins sur pâturages dont Helichrysum argyrosphaerum DC *constitue la plante principale. L'alimentation expérimentale de moutons avec cette plante a suscité la même syndrome, ce qui a confirmé sa toxicité. Tandis que aucun de ces animaux était atteint de cécité et un seul mouton a développé une paralysie, les auteurs ont pu démontrer des lésions de spongiosité, typiques de cette encephalopathie, dans le cerveau et le tractus optique de tous les animaux d'expérience. Les lieux de prédilection de cette lésion sont la matière blanche autour des ventricules laterals, le tractus optique, les faisceaux pyramidals et la* brachium pontis. *Un grossissement du tractus optique entrâine un amollissement du cerveau, un oedème papillaire et des altérations de la rétine.*

Des vieux moutons ont manifesté une cataracte à peu prés 2 à 3 mois après l'apparition de la cécité. Les données circonstancielles et pathologiques font soupconner que les cataractes sont dues à l'intoxication chronique à Helichrysum, *supposition pas encore confirmée lors de cette enquête.*

Introduction

Plants of the genus *Helichrysum* are widely used for domestic and medicinal purposes by the indigenous peoples of Southern Africa (Watt & Breyer-Brandwijk, 1962), but little is known about their toxicity.

The following species are thought to be toxic: *H. blandowskianum* (McClennan, 1938), *H. apiculatum* (cited by Pammel, 1911), *H. diosmifolium* and *H. lucidum* (Hurst, 1942) in Australia, and *H. cephaloideum* (Van der Walt & Steyn, 1940) in South Africa.

Two South African species were tested for toxicity with negative results, namely a *Helichrysum* sp., probably *H. krausii* (Steyn, 1929); and *H. nudifolium* (Whelan & Whitaker, 1952).

McClennan (1938) tested the toxicity of *H. blandowskianum* by dosing crude extracts of the plant to sheep and by administering the extracts orally and intravenously to rabbits. Within an hour of dosing a combination of hydrochloric acid, ether and alcohol extracts to a ewe, it became blind, suffered severe respiratory distress and died. The *post mortem* examination revealed a pale and friable liver, congestion of the anterior lobes of the lungs, froth in the trachea, and subendocardial haemorrhages. Although some extract was apparently dosed into the lungs, the resultant lung condition was not considered serious enough to cause sudden death. A combination of the ether and alcohol fractions produced similar signs and clonic spasms in a lamb which died within 5 h of being dosed. The autopsy features included general venous congestion, hydropericardium and haemorrhages in the heart, a dark and swollen liver and nephrosis. The hydrochloric acid fraction was not toxic. Pullar (1939), on the other hand, failed to induce poisoning with 2 kg of dry *H. blandowskianum* plants administered to a sheep in 14 days.

Early in November 1938, Van der Walt & Steyn (1940) poisoned a 39 kg sheep with 600 g of *H. cephaloideum* obtained from Bathurst, Cape Province. The clinical signs manifested on the day after dosing were apathy, diuresis, ruminal stasis, diarrhoea, tachycardia and polypnoea. Later severe constipation set in and the sheep died on the 20th day after being injected with carbamylcholine chloride. The main *post mortem* features were oedema of the lungs, gastrointestinal stasis, hyperaemia of the abomasum and small intestine, and fat necrosis.

Juritz (1914) investigated the toxicity of a plant, tentatively identified as a *Helichrysum* sp., in connection with the death of a woman in 1908. Tests on a dog and guinea-pigs indicated that the plant was a depressant, an emetic, and a slight purgative, but Juritz did not regard it as being particularly toxic. He also reported on the deaths of 2 people who died in 1912 after drinking a tea, brewed presumably from *H. serpyllifolium*. The plant, which had no known toxic properties, could not be incriminated in the fatalities.

Steyn (1929) dosed 350 g of *Helichrysum* sp. (probably *H. krausii*) to a sheep without any toxic effect. Negative results were also obtained by Whelan & Whitaker (1952) when they injected infusions and extracts of *H. nudifolium* into the ventral lymph sac of clawed toads (*Xenopus laevis*).

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H. argyrosphaerum has long been suspected of poisoning stock in South Africa but, although the plant was tested twice for toxicity, this suspicion could not be experimentally confirmed. On the first occasion Van der Walt (1944) dosed 3,3 kg of *H. argyrosphaerum* from Windhoek to a 27,3 kg sheep with a negative result. The second investigation was prompted by an unexplained outbreak of stiffness and posterior paresis and/or paralysis amongst cattle in the Gobabis and Windhoek areas of South-West Africa, during September 1968. The outbreaks started when cattle were put on pastures consisting predominantly of *Helichrysum* and stopped when they were removed. T. W. Naudé (Onderstepoort, personal communication, 1973) dosed dry plants, composed mainly of *H. argyrosphaerum,* with some *H. lepis,* from the affected farms, to 2 sheep. One sheep received 11,9 kg of the dry plants in 28 days and the other 12,3 kg in 30 days. No ill effects were observed and the sheep were discharged from the experiment without *post mortem* examination.

In this paper circumstantial and experimental evidence will be presented that *H. argyrosphaerum* causes paresis, paralysis, blindness and encephalopathy in sheep.

History of Field Outbreak

During August, September and October 1972 (late winter and spring) outbreaks of blindness, sometimes associated with paresis or paralysis, were reported amongst ruminants on several farms in the southern and central areas of South West Africa. An investigation revealed that the blindness was of a non-inflammatory, amaurotic type, characterised by mydriasis. It affected sheep more commonly than cattle. The morbidity varied from 1–29% and, although mortality was low, practically all the animals had to be slaughtered eventually because of a hopeless prognosis. Outbreaks were confined to overstocked farms or camps where the grazing consisted mainly, or sometimes almost exclusively, of a luxuriant flowering stage of *H. argyrosphaerum* ("sewejaartjies"). Apart from overgrazing, it was evident that droughts and late autumn rains had favoured the growth of this composite which is usually regarded as an excellent fodder plant.

At the beginning of November, a second type of blindness, caused by cataracts, made its appearance on most of these farms, as well as on 3 other farms where the amaurotic type had not been recorded. In each case *H. argyrosphaerum* was a prominent or pre-dominant plant on the spring pasture. Exceptionally large numbers of the pioneer plant *Requiena sphaerosperma* ("springbokopslag") were also noticed on some of the farms.

By the end of February 1973, blindness of one or both types had been recorded on 20 farms in 4 districts.

Field Investigation

The disease syndromes were studied on several farms.

Clinical signs

The first syndrome of blindness, that of amaurosis in sheep, was characterised by complete or partial bilateral mydriasis. Both eyes were usually affected to the same degree but in exceptional cases the pupillary reflex of one eye was either decreased or normal. The ocular media were transparent and normal, but ophthalmoscopic examination revealed papilloedema and congestion of the vessels in the central part of the fundus. Both sexes were affected irrespective of age, but on most farms a bias towards younger animals (2–4 tooth stage) was noticed.

In addition to blindness, signs of nervous disorder were apparent in 0–24% of the affected animals. The nervous signs took the form of nystagmus in 11% of cases, and paralysis or paresis in another 11%. Only one exception was encountered which had paresis in the absence of blindness. Other nervous signs included ataxia, chorea of the head and neck muscles, and a peculiar star-gazing or oblique posture of the head, accompanied by circling movements. Some animals had a mild febrile reaction.

The disease had a prolonged course and the prognosis was poor. Although a few cases were purported to have recovered, these claims could not be verified. Mortality was low and only a few of the recumbent animals died within a week. Most of the sheep, however, remained blind and eventually had to be slaughtered.

On a few of these farms, where both sheep and cattle were kept, a small number of young oxen aged between 2–3 years developed stiffness, lameness and paresis. The highest incidence of this syndrome was 18%. One or more of either front or hind legs, or both, were affected. The fore limbs were kept in extension by some animals, while others refrained from extending or using the affected limbs at all. Locomotion seemed to be painful and lameness could be precipitated by chasing the oxen. Several animals became recumbent as a result of this treatment, but they usually recovered within 1 or 2 weeks. Occasionally diffuse swellings were noticed between the elbow and carpal joint. Nervous signs and blindness were never encountered on the 2 farms with the highest incidence of the disease, but a few cases of blindness and paralysis were reported amongst calves on other properties. A small number of unidentified *Geigeria* plants grew on 2 of the farms.

The 2nd syndrome of blindness in sheep started about 3 months after amaurosis was noticed. It was characterised by cataracts which were sometimes associated with paresis, paralysis or circling movements. In the majority of cases the pupillary reflex, although reduced, was still present, but sometimes this reflex was absent. Only sheep were affected, and cataracts were encountered only in adult or aged animals. A few amaurotic sheep also developed cataracts, but cataracts also occurred amongst sheep on farms with no history of amaurosis.

A syndrome of paresis, very similar to that of the oxen, affected 25% of a flock of 440 sheep on 1 farm. Again the paresis was precipitated by handling. Most of the sheep recovered within an hour or 2, but some remained ataxic for 3 days. A few of the paretic animals also suffered from amaurosis, but, apart from blindness, this syndrome closely resembled vermeersiekte. However, although *Geigeria* plants, which cause vermeersiekte (Du Toit 1928; Steyn, 1949), grew on this farm, the number of plants seemed inadequate to cause such a severe outbreak. *Helichrysum* species, on the other hand, were abundant. One sheep developed cataracts 2 months after first becoming paretic.

Goats (when present) seemed to be resistant and only 1 unconfirmed case of blindness was reported.

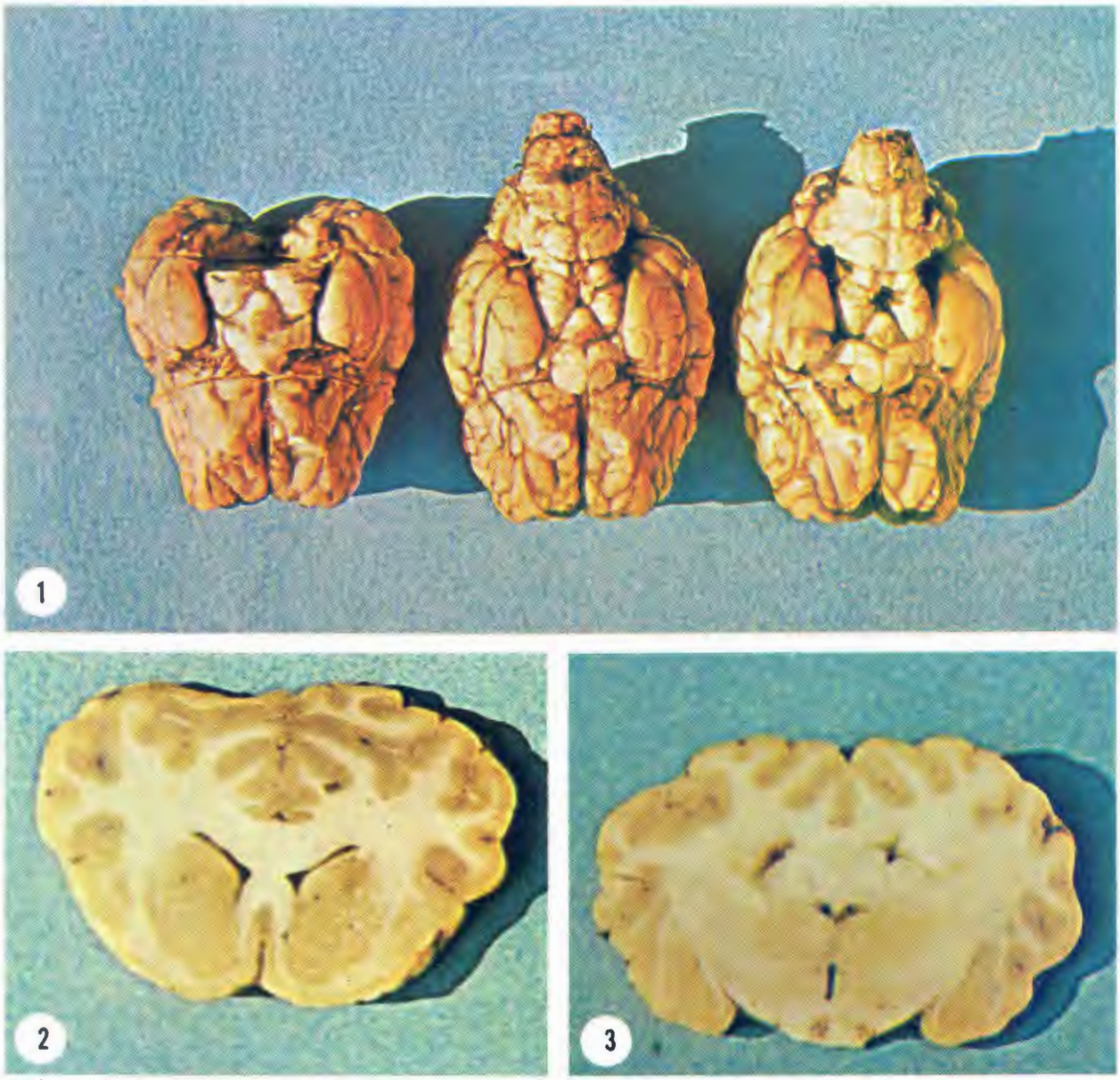

FIG. 1 Various degrees of chiasmal swelling and increase in width between pyriform lobes
FIG. 2 and 3 Swollen white substance, especially in peri-ventricular zone of affected brain

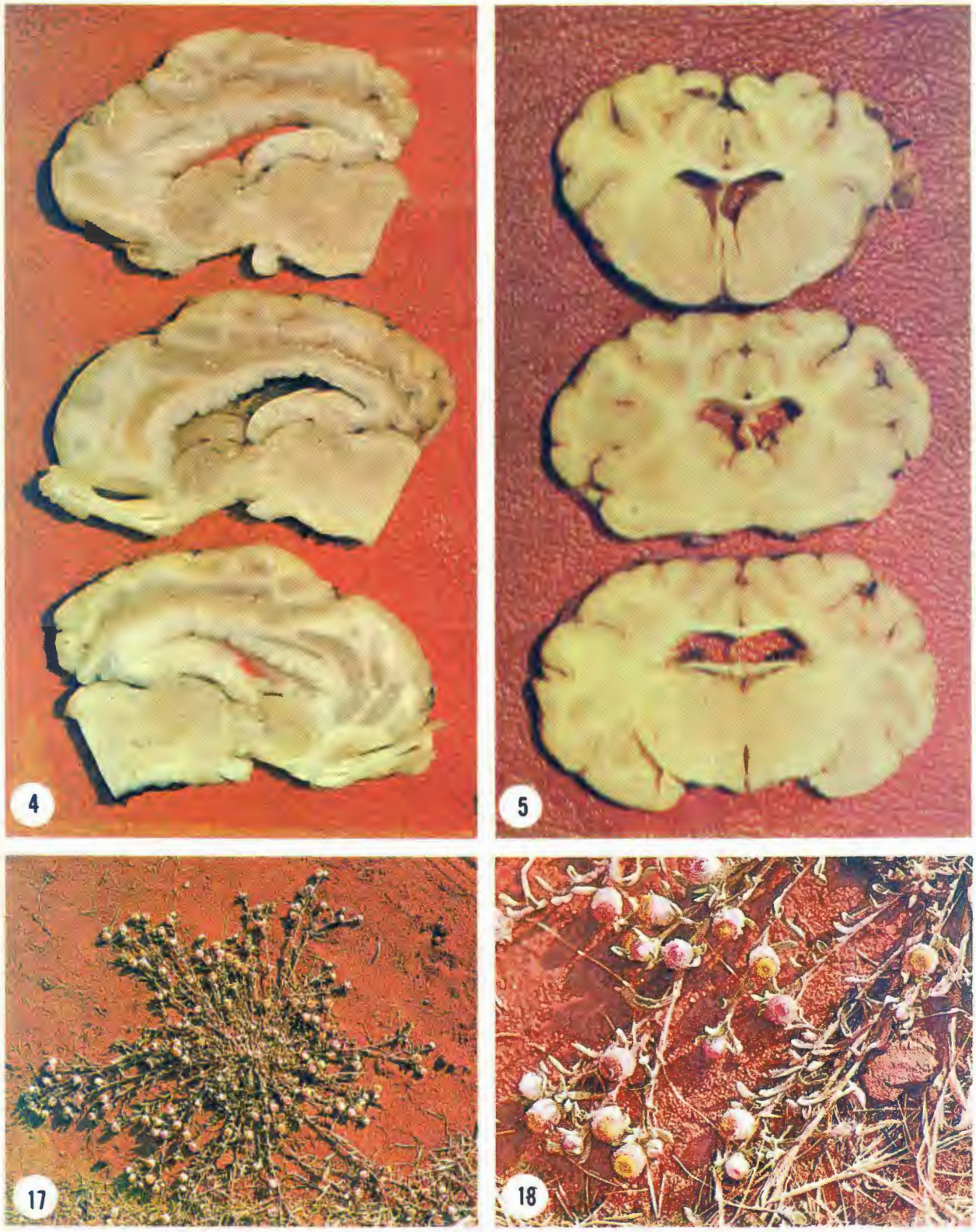

FIG. 4 Affected brain, illustrating swollen parts and undulations in *corpus callosum*
FIG. 5 Brain of normal (control) sheep

FIG. 17 and 18 *Helichrysum argyrosphaerum:* plant and flowers

Macroscopic pathology

Complete autopsies were done on 12 sheep and a 4-tooth ox. The heads of another 7 sheep, including those of 4 aged animals with cataracts, and 1 amaurotic calf were examined. The other animals were either young or adult sheep and, except for 1 sheep that died naturally, all were slaughtered.

Amaurotic cases (sheep and 1 calf)

Eyes: Swelling of the fundus and optic disc was noticed in several animals. The optic fasciculi and the optic chiasm were usually swollen and more fragile than normal. (Note: This change was always easier to detect after fixation.) The swelling was more conspicuous in localised areas of the optic fasciculi which coiled and buckled as a result of expansion. On section the lesions appeared greyish white and gelatinous, occasionally containing distinct white islets of unaffected tissue. In the calf these lesions were accompanied by congestion and haemorrhages in the optic fasciculi. Swelling of the optic chiasm gave the impression that the optic fasciculus was compressed at the optic foramen, but this was evidently due to swelling rather than lesions in the optic foramina.

Brain: Apart from chiasmal swellings, changes on the external surface were usually not easily detectable. In advanced cases, changes indicative of swelling and oedema, such as a decrease in consistency and flattening of gyri or lengthening of the distance between the piriform lobes at the base of the brain (Fig. 1), were sometimes noticed. On coronal or sagittal section of the fixed brain, the white matter around the lateral ventricles (periventricular areas) was distinctly swollen, gelatinous, and off-white in colour (Fig. 2 and 3; cf. normal brain of control sheep, Fig. 5) and the ventricular surface of the *corpus callosum* and *centrum semiovale* was conspicuously undulated (Fig. 4). Other periventricular areas that were swollen included the *septum pellucidum,* hippocampus (*fimbria, alveus,* commissure) and fornix. Frequently the *brachium pontis* was affected. One fatal case had a prominent unilateral swelling of the midbrain.

Liver: The livers of some sheep were mottled in appearance, with light pale-brown zones situated either peripherally or centrilobularly, and in such cases the consistency was slightly decreased. Bile stasis occurred in the fatal recumbent case.

Kidneys: Renal lesions were also an inconstant finding, but when these were present the kidneys had a slightly variegated greysish-brown colour pattern and a mildly decreased consistency.

Muscles: Slight localised degeneration was observed in the muscles of the limbs of a few recumbent sheep.

Cataractous sheep

Sheep with cataracts did not reveal any appreciable swelling of the optic fasciculi or chiasm, but the periventricular areas were affected as described above.

Paretic ox

The 1 ox which was autopsied deserves special mention. No lesions were detected in the eyes, optic-fasciculi, brain, liver and kidneys, but wide-spread lesions were present in the skeletal muscles. These muscles included those of the limbs, the *longissimus dorsi* and *psoas* group. The affected portions were pale greyish-brown, sometimes with dull greyish-white spots, and, in certain muscles, such as the *longissimus dorsi* and *psoas minor,* ruptures with haemorrhages, or even haematomas, were present. The lesions were bilateral, but usually not symmetrical.

Histopathology

Specimens of various organs and tissues from 24 sheep and 1 calf with amaurosis, 14 sheep with cataracts, and 1 ox with paresis, were collected or submitted in either buffered or unbuffered 10% formalin. The brains, however, were suspended in approximately 50% formalin. Suitable tissue blocks from these specimens were embedded routinely in paraffin wax, sectioned at 3–5 μm thickness and stained with haematoxylin and eosin (HE). Special staining techniques, such as Luxol fast blue (LFB), periodic acid-Schiff (PAS), PAS Alcian blue and Alcian blue at pH 2,5 (Anon, 1960) were occasionally employed on the brain, and oil red O (ORO) on livers and kidneys.

The organs and tissues of the amaurotic bovine case (calf) included eyes, optic fasciculi, optic chiasm, brain, spinal cord, gasserian ganglion and trigeminal nerve. The changes in these sections were similar to those of sheep and are consequently dealt with under the same heading.

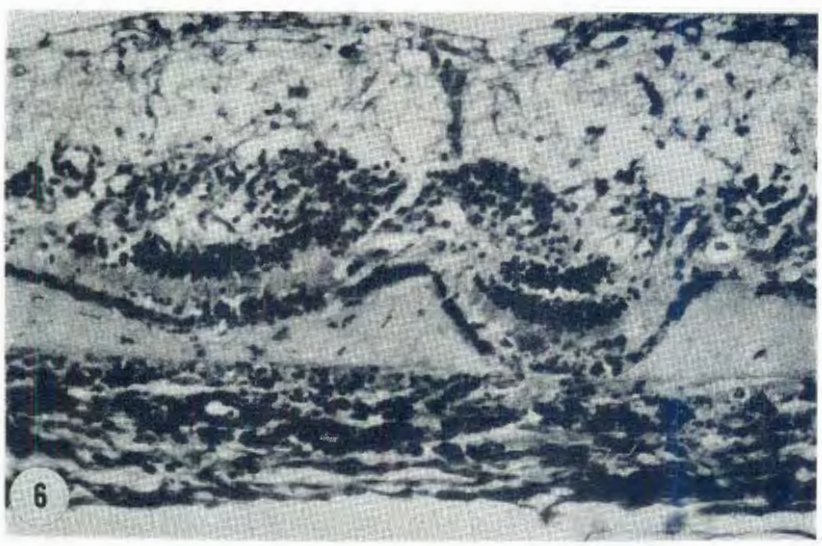

FIG. 6 Retina and choroid: Oedema and congestion, patchy distorting necrosis and porosity of nerve fibre layer. HE×200

Eyes

(a) *Amaurotic sheep and calf:* The choroid and retina, especially in the region of the fundus and optic papilla, were usually mildly to prominently congested and oedematous (Fig. 6). Very mild to mild haemorrhages occurred within these 2 layers and sometimes within the vitreous humor. Appreciable buckling of the retina near the optic disc was observed in some animals. A progressive necrotic lesion, characterised by the disappearance of various layers, occurred in the retina. It commenced in the layer of rods and cones near the optic papilla and progressed anteriorly and towards the innermost layers up to, and occasionally even including portions of, the inner nuclear layer (Fig. 6). The lesion was frequently patchy, especially towards the innermost layers, with the result that it was often encountered at various intervals in the retina. Ignoring the fact that retinas were not always present in the sections, an approximate incidence of 40% retinal lesions was encountered.

The nerve fibre layer of a few animals revealed a mild porosity and very mild haemorrhages near the optic disc. Segmental thickening of the wall of one central vein, due to the accumulation of a basophilic mucoid substance in the optic papilla, was seen in 1 sheep.

(b) *Cataractous sheep:* The lesions in the lenses of the 14 sheep affected with cataracts were confined mainly to the epithelium and cortex, but the nucleus was also frequently involved. However, since all the sheep were aged, the presence of possible concomitant, coincidental, senile changes cannot be disregarded.

Proliferation, swelling and eventual degeneration and necrosis of the epithelial cells occurred in association with various degenerative and necrotic lesions in the cortex. These included homogenisation and acidification or the formation of a less dense, slightly basophilic substance in cracks and clefts. Morgagnian globules (Hogan & Zimmerman, 1962) of varying colour intensities were frequently present and clear clefts were occasionally encountered. In those cases where the cracks with the morgagnian globules extended into the nucleus, the nuclear tissue was intensely acidophilic and homogenised. Fibrous metaplasia of the epithelium with eventual hyalinisation was found in 2 animals.

Optic fasciculus

A very pronounced bilateral *status spongiosus* was present in all the amaurotic cases. Malacia with gitter cell mobilization (Fig. 9 and 10) occurred in all animals except 3 sheep and 1 calf, which revealed lysis only. Cavities, which were considerably larger in size than the vacuoles in the purely spongy lesions and evidently due to lytic necrosis, were noticeable in some animals (Fig. 11). The malacic changes were usually within and close to the point of buckling, and were apparently a result of compression of the fasciculus and blood vessels. Hence congestion and haemorrhages, notably in the calf, as well as segmental mucoid changes and proliferation of the intima of some arteries and some veins around the optic fasciculi, were observed in a few sheep. Very mild, localized, mixed cell, perivascular infiltration and proliferation were seen in 20% of the cases, and fibrosis and gliosis in 28%.

Only 50% of the sheep with cataracts had either a very mild or mild *status spongiosus,* and no malacia was present. Gliosis was noticeable in 25%.

Optic chiasm

In the amaurotic cases a *status spongiosus* was invariably present, but it was often milder than in the optic fasciculi. A very small number of gitter cells were seen in approximately a third of the animals, and larger cavities than those described in the optic fasciculi occurred in a few sheep.

Eight optic chiasms from cataractous sheep were examined, and all of them had very mild to moderate spongiosity without malacia.

Brain

The most outstanding lesion was a bilateral symmetrical *status spongiosus* of the white matter (Fig. 7, 13, 14, 15 & 16) which was asymmetrical and much more pronounced in the midbrain and thalamus of the fatal case than in the other animals. Both amaurotic and cataractous cases were identical as far as the type of lesion, predilection sites and distribution were concerned, the only difference being that some of the latter group showed milder lesions.

A definite preferential sequence existed, but this sequence was masked in very advanced cases where the entire white substance was affected. The periventricular areas (*vide supra*) (Fig. 7) and the *brachium pontis* had the highest degree of prevalence and severity. The former included the hippocampus (fimbria, alveus and commissure especially), *corpus callosum,* subcallosal tract, fornix, *centrum semiovale*—involving prominently the optic acoustic and auditory radiations—and the *septum pellucidum.*

Next in order of preference and severity were the optic tracts, lateral geniculate and some pathways of the pyramidal and extra-pyramidal tracts. The pyramidal system, however, was more regularly involved than the extra-pyramidal and the pathways concerned were the central cerebral white matter, cerebral peduncles, internal capsule, pontile tracts and pyramids. The latter were invariably mildly or very mildly affected.

Areas found to be somewhat less vulnerable were the thalamic tracts, the central cerebellar white matter and the *corona radiata* of the cerebral white matter. The convolutional (subcortical) and foliar white matter and the midbrain were noticeably affected only in very advanced cases and very mildly affected in moderate cases. Other areas occasionally found to be involved, but which could not be surveyed in all the animals, were the rostral commissure, restiform body, medial geniculate and the medial longitudinal fasciculi.

The vacuoles were invariably clear and did not appear to contain any material, but occasionally a faint tint suggestive of a tinctorial substance was seen in HE sections. Very mild glial swelling was occasionally noticeable in mildly affected zones or near the periphery of lesions.

LFB stain failed to reveal unequivocal evidence of demyelination, but the lesions, owing to their state of spongiosity, did stain somewhat paler than the surrounding unaffected areas. Except for showing strands of an unknown, very pale staining material in some of the vacuoles, the other special stains failed to demonstrate mucopolysaccharides in this site.

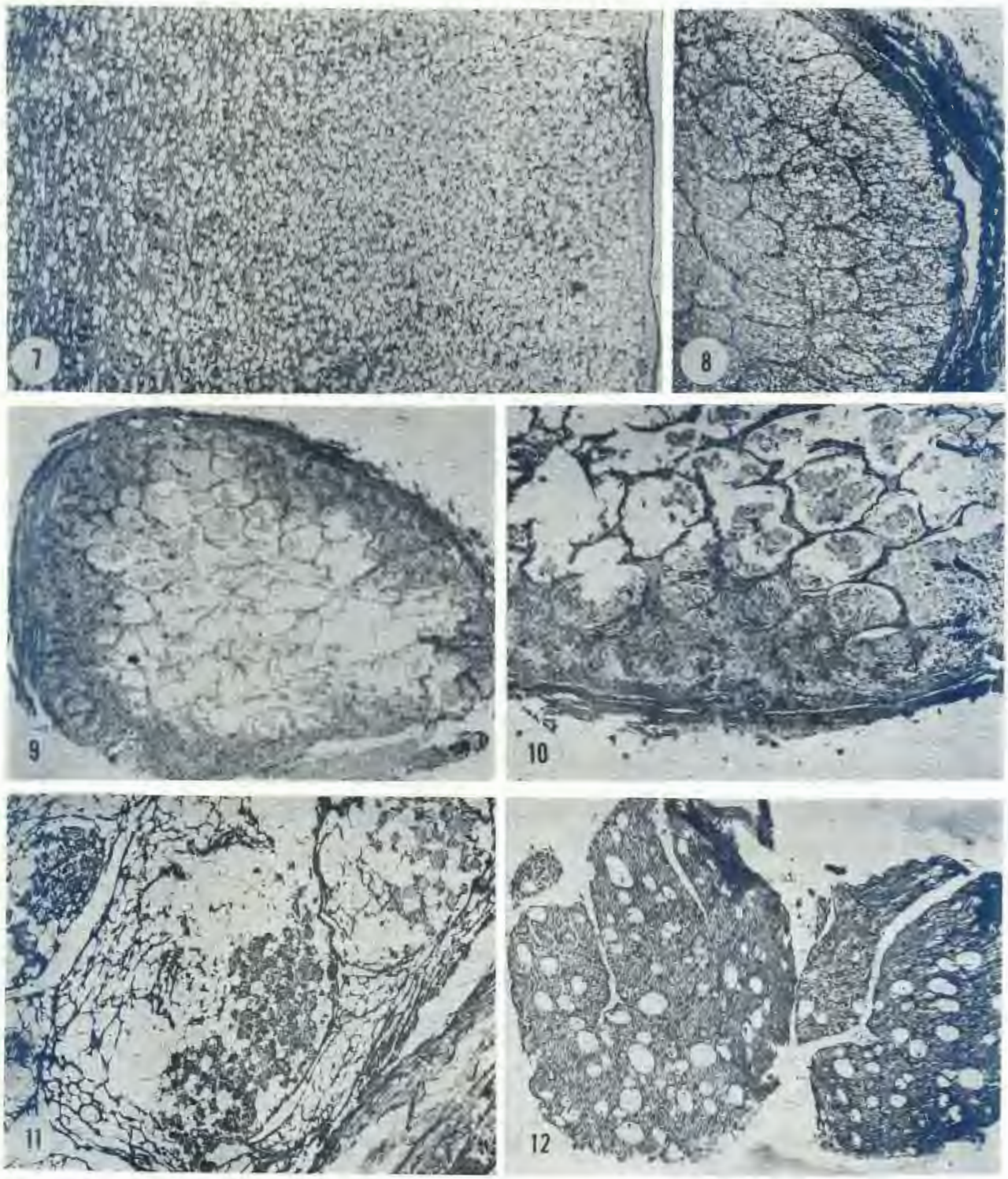

FIG. 7 Periventricular area (*corpus callosum*): *status spongiosus*. HE×75
FIG. 8 Optic fasciculus, showing a moderate *status spongiosus*. HE×35
FIG. 9 Entire optic fasciculus, showing malacia. HE×20
FIG. 10 Optic fasciculus: Malacic area. HE×35
FIG. 11 Optic fasciculus: Large cavities in association with aggregates of gitter cells. HE×75
FIG. 12 Nerve with mild spongiosity. HE×75

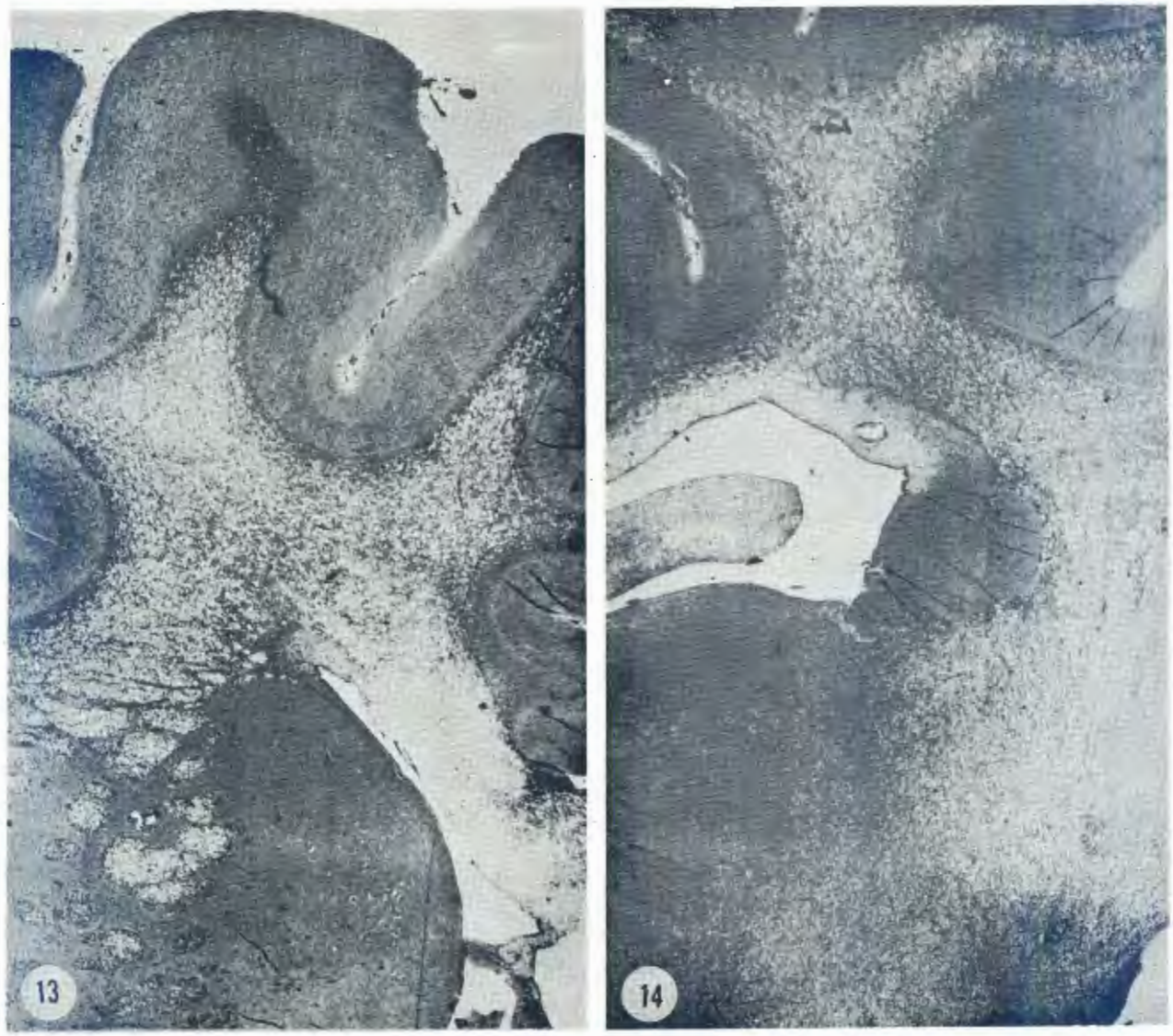

FIG. 13, 14, 15 and 16 Brain sections at very low magnification, showing various areas and degrees of spongiosity of the white matter. HE

Spinal cord

Tissues could not be examined from all the cases, but 40% of the available specimens from amaurotic animals and 1 cataractous sheep had spongy lesions, most of which were mild. The highest incidence was recorded in Lissauer's tract, the *fasciculus cuneatus* and *fasciculum gracilis*. Other affected areas were the ventral spinothalamic and ventral spinocerebellar tracts. In 2 animals a narrow peripheral zone of the white matter was also very mildly affected. The lesions usually occurred in all the segments of the cord.

Nerves

A mild spongiosity was seen in several nerves (Fig. 12), such as the trigeminus, intermuscular and spinal nerves of the amaurotic animals. As the nerves were not always examined, the precise incidence can not be given. Some of the myelin sheaths of one cataractous sheep were distended and contained either amorphous or granular eosinophilic material, while another nerve showed peculiar delicate fibrous configurations. Both changes were interpreted as being types of degeneration.

Other organs

(a) *Amaurotic sheep:* Either very mild or mild nephrosis occurred in approximately 40% of the animals. The lesions consisted mainly of fatty changes, as borne out by the ORO stained sections. Hyalin droplet degeneration was seen in 1 sheep. Fatty changes, sometimes more prominent than in the kidneys, as well as occasional cloudy swelling and a type of eosinophilic coagulation of the cytoplasm of hepatocytes, were present in the livers of about 60% of the cases. The latter change was characterised by the formation of a single large globule in each hepatocyte. This globule differed from hyalin globules by being less homogeneous, somewhat irregular or rough in outline and separated by a narrow clear space from the periphery of the hepatocyte. The prominent fatty changes seen in a few sheep (such as the fatal case) had a peripheral distribution, whereas in most of the mild cases these changes were centrilobularly situated. Very mild cloudy swelling of the myocardium was present in exceptional sheep. A seemingly unrelated coincidental, mild, localized, mononuclear myocarditis occurred in 1 sheep. Three sheep had mild

FIG. 15 and 16 See Fig. 13 and 14

localized muscular lesions, such as cloudy swelling, Zenker's changes of individual fibres, atrophy and mild localized sarcolemmal proliferation. In addition, mild vacuolarity was noticeable in the pancreas of 1 sheep.

(b) *Cataractous sheep:* Very mild fatty changes were present in the livers and kidneys of a few sheep. Additional mild hepatic changes seen occasionally were purplish brown pigmentation of the Kupffer cells (probably lipofuscin pigment) and proliferative biliary and fibrous changes in the portal areas. Two sheep, which originated from a camp containing both *Helichrysum* and *Geigeria* plants, had prominent myocardial and muscular lesions. Hydropic and suspected fatty degeneration and coagulative necrosis, along with focal disseminated areas of fibrosis, occurred in the heart. Fibrillar disintegration and replacement by a basophilic granular substance were present in portions of the skeletal musculature. The oesophagus was oedematous and contained a small number of either degenerated or necrotic fibres. One sheep had peculiar myocardial and muscular lesions, the fibres being vacuolated and containing small quantities of a reddish, purplish or golden brown substance. Both small and large vacuoles were present, the latter seemingly formed by coalescence of the smaller ones and probably arising from fatty changes followed by lipofuscin formation.

Histopathology of the paretic ox

The only ox that was autopsied did not have lesions in the eyes, brain, liver and kidneys, but a very mild localized spongiosity was noticeable in the optic fasciculus. The skeletal muscles, however, revealed very severe and wide-spread degeneration, necrosis, oedema and haemorrhages. Rupture of muscle fibres resulted in haematomas and, in some other areas, mild sarcolemmal proliferation, macrophage mobilization and regeneration were evident.

Trace Element Analys s

The most important feature of the trace element analysis (Table 1) was that the liver copper values of 4 cataractous sheep were elevated. *Helichrysum* plants had a copper content of 12 ppm.

TABLE 1 Trace element analysis of ovine and bovine liver specimens (wet basis) and dry *H. argyrosphaerum* plants collected during the field outbreak of blindness

Animal	Farm	Cu p.p.m.	Co p.p.m.	Mg p.p.m.	Mn p.p.m.	Fe p.p.m.	Zn p.p.m.	P %
Amaurotic sheep	A	69	11,2	241	5,0	156	82	0,16
Cataractous sheep	A	78	—	226	3,0	116	50	0,126
Cataractous sheep	A	118	—	232	2,6	116	48	0,123
Cataractous sheep	A	167	—	230	3,0	83	62	0,128
Cataractous sheep	B	530	11,5	120	3,2	190	108	0,21
Cataractous sheep	C	465	—	138	3,9	105	109	0,28
Cataractous sheep	D	240	—	110	3,3	165	75	0,39
Lame ox	E	16,6	13,1	157	5,2	152	118	0,20
H. argyrosphaerum	—	12	—	—	—	—	—	—

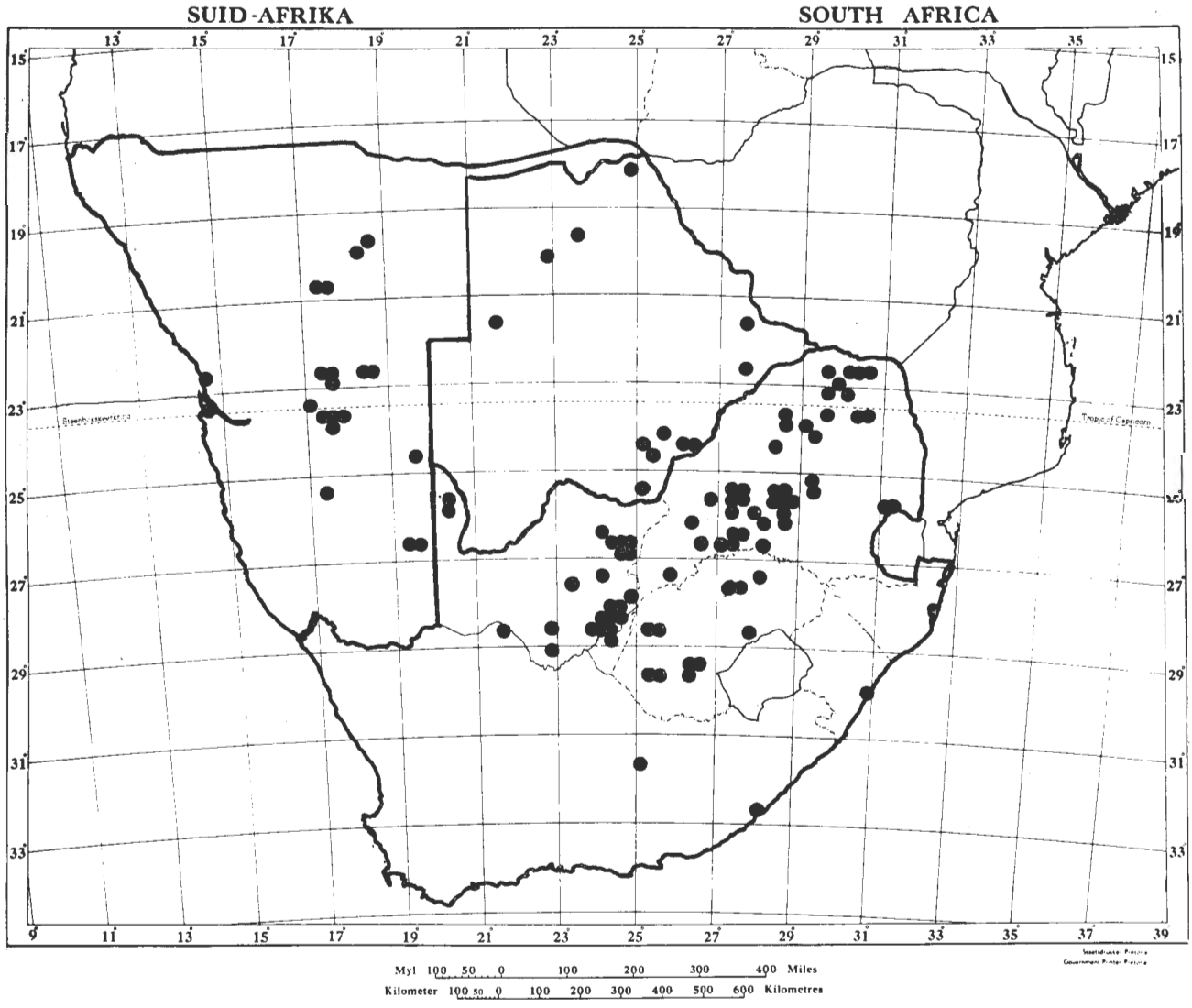

FIG. 19 Distribution of *Helichrysum argyrosphaerum*

DESCRIPTION AND DISTRIBUTION OF THE PLANT

Family: Compositae.

Name: Helichrysum argyrosphaerum DC.

Common names: Wild everlasting, "Poprosie", "Sewejaartjie".

Description (Moeser, 1910; Merxmüller, 1967).

A prostrate annual, forming mats up to 50 cm in diameter, the branches often ascending up to 15 cm high. *Root* woody and somewhat thickened, long and simple. *Stems* numerous, radiating from the crown of the rootstock, half-herbaceous or suffruticose, slender, simple or branched, rather woolly. *Leaves* alternate, sessile, entire, up to 2,5 cm long; linear-oblong, obovate or spatulate, very pilose, grey-green, spreading horizontally. *Capitula* about 1 cm in diameter, sessile, solitary or a few together at the ends of the branches and branchlets, subglobose, subtended by leaves, heterogamous with about 200–300 yellow to brownish disc-florets. *Involucre* glabrous, bracts, membranous, imbricated in many rows, ovate-oblong, subacute or obtuse, erect or spreading, scarcely longer than the florets, outer bracts silvery-white, inner rosy to purple. *Receptacle* naked and flat. *Marginal florets* few, female, corolla-tube filiform, minutely toothed, ovary ellipsoid, style filiform, style-branches narrow-linear. *Disc-florets* bisexual, corolla-tube tubular, glabrous, 5-toothed, anthers linear, with a lanceolate appendage, ovary ellipsoid, style linear, style-branches hairy. *Achenes* papillose, pappus bristles in one row, free, scabrid, white. *Flowering time* throughout the year, but mostly from July to October.

The plant occurs in South West Africa, Cape Province, Natal, Orange Free State, Transvaal, Botswana and also further north into tropical Africa. It has been recorded in the following districts: *South West Africa:* Okavango, Grootfontein, Outjo, Otjiwarongo, Gobabis, Okahandja, Swakopmund, Karibib, Windhoek, Rehoboth, Maltahöhe, Gibeon, Keetmanshoop.

Cape: Gordonia, Vryburg, Kuruman, Barley West, Warrenton, Hay, Herbert, Kimberley, Prieska, Middelburg, Kentani.

Natal: Pinetown.

Orange Free State: Heilbron, Kroonstad, Boshof, Bloemfontein, Ficksburg, Fauresmith.

Transvaal: Soutpansberg, Potgietersrus, Pietersburg, Waterberg, Rustenburg, Warmbad, Groblersdal, Pretoria, Witbank, Middelburg, Barberton, Lichtenburg, Witwatersrand, Klerksdorp, Potchefstroom, Vereeniging, Bloemhof.

Botswana: Ngamiland, Ghanzi, Chobe, Francistown, Central districts, Gaborone, Kgatleng, Lobatse, Kweneng, Ngwaketse.

H. argyrosphaerum prefers red sand or sandy loams, but it will often grow in stony or even gravel soils. It is also rather common on calcarious soils and is occasionally found on turf or alluvial soil.

The plant can grow in exposed places, such as bare patches, cleared ground, old termite mounds, the banks of furrows and the northern aspect of hills. It is also often seen along railway lines, roadsides, on cultivated or fallow lands and disturbed ground. In addition 'sewejaartjies' commonly occur on flats, floors of pans, dunes, sandy, dry river beds, granite plains and dolerite kopjes.

It is found in grassveld with *Aristida, Schmidtia* and *Themeda* spp. and in bushveld with *Acacia, Terminalia, Boscia, Combretum* and *Colophospermum mopane* trees. *H. argyrosphaerum* is also often associated with xerophytic shrubs such as *Euryops* and *Rhigozum.*

This composite may become abundant wherever the veld is heavily grazed, but it is generally regarded as an excellent fodder crop for antelope, cattle and especially sheep.

TABLE 2 Mass of *H. argyrosphaerum* dosed daily to sheep at Onderstepoort

Dry material				Refrigerated green material			
Sheep 1 (live mass 38,5 kg)		Sheep 2 (live mass 53,0 kg)		Sheep 3 (live mass 36,0 kg)		Sheep 4 (live mass 31,5 kg)	
No. of consecutive days dosed	Daily dosage rate g/kg	No. of consecutive days dosed	Daily dosage rate g/kg	No. of consecutive days dosed	Daily dosage rate g/kg	No. of consecutive days dosed	Daily dosage rate g/kg
2	20	1	15	1	15	1	15
4	0*	1	20	4	20	4	20
7	15	4	0*	3	40†	3	40†
3	20	7	15	1	60†	1	60†
4	0*	3	20	2	30	2	30
5	15	4	0				
2	0*	3	15				
5	15	1	0*				
2	0	1	15				
7	15	2	0				
		5	15				
		2	0				
		7	15				

* Rumen impacted
† Administered in divided doses, am and pm

Experiments at Onderstepoort Veterinary Research Institute

Materials and methods

Green flowering *H. argyrosphaerum* plants from a toxic camp at Windhoek were flown to Onderstepoort on 30 August 1972. Upon arrival the consignment was divided into 2 parts: one part was refrigerated at 4 °C and the other dried in the shade for 5 days. The dry and refrigerated materials were separately milled and dosed per ruminal fistula to Merino sheep at the following rates (see also Table 2):

Dry plants

Sheep 1, a 4-tooth wether of live mass 38,5 kg, received 15,3 kg of the dry plants in 41 days. In a second experiment 20,5 kg of the same material was given to Sheep 2, a mature wether with a mass of 53,0 kg. After the dosing was completed, the sheep were kept under observation for 15 and 17 days.

Refrigerated green plants:

Sheep 3, a 4-tooth wether of live mass 36,0 kg, received 12,6 kg of the green plants in 11 days, and Sheep 4, a 4-tooth wether of live mass 31,5 kg, was given 10,8 kg of the green plant over the same period. Both sheep were kept under observation for 30 days after dosing was completed.

The sheep were fed on a standard Onderstepoort ration and examined daily for clinical reactions.

Periodically chemical pathological determinations were done on the blood. These included blood urea nitrogen, serum glutamic oxalacetic transaminase, serum glutamic pyruvic transaminase, bilirubin, total plasma proteins, glucose and serum calcium, sodium and potassium.

At the end of the observation period all the sheep were slaughtered for autopsy. Specimens from various organs were collected, fixed and prepared for microscopic examination as described earlier.

Results

Clinical signs and chemical pathological changes

Dry plants: The sheep that were dosed with dry *H. argyrosphaerum* plants reacted as follows:

Sheep 1: The most conspicuous clinical signs were progressive paresis and apathy. On Day 44, i.e. 3 days after dosing had ceased, the sheep was found in sternal recumbency. It could rise when prodded, but had difficulty in maintaining the upright position. The paresis gradually worsened until, on Day 48, the sheep could no longer rise unassisted. At this stage the animal still lay on the sternum but the legs were often held in unphysiological positions, e.g. with one hind leg extended backwards. By Day 55 the wether could barely lift its head from the floor.

The paresis was accompanied by growing apathy. The sheep gradually lost awareness of the surroundings, but, despite this 'dumbness', would compulsively consume food and water placed before it.

Other clinical signs included congestion of visible mucosae, transient icterus (Fig. 20), loss of mass (7 kg) and a terminal systolic cardiac murmur. Vision was not notably impaired.

Sheep 2: Apart from mild digestive disturbance, due to periodic ruminal impaction and very mild transient icterus (Fig. 20), no conspicuous clinical abnormalities were observed.

The most prominent changes in the blood chemistry of sheep 1 and 2 were a moderate elevation of the serum glutamic oxalacetic transaminase (SGOT) accompanied by mild transient bilirubinaemia when the transaminase level reached maximal elevation (Fig. 20).

Refrigerated green plants: The administration of green plants produced no apparent ill effects in Sheep 3 and 4.

Pathology

Sheep 1: Macroscopically the brain was very flabby, oedematous and friable. The periventricular areas were markedly swollen and semi-gelatinous in appearance, forming prominent undulations on their ventricular surface. Both the optic chiasm and optic tracts were also mildly swollen. The sheep was cachectic, and localized intermuscular oedema as well as a few localized muscular haemorrhages and areas of degeneration were observed. A moderate hydropericardium and mild hepatic fibrosis were also present. These lesions were all confirmed by the histopathological examination. A most marked *status spongiosus* was present in the brain. Both in type and distribution the lesions were identical to those seen in cases of amaurosis and cataracts, the only exception being that the lesions were so marked and wide-spread that even some of the nuclear areas in the midbrain and thalamus were mildly affected. A similar moderate lesion occurred in the optic fasciculis (Fig. 8). The periphery of the spinal cord was very mildly vacuolar. The skeletal muscles had areas of congestion, haemorrhages and oedema, accompanied by degeneration and necrosis. Mild spongiosity was present in the trigeminal and intermuscular nerves. The liver showed very mild fatty changes, localized mononuclear cell infiltration and fibrous proliferation in both portal and centrilobular areas. Mild lipofuscinosis was also present. The eyes and all the other tissues were normal. *Sheep* 2: It revealed swelling around the lateral ventricles which proved to be a severe *status spongiosus*. This was identical to that of natural amaurotic cases in both type and pathoclisis. The periventricular areas, lateral geniculate, optic tracts, optic chiasm, cerebral peduncles, central cerebral white matter, internal capsule and *brachium pontis* were affected. Very mild lesions occurred in the convolutional white matter and cerebellum. Portions of the optic fasciculi were distinctly affected, but malacia was never seen. Mild proliferative reactions were noticeable in the portal areas of the liver, probably due to the presence of *Stilesia hepatica.*

Sheep 3 *and* 4: Although the autopsies of both animals were negative, a mild *status spongiosus* was found microscopically in the periventricular areas, optic tracts and optic chiasm.

Experiments in South West Africa

Materials and methods

Toxicity trials were conducted at 4 different places, viz. Windhoek, Kalahari Experimental Farm, Gobabis and Carolahof. With the exception of Gobabis, where the experiment commenced about 6 weeks after an outbreak of amaurosis had ceased, the trials were conducted during a prevailing outbreak. The former 2 places were outside the enzootic area, but the latter were situated on affected farms.

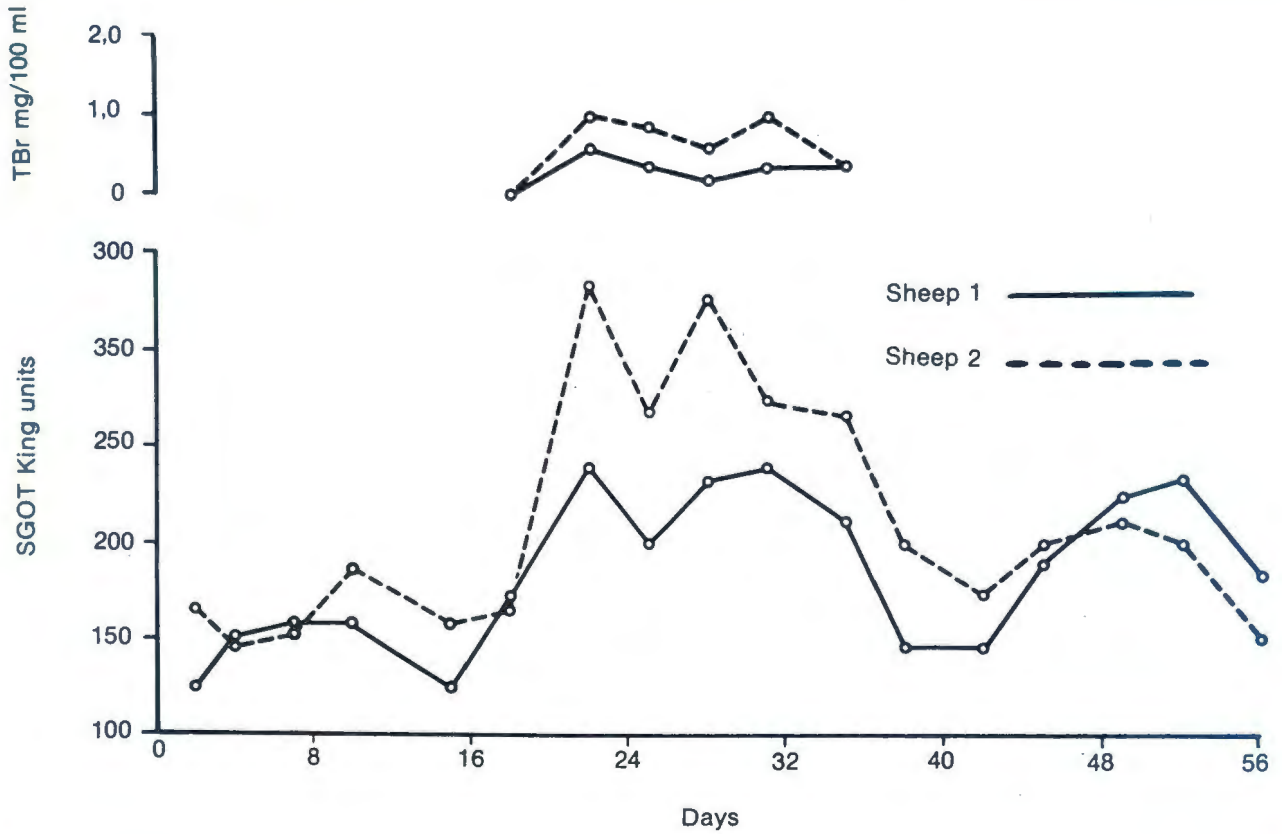

FIG. 20 Changes in the total bilirubin (TBr) and serum glutamic oxalacetic transaminase (SGOT) in the blood of sheep dosed with *H. argyrosphaerum*

TABLE 3 *Helichrysum* toxicity trial: Windhoek

No. of animal	2PK3	45ST	PR237	8PT2
Sex and age of animal	Young wether	Young wether	Young ram	Young wether
Mass	23,5 kg	23,5 kg	31 kg	27 kg
No. of days in test	16	20	20	20
Lowest daily intake	100 g	250 g	550 g	100 g
Highest daily intake	650 g	700 g	800 g	800 g
Average daily intake per kg of body mass	20 g/kg	25 g/kg	21 g/kg	20 g/kg

Four sheep were exposed in each experiment and 4 served as controls. They varied in age, but were mainly young animals. No chemical pathological analyses were done. All the sheep were slaughtered within 36 days and, at autopsy, histopathological specimens were collected from various organs and treated as previously described.

The Windhoek trial commenced on 9 October 1972. The flowering plants were collected *in toto* in an affected area during the early morning and transported to Windhoek where they were stored loosely packed in flat layers. The material was replaced every 4th–7th day, i.e. before the plants were completely dry. Only the branches with the leaves and flowers were offered to the sheep, and each animal received 1 kg daily. The total daily intake was calculated by determining the mass of the residue (Table 3) before it was discarded.

This was the sole diet for 16–20 days, except that occasionally, whenever the plants became too dry and unattractive, about 0,2 kg of good quality maize meal was added to the *Helichrysum* ration of each animal. Dry lucerne hay (600 g) was given once to sheep 8PT2 when it developed diarrhoea on the 4th day.

All the sheep were slaughtered 4–8 days after feeding of *Helichrysum* was terminated. Only good quality lucerne hay was fed during the interim.

On the Kalahari Experimental Farm the entire plant, including the roots, was offered. Since the plants were collected near by, the sheep obtained fresh flowering material more regularly. The daily intake was not calculated. The sheep were fed for 18 days, after which only lucerne hay was given. All animals were slaughtered after 26 days.

At Carolahof freshly collected flowering *Helichrysum* was given *ad libitum* for 27 days to 4 sheep in an open-air enclosure. The plants were collected 4 times daily and the residues were regularly removed. No other food was supplied and the daily consumption was not calculated.

In the Gobabis trial the sheep were put on a leash and allowed to graze on dry or semi-dry *Helichrysum* which had passed the flowering stage. Whenever necessary the animals were moved to a new stand from which all other plants had been removed. This was continued for 36 days before the animals were slaughtered for autopsy purposes.

Results

Clinical signs

Except for 1 sheep in Windhoek which developed a diarrhoea on the 4th day, and another on the Kalahari Experimental Farm that showed a mild behavioural disturbance for 1 day, nothing untoward was noticed.

Pathology

Except for the sheep in the Gobabis experiment which were negative, the exposed animals all proved to be histopathologically positive for brain lesions. A moderately to severe *status spongiosus* occurred in which the predilection sites were similar to those of natural amaurosis. The optic chiasm and optic fasciculi of all the sheep also contained similar very mild (18%) to moderate (82%) lesions, but malacia was never encountered. One sheep had mild spongy lesions in the spinal cord. Very mild or mild fatty changes were observed in the livers (45%) and kidneys (29%). No lesions were noticeable elsewhere.

The controls were negative except for 2 sheep from the Kalahari Experimental Farm which showed a very mild porosity of the periventricular area. This was comparatively insignificant and only indicated a previous slight exposure to some toxic agent such as *Helichrysum*.

Discussion

The results of the feeding experiments proved that a *status spongiosus* of the brain, spinal cord, optic fasciculi and nerves, followed by paralysis, is caused by the ingestion of *H. argyrosphaerum* in large quantities. Although overt blindness did not develop, this was probably because the lesion had not progressed sufficiently to cause this symptom, since the entire pathological picture simulated that of natural amaurosis and paresis. Furthermore, it was shown that both dry and fresh plant material were toxic in the flowering stage, but that a later growth phase was probably non-toxic.

Cataracts appeared on most of the farms on which outbreaks of amaurosis had occurred, the interval being approximately 2–3 months. Some farmers even claimed that a few cases of amaurosis became cataractous. There is therefore some reason to believe that the development of cataracts could be a chronic manifestation of the disease in aged sheep with subclinical amaurosis. This may be deduced from the presence of a spongiosity with the same distribution as in amaurosis. Swelling of the optic fasciculus with subsequent papilloedema and even retinal detachment. or a prolonged toxic effect, could possibly give rise to such cataracts, However, experimental proof for this is still lacking, and more extended feeding experiments are indicated to verify this suspicion.

The severe muscular lesions seen in some cattle in the absence of blindness or a *status spongiosus* is confusing because, apart from their severity, these lesions closely resembled those of *Geigeria* poisoning (Pienaar, Kriek, Naudé, Adelaar & Ellis, 1973). However, the small number of *Geigeria* plants present in relation to the large number of cattle affected argues against *Geigeria* poisoning. Sheep, grazing with the cattle, developed the typical syndrome of amaurosis and paresis, but muscular lesions, which were mild, were present in only some of them. Furthermore, on 1 farm sheep had myocardial and oesophageal lesions in addition to muscular lesions. It would therefore appear that either outbreaks of *Helichrysum* poisoning were complicated by *Geigeria* poisoning, or that *Helichrysum* can also produce a muscular syndrome. Another possible explanation is the existence of synergism between *Helichrysum* and *Geigeria* poisoning. Since species of *Helichrysum* are very similar in appearance and, as a survey of the various species was not conducted on all the farms, the possibility of poisoning by one other than *H. argyrosphaerum* should also not be overlooked.

Although the precise nature of the *status spongiosus* was not determined, it is thought to be a gliogenic type (Jellinger & Seitelberger, 1970) due to glial dystrophy rather than oedema. The vacuoles may be intramyelinic, intra-axonal or intra-oligoglial, or may affect more than one of these tissues simultaneously. Many causes of such spongiosity, including hepatic disease due to poisoning with pyrrolizidine alkaloids, copper, and ammonia (Hooper, 1972), are known, but it is not within the scope of this communication to deal with all of them.

A small, statistically inadequate trace element survey revealed that the liver copper levels of some cataractous sheep were elevated. Since the copper content of *Helichrysum* plants was normal, the elevated hepatic copper values could be due to hepatotoxic changes or merely coincidental. In this connection it must also be mentioned that typical cases of chronic copper poisoning were never seen on these farms.

Amaurosis in ruminants is known to have many toxic causes, but from a viewpoint of differential diagnosis in South Africa, as far as plants are concerned, poisoning by *Ornithogalum* spp. (Van der Walt & Steyn, 1941) and *Brassica* spp. (Steyn, 1949) should be considered. The precise lesions of poisoning with the aforementioned plants, however, are unknown.

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