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THE PATHOLOGY OF BLINDNESS IN NEW-BORN CALVES CAUSED BY HYPOVITAMINOSIS A

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ABSTRACT

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Blindness attributed to vitamin A deficiency afflicted 47 out of 197, and 15 out of 29 new-born dairy calves on 2 farms. Other clinical signs included doming of the forehead, thickening of the carpal joints, incoordination and weakness.

Gross lesions in 8 of the calves examined consisted in hydrocephalus and thickened occipital and sphenoid bones. In 4 of these calves the optic nerves were constricted as a result of a reduction in size and dorsoventral narrowing of the optic canals. Microscopical changes in the optic nerves were characterized by necrosis, demyelination and fibrosis.

Oedema or gliosis of the optic disc occurred in some of the calves. Retinal lesions included atrophy and gliosis of the ganglion cell layer and the nerve fibre layer. Three of the calves showed focal retinal dysplasia with occasional rosette formation.

INTRODUCTION

Vitamin A (retinol) is an essential ingredient in the rations of cattle. Plant carotenoid pigments, β-carotene of which is the most important, are the major natural source (Miller, 1979).

Hypovitaminosis A is a well-described syndrome in cattle. In adult cattle clinical signs comprise ataxia, convulsions and blindness (Moore, 1941; Divers, Blackmon, Martin & Worrell, 1986; Booth, Reid & Clark, 1987), and those in calves include poor growth, decreased appetite, diarrhoea, incoordination, convulsions, blindness and exophthalmos (Helmboldt, Jungherr, Eaton & Moore, 1953; Abrams, Bridge, Palmer, Spratling & Sharman, 1961; Spratling, Bridge, Barnett, Abrams, Palmer & Sharman, 1965; Nielsen, Mills, Woelfel & Eaton, 1966). Hypovitaminosis A in calves born to dams fed a deficient ration is less well documented. Calves are born dead, or are weak, incoordinated and blind at birth (De Schweinitz & De Long, 1934; Moore, Huffman & Duncan, 1935).

Three types of blindness have been reported in vitamin A-deficient calves (Hayes, Nielsen & Eaton, 1968): night blindness, associated with a deficiency of vitamin A aldehyde in the formation of the visual pigment rhodopsin and often reversible (Barnett, Palmer, Abrams, Bridge, Spratling & Sharman, 1970); degenerative changes in the outer retinal layers resulting from a prolonged deficiency (Cohrs, 1955); and narrowing of the optic canal with constriction of the optic nerve which leads to irreparable loss of vision (Abrams *et al.*, 1961; Spratling *et al.*, 1965).

Vitamin A deficiency in cattle is rarely recognized in the Republic of South Africa (RSA). In an early report Du Toit, Malan & Groenewald (1934) mentioned blindness and weakness in new-born calves and speculated on the possible role of a vitamin A deficiency. No work on hypovitaminosis A in cattle has since been published in the RSA. In this report are described the pathological findings in blind new-born calves on two farms which resulted from a vitamin A deficiency.

HISTORY OF OUTBREAKS

Farm 1: The first outbreak involved 240 Friesland heifers on a farm near Heidelberg, Transvaal, where approximately 600 cows were milked daily. From about 4 months of age the heifers were fed *ad libitum* a ration consisting of 60 % spent brewer's grain, 30 % roughage (wheat straw and *Eragrostis curvula* hay), 5 % fish meal and yellow maize meal, and 5 % ground sorghum grain or yellow maize cobs (depending on availability). No vitamin a or vitamin A equivalents were supplemented in the ration or given parenterally. The heifers were vaccinated against brucellosis at 6–7 months of age and had no access to natural pastures except in March 1984, at 14–15 months of age, when they were put on natural veld for 4 weeks. They were inseminated during April and those that did not conceive were mated in May. Seventy calves were born from the heifers during December 1984, 61 of which were born dead and 9 were blind, weak and unable to suckle, and died within 1–3 days. From January to March 1985, a further 28 dead and 38 blind calves were born. Several of the blind calves were weak, incoordinated and died soon after birth. Doming of the forehead occurred in the majority of blind calves, exophthalmos was occasionally noticed and in about 15 calves the carpal joints appeared thickened. The heifers maintained good health and post-partum complications were low. Sixty-one clinically normal calves were born during the period January to May 1985.

In addition to the ration fed to the heifers, pregnant cows received dry lucerne and were allowed to graze natural veld 4–8 weeks before partus. Eight weeks before calving the cows were also given a vitamin A, D and E preparation ('Intravit A', Agricura) parenterally at a dosage rate of 1 m*l*/250 kg. According to the farmer, calves born to these cows were clinically normal.

Farm 2: The 2nd outbreak occurred on a farm near Sasolburg, Orange Free State, where 130 cows were milked daily. Thirty-five Friesland heifers were kraaled from 4 months of age and fed *ad libitum* a ration containing 97,4 % ground sorghum grain, 2 % urea and 0,6 % dicalcium phosphate. The sorghum was stored at room temperature from July 1986. Chicken manure and roughage (*Themeda triandra* hay) were also freely available. Each animal was injected intramuscularly with 3 m*l* of vitamin A, D and E ('Vitadex', Milborrow) during July 1986. The heifers were inseminated at 15–17 months of age.

During January to May 1987, 6 full term dead, 15 blind and 8 clinically normal calves were born. The

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TABLE 1 Age, clinical signs and pathological lesions in the optic canal, optic tract and eyes of calves with hypovitaminosis A

Calf No.	Origin	Age	Clinical signs	Macroscopical lesions		Microscopical lesions		
				Optic canal and intracranial part of the optic nerve	Orbital part of the optic nerve	Optic canal and intracranial part of the optic nerve	Orbital part of the optic nerve	Eye
1	Farm 1	3 h	Blindness, doming of the forehead, thickened carpus and weakness	NE	Slight reduction in diameter and yellowish-brown on the cut surface	NE	Necrosis and demyelination	Atrophy and gliosis of ganglion cell and nerve fibre layers and papilloedema
2	Farm 1	6 h	Blindness, doming of the forehead, thickened carpus and weakness	NE	Slight reduction in diameter and yellowish-brown on the cut surface	NE	Necrosis and demyelination	Atrophy and gliosis of ganglion cell and nerve fibre layers and papilloedema
3	Farm 1	5 h	Blindness, doming of the forehead, thickened carpus, weakness, and nystagmus	NE	Thin fibrous cord	NE	Fibrosis	Atrophy and gliosis of ganglion cell and nerve fibre layers
4	Farm 1	10 days	Blindness, doming of the forehead and incoordination	NE	Thin fibrous cord	NE	Fibrosis	Atrophy and gliosis of ganglion cell and nerve fibre layers, gliosis of optic disc and congestion of retinal veins
5	Farm 1	14 days	Blindness and doming of the forehead	Reduction in size and dorsoventral narrowing of the optic canal with constriction of the nerve	Thin fibrous cord	Reduction in size and dorsoventral narrowing of the optic canal with fibrosis of the nerve	Fibrosis	Atrophy and gliosis of ganglion cell and nerve fibre layers, papilloedema and retinal dysplasia
6	Farm 1	3 days	Blindness and doming of the forehead	ditto	Thin fibrous cord	ditto	Fibrosis	Atrophy and gliosis of ganglion cell and nerve fibre layers, gliosis of optic disc, retinal dysplasia and rosette formation
7	Farm 2	19 days	Blindness and doming of the forehead	ditto	Thin fibrous cord	ditto	Fibrosis	Atrophy and gliosis of ganglion cell and nerve fibre layers, gliosis of optic disc, congestion of retinal veins and retinal dysplasia
8	Farm 2	47 days	Blindness and doming of the forehead	ditto	Thin fibrous cord	ditto	Fibrosis	Atrophy and gliosis of ganglion cell and nerve fibre layers, gliosis of optic disc and congestion of retinal veins
9	Control	14 days	–	–	–	–	–	–
10	Control	20 days	–	–	–	–	–	–

NE Not examined — No lesions

majority of the blind claves showed doming of the forehead, and a few were weak at birth and died several days later. Approximately 10 heifers showed mild pupillary dilation and/or varying degrees of corneal opacity. Blindness was not clinically apparent when these animals were examined by daylight.

The cows on the farm received the same ration as the heifers but were allowed to graze natural veld 2–8 weeks before calving. These animals gave birth to clinically normal calves.

Materials and Methods

Animals

Necropsies were performed on 6 calves from Farm 1 and 2 calves from Farm 2 as well as 2 control Friesland calves (Table 1). The control animals were obtained from the dairy herd at the Veterinary Research Institute, Onderstepoort. During gestation, the dams of these calves were fed lucerne hay *ad libitum* and daily 5–7 kg dairy meal which contained a minimum of 10 000 I.U. vitamin A/kg meal.

Pathology

All the calves were killed by exsanguination following barbiturate anaesthesia. The heads of Calves 5 & 9 were perfused with 10 % buffered formalin through the carotid arteries. The skull of each calf was opened by a longitudinal section in the sagittal plane and the brain, eyes and orbital parts of the optic nerves removed. One half of a skull from Calves 5 & 9 was boiled and the flesh removed in order to study the gross bone lesions in more detail. The intracranial part of the optic nerves of Calves 5–10 were removed by cutting a block of sphenoid bone (optic block) approximately 50 × 30 × 30 mm in size, as described by Hayes *et al.* (1968). The optic canal and intracranial part of the optic nerves were not examined in Calves 1–4.

The eyes and optic nerves, optic blocks, optic chiasma and various parts of the cerebrum, cerebellum and spinal cord were fixed in 10 % buffered formalin. One eye of each of Calves 5–10 was fixed in Zenker's solution (Luna, 1968). After fixation, the optic blocks were decalcified in 10 % formic acid and trimmed to expose either the transverse or longitudinal surfaces of the optic nerve in the bony canal. All tissues were processed routinely and stained with haematoxylin and eosin (HE). Selected sections were stained with luxol fast blue-periodic acid-Schiff-haematoxylin (LFB-PAS-H) and luxol fast blue-Holmes silver nitrate (LFB-H) (Margolis & Pickett, 1956), Schmorl's method for lipofuscin, Berlin blue for iron (Pearse, 1961) and Masson's trichrome for collagen (Luna, 1968).

Apart from these specimens, a wide range of tissues from Calves 1–10, including the parotid salivary glands and a 50 mm portion of the parotid duct overlying the angle of the mandible in Calves 5–10 was fixed in 10 % buffered formalin and processed for histopathology.

Chemical pathology

On a visit to Farm 2, blood was collected in tubes from 15 heifers and immediately wrapped in aluminium foil. The plasma was removed, frozen and vitamin A and β-carotene levels were determined by means of a high pressure liquid chromatography method (Vuilleumier, Keller, Gysel & Hunziker, 1983).

Virology

Serum samples from 3 colostrum-deprived calves (Calves 1–3) and 10 heifers (5 of which gave birth to blind and 5 to clinically normal calves from each of the farms were tested for the presence of antibodies to the viruses of Rift Valley fever (RVF), Wesselsbron disease (WSD), bluetongue (BT), Akabane disease (AD) and bovine viral diarrhoea-mucosal disease (BVD-MD). The methods employed were the haemagglutination inhibition test for RVF and WSD (Clarke & Casals, 1958), the complement fixation test for BT and AD (McIntosh, 1956), and the microtitre neutralization test for BVD-MD (Frey & Liess, 1971).

Results

Clinical signs

The clinical signs are summarized in Table 1. Calves 1–8 were blind, the pupillae severely dilated and the pupillary light reflexes absent. Doming of the frontal bones was most prominent in Calves 1–3 and the carpal joints of these 3 animals were moderately thickened. Calves 1–3 were weak and unable to stand. Clinical signs in some of the calves included incoordination and nystagmus (Table 1).

Macroscopical pathology

Doming of the skulls in Calves 1–8 was due to a convexity of the frontal and parietal bones. Digital impressions and ridges were absent on the internal surface of the calvarium. The occipital bones and, to a lesser extent, the sphenoid bones were thickened (Fig. 1 & 2) and the bone trabeculae reduced in number, giving them a porous appearance (Fig. 3 & 4). Sagittal mid-line sections of the heads of Calves 1–8 revealed moderate internal hydrocephalus and dorsoventral compression of the cerebellum and, to a lesser degree, of the cerebrum. The posterior part of the *vermis cerebelli* was flattened dorsoventrally and herniated through the foramen magnum in 5 of the calves (Fig. 1 & 2).

Transverse sections through the optic nerve and optic canal in Calves 5–8 showed a reduction in size and dorsoventral narrowing of the canal with constriction of the nerve (Fig. 5 & 6). The constricted nerve was yellowish-brown and was located in the lateral angle of the bony canal. Several dilated blood vessels were present in the medial aspect of the canal. The optic canal in Calf 5 was severely narrowed and had a slit-like appearance (Fig. 3 & 4). In Calves 1–8 the orbital part of the optic nerves was reduced in diameter, except for a portion 3–5 mm in length immediately posterior to the eye. The affected portions of the nerves in Calves 3–8 were represented by thin fibrous cords 2–3 mm in diameter, whilst the nerves were only slightly thinner than normal in Calves 1 and 2, and yellowish-brown on the cut surface. No lesions were present in the other organs of Calves 1–8.

Microscopical pathology

Optic canal and intracranial part of the optic nerve: Lesions were noticeable bilaterally in the bone plates which consitute the optic canal, the dura mater and leptomeninges, and the optic nerve (Fig. 7–11). The canal was distinctly smaller than normal and narrowed dorsoventrally (Fig. 7). Bone plates ventral and lateral to the nerve appeared more compact when compared to those of the controls; they were thin in some areas and showed several metachromatic arrest lines; central canals were smaller and more widely spaced; and osteocytic lacunae

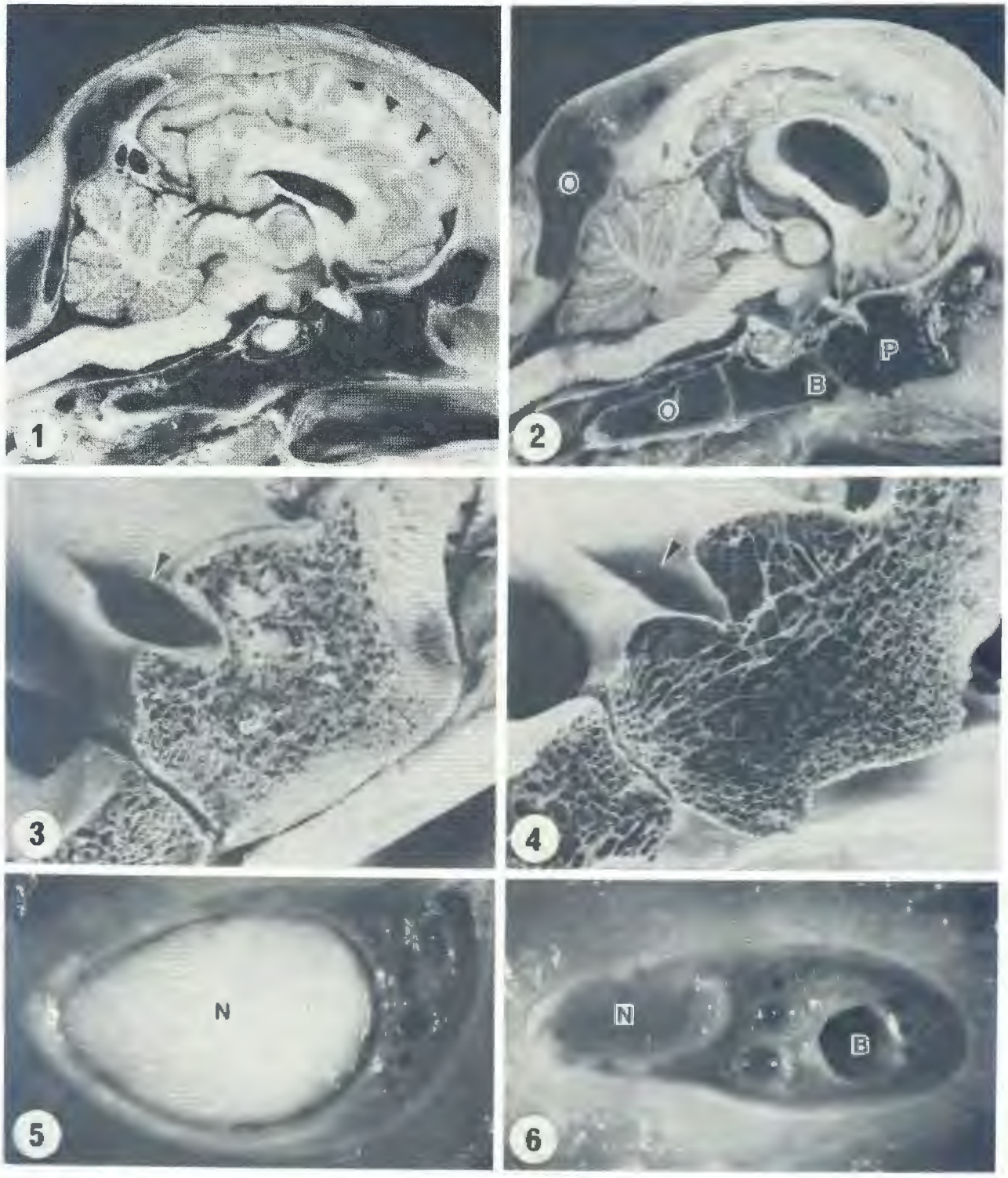


FIG. 1 Normal calf: sagittal mid-line section of the skull.

FIG. 2 Thickening of the occipital (O) and to a lesser degree basisphenoid (B) and presphenoid (P) bones in Calf 5. There is hydrocephalus and compression of the cerebellum with slight prolapse of the caudal portion of the vermis.

FIG. 3 Normal calf: sagittal mid-line section through the presphenoid bone. The optic canal has a wide oval contour (arrowhead).

FIG. 4 Presphenoid bone in Calf 5 is slightly thicker than normal and porous. The optic canal is narrowed (arrowhead).

FIG. 5 Normal calf: transverse section of optic nerve (N) in the optic canal.

FIG. 6 Transverse section of the optic nerve and optic canal in Calf 5 demonstrating dorsoventral narrowing of the canal and constriction of the nerve (N). Several dilated blood vessels (B) are located in the medial portion of the canal.

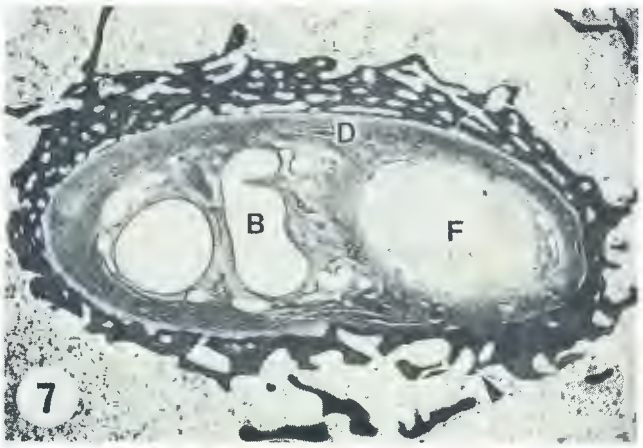
seemed reduced in number (Fig. 8 & 9). The inner surfaces of the bone plates were sligthly irregular, were not indented by cavities from the periosteum, and osteoclastic activity was decreased. In addition, osteoblasts, which normally line the outer surfaces of these plates, were markedly reduced in number (Fig. 8 & 9).

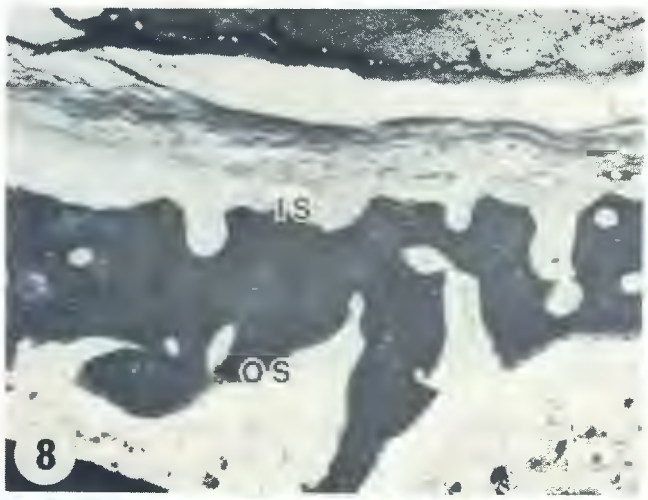
The dura mater in the optic canal and dorsally on the sphenoid bone, especially at the site of entry of the nerve, was moderately thickened by fibrous con-

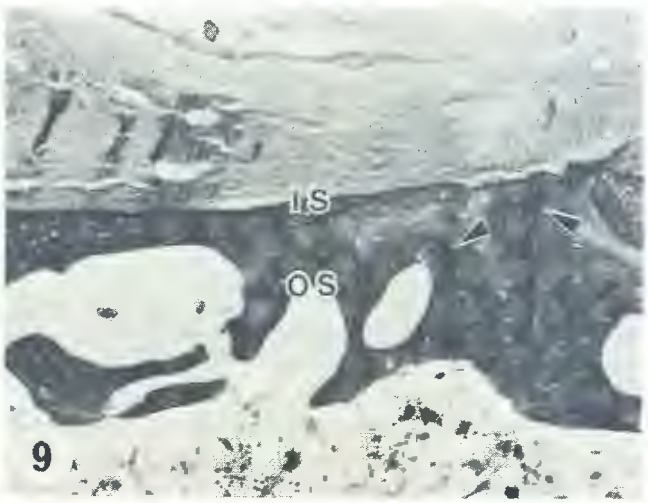
nective tissue (Fig. 10). The pia-arachnoid also showed fibroplasia and the subarachnoid spaces dilated in some areas.

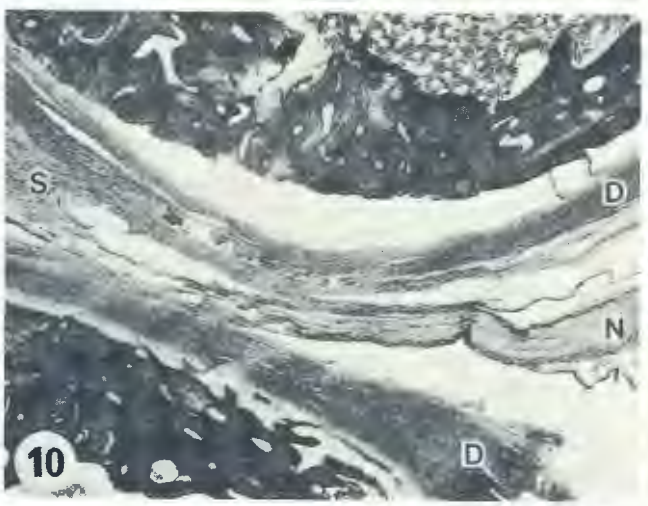
The intracranial part of the optic nerves was severely constricted (Calves 5–8), resulting in atrophy and progressive loss of nerve fibres as the nerve entered the optic canal. In 2 of the calves the nerve was replaced by irregularly arranged bundles of collagen (Fig. 10). The fibrotic portion was often vacuolated and infiltrated by moderate numbers of macrophages containing pigment, resembling lipofuscin. Fine fibrous connective tissue strands traversed the optic canal in the other 2 calves (Fig. 11).

Orbital part of the optic nerve: The lesions in the optic nerves were bilaterally distributed and varied among the affected calves. On cross-section, necrosis and demyelination of nerve bundles was evident in about half of the nerve in Calf 1 (Fig. 12–15) and throughout the entire nerve in Calf 2 (Fig. 16 & 17). Thickened fibrotic pial septa isolated necrotic nerve bundles. Fragmentation and loss of axons and myelin in areas of necrosis were demonstrated in sections stained with LFB-H and LFB-PAS-H. Focal accumulations of neutrophils and macrophages containing lipofuscin, haemosiderin and breakdown products of myelin were seen in necrotic areas.









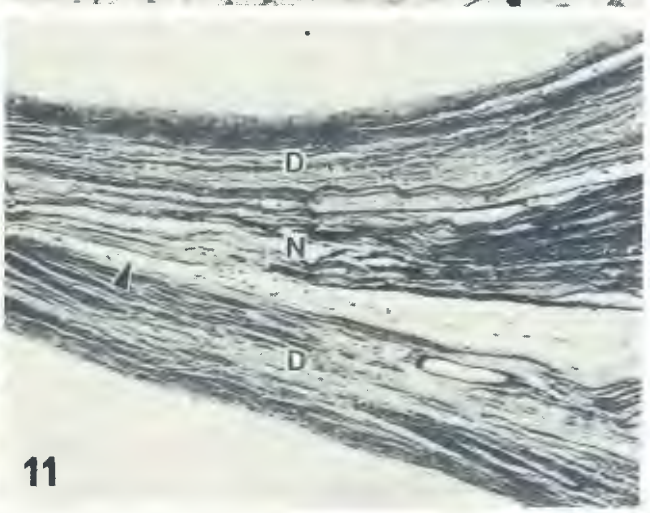


FIG. 7 Dorsoventral narrowing of the optic nerve in a transverse section of the optic canal (Calf 5). Dura mater is thickened (D), the nerve is replaced by fibrous connective tissue (F) and dilated blood vessels are evident in the medial portion of the canal (B). HE × 20

FIG. 8 Normal calf: portion of the bone plate ventral to the optic nerve. The inner surface (IS) and outer surface (OS) are indented by cavities from the periosteum and bone marrow. HE × 70

FIG. 9 Area indicated by arrowhead in Fig. 7: inner surface (IS) and outer surface (OS) of the ventral bone plate in Calf 5 are smooth. The bone plate is more compact than normal and contains several metachromatic arrest lines (arrowheads). HE × 70

FIG. 10 Transverse section of the optic nerve and optic canal in Calf 7. The nerve is atrophied (N) as it enters the canal and is replaced by fibrous connective tissue (S). Note fibrosis of dura mater (D). HE × 40.

FIG. 11 Intracranial part of optic nerve (N) in Calf 6. Note thin fibrous connective tissue strands (arrowhead) and fibrosis of the dura mater (D). Masson's trichrome × 80

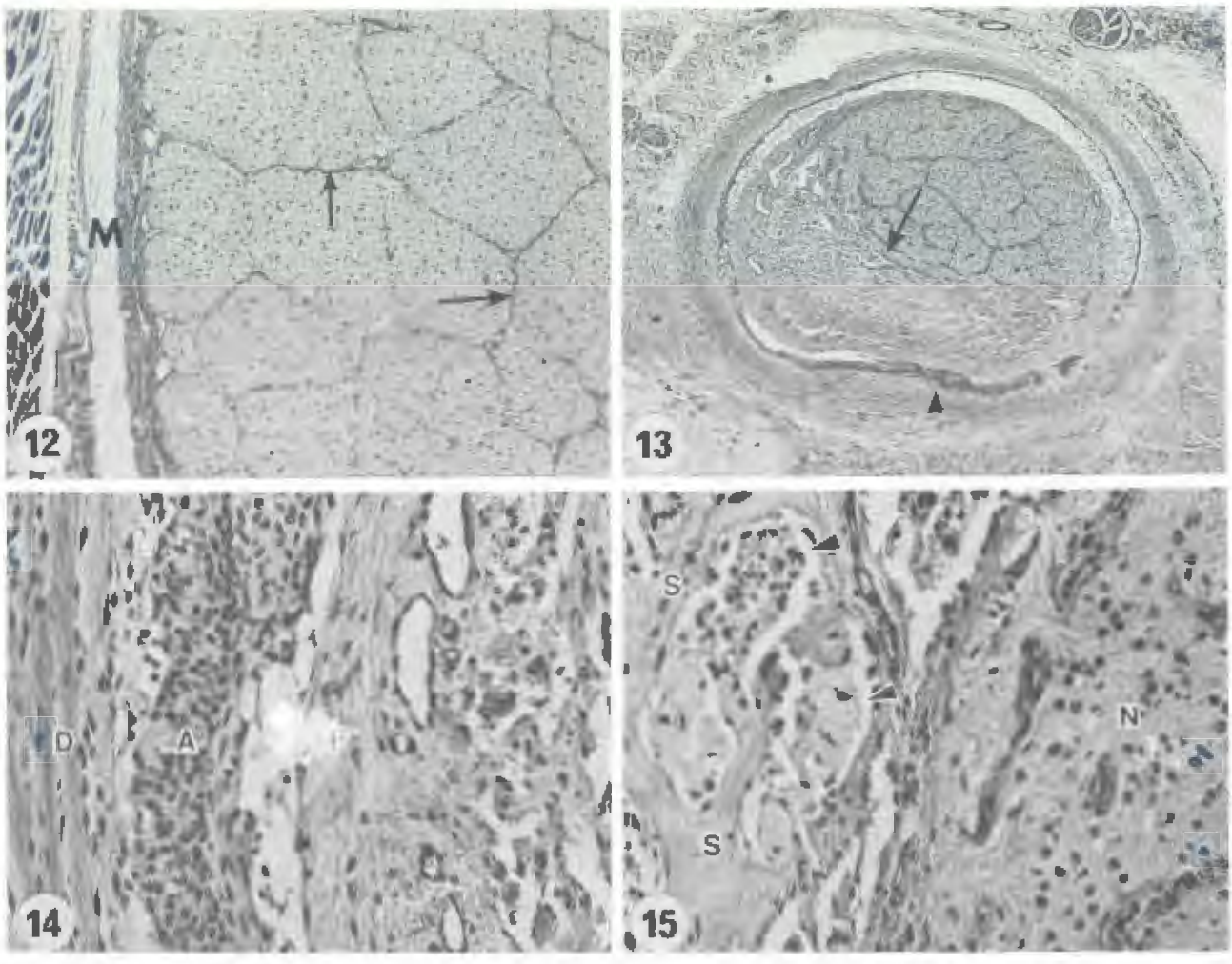


FIG. 12–15 Sections of the orbital part of the optic nerve.

FIG. 12 Normal calf: transverse section to show relationship between nerve, meninges (M), and pial septa (arrows). HE × 50

FIG. 13 Necrosis of nerve bundles and thickening of pial septa in a portion of the nerve in Calf 1. The dura mater and leptomeninges are thickened. HE × 30

FIG. 14 Area indicated by arrowhead in Fig. 13: the dura mater (D) is thickened and there is a cellular proliferation of the arachnoid (A) (Calf 1). Note fibrosis of pia mater (P) and pial septa, and dilation of subarachnoid space. HE × 250.

FIG. 15 Area indicated by arrow in Fig. 13: necrotic nerve bundles are infiltrated by macrophages (arrowheads) and isolated by fibrotic pial septa (S) (Calf 1). Astrocytic gliosis and vacuolation of nerve fibres in the more viable part of the nerve are evident (N). HE × 250

Mineralized deposits were noted occasionally in these areas. Variable numbers of macrophages also infiltrated the leptomeninges and dilated subarachnoid spaces. Lesions in the remaining portion of the nerve in Calf 1 included gliosis, multifocal vacuolation of nerve bundles and a loss of axons and myelin (Fig. 15).

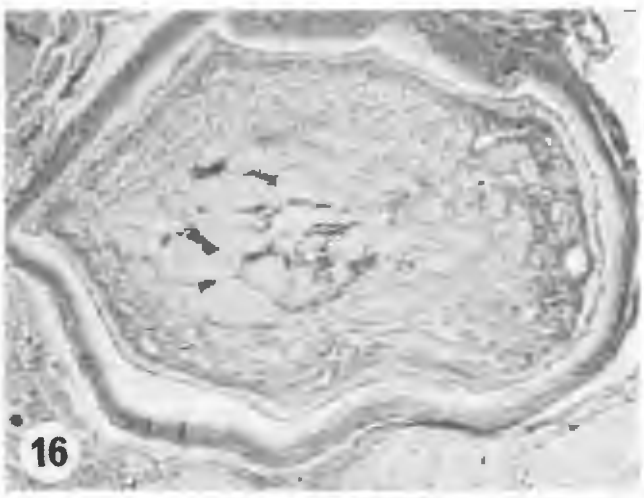
In Calves 3–8 the nerves were reduced in diameter almost along their entire length and the nerve bundles were replaced by irregularly arranged fibrous connective tissue which was infiltrated by pigment containing macrophages and small accumulations of lymphocytes (Fig. 18 & 19). Moderate fibrosis of the dura mater was evident and many fibroblast-like cells and fibrosis resulted in thickening of the leptomeninges (Fig. 19).

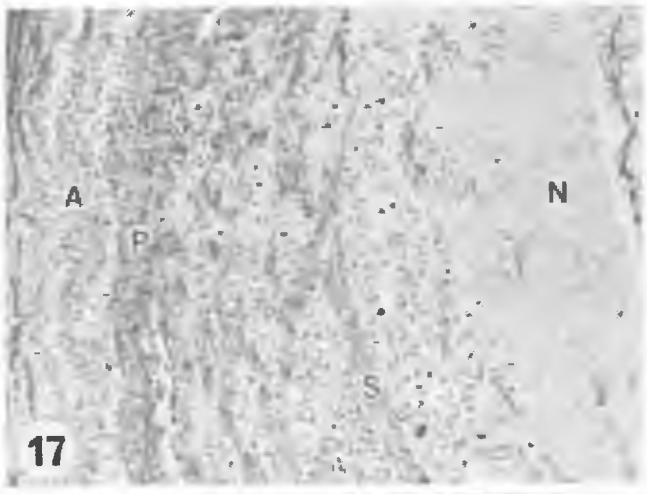
In the 3–5 mm long portion immediately posterior to the eye, the lesions were characterized by astrocytic gliosis, demyelination, and mild vacuolation of myelin and fibrous thickening of pial septa.

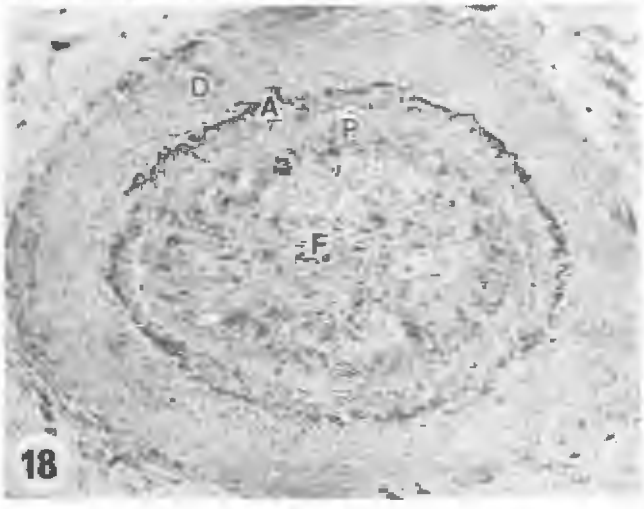
Optic chiasma: Mild gliosis and focal vacuolization were noticed in sections of the optic chiasma in 4 of the calves.

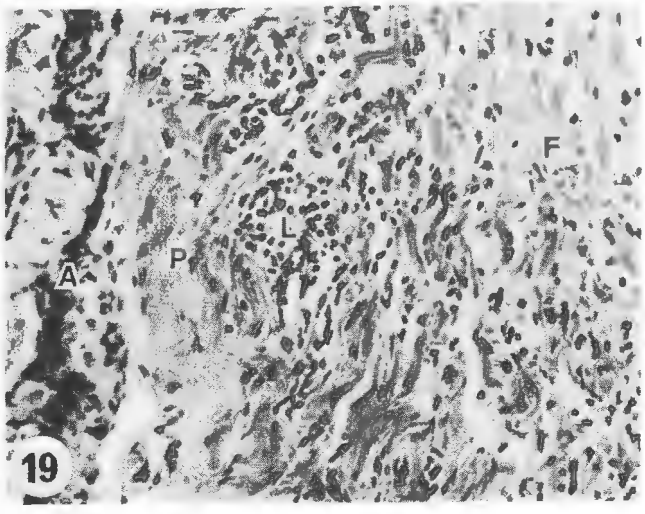
Eye: The ocular lesions are summarized in Table 1. In 3 of the blind calves there was bilateral mild to moderate papilloedema. In 4 other animals the optic discs were enlarged as a result of astrocytic gliosis and congestion (Fig. 20 & 21).

All affected animals showed a marked reduction, or, in some parts, an absence of ganglion cells. The nerve fibre layer appeared thinner when compared with that of the controls and a mild but widespread gliosis was present in this layer as well as in the ganglion cell layer (Fig. 22 & 23). In Calves 5–8 the nerve fibre layer was vacuolated and Muller's fibres were prominent. There were areas of dysplasia of the central retina in Calves 5–7 (Fig. 24 & 25). The layer of rods and cones and the outer nuclear layer were absent and a few of the outer nuclear cells were pycnotic. The inner nuclear layer was slightly distorted and depleted of cells (Fig. 25). The pigment epithelium was hyperplastic and hypertrophic and formed clusters of cells, occasionally surrounded by fine fibrillar, eosinophilic material. Several large pigment-containing cells infiltrated the outer retinal layers. A rosette, which consisted of a peripheral









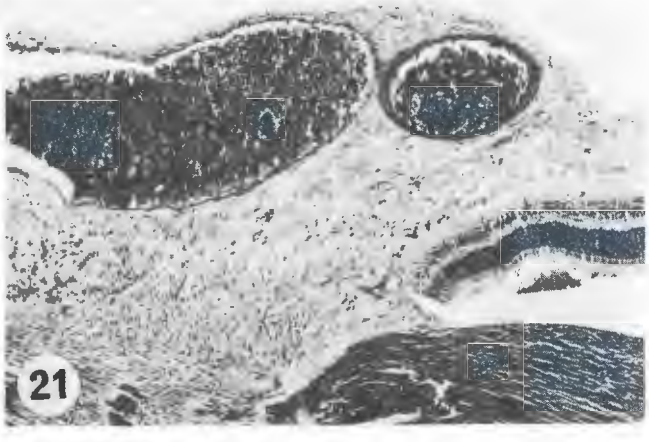


FIG. 16–19 Sections of the orbital part of the optic nerve.

FIG. 16 Necrosis of nerve bundles throughout the entire nerve in Calf 2. Masson's trichrome × 20

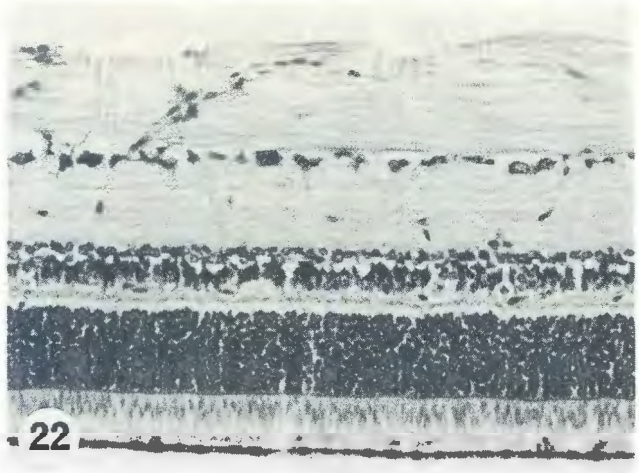
FIG. 17 Necrosis of nerve bundles (N) (longitudinal section). The arachnoid (A), pia mater (P) and pial septa (S) are thickened. HE × 60

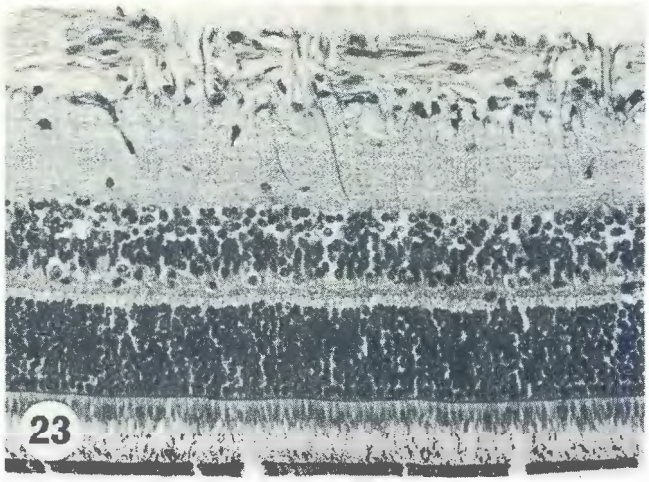
FIG. 18 The nerve is replaced by fibrous connective tissue (F). There is fibrosis of the dura mater (D) and pia mater (P), and cellular proliferation of the arachnoid (A) (Calf 8). HE × 80

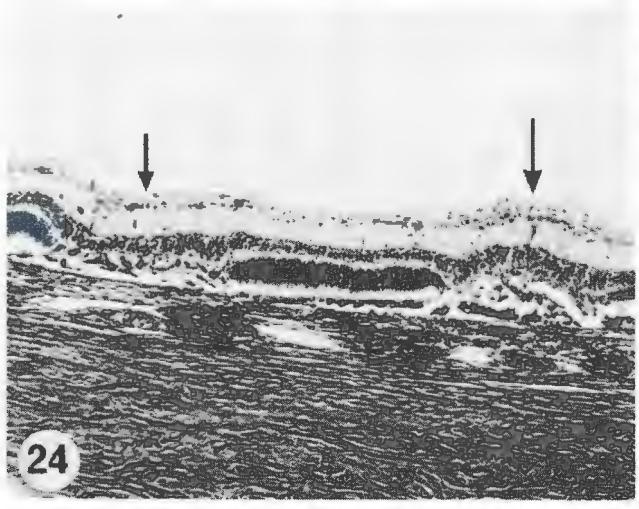
FIG. 19 Fibrosis of nerve bundles (F) and the pia mater (P) (Calf 7). Focal accumulation of lymphocytes (L) are noticed in the fibrotic portion and the arachnoid (A) is thickened. HE × 180

FIG. 20 Normal calf: portion of the optic papilla. Zenker's fixative, HE × 80

FIG. 21 Mild swelling and gliosis of the optic papilla with congestion of retinal vessels in Calf 7. Zenker's fixative, HE × 80







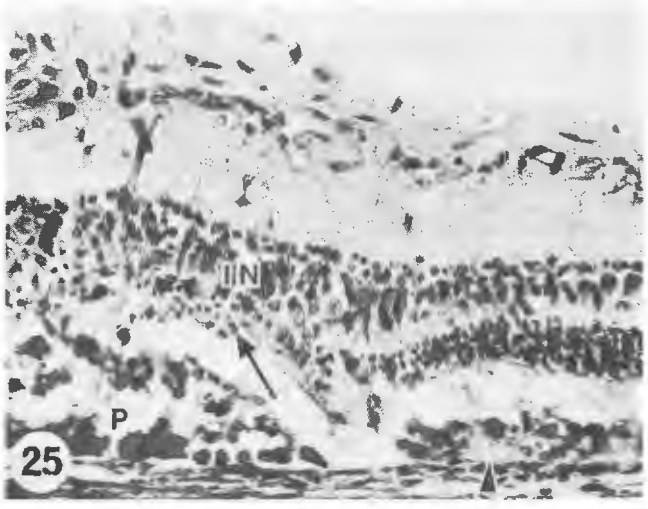


FIG. 22 Retina of a normal calf. Zenker's fixative, HE × 200

FIG. 23 Atrophy and gliosis of the ganglion cell layer and nerve fibre layer in the retina of Calf 8. The nerve fibre layer is vacuolated and Müller's fibres appear prominent. Zenker's fixative, HE × 200

FIG. 24 Areas of retinal dysplasia in Calf 7 (arrows). Zenker's fixative, HE × 70

FIG. 25 Area indicated by large arrow in Fig. 24: the outer nuclear layer and the photoreceptor layer are absent, the inner nuclear layer is slightly distorted (IN) and a few inner nuclear cells are pycnotic (arrow). There is hypertrophy and hyperplasia of pigment epithelium (P) forming a cluster of cells (arrowhead). Zenker's fixative, HE × 200

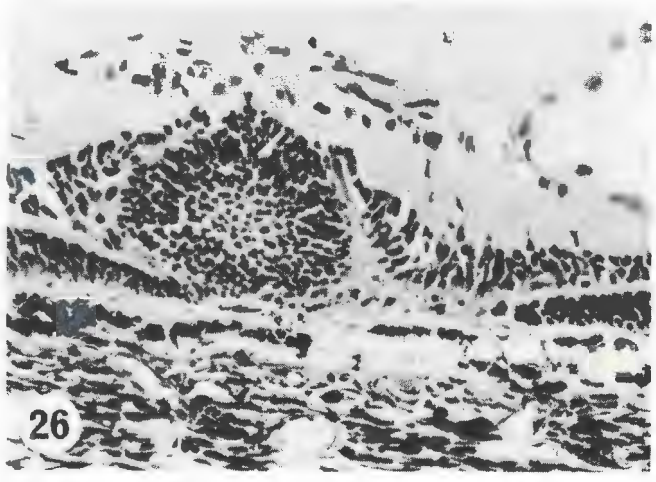


FIG. 26 Focal retinal dysplasia and rosette formation in Calf 6. HE × 150

layer of outer nuclear cells and an inner layer resembling photoreceptor cells, was closely associated with the dysplastic lesion in Calf 6 (Fig. 26). Adjacent to the disc in Calf 7 a retinal fold was evident.

Brain: Focal loss of the granular and molecular layers and Purkinje cells in the herniated portions of the cerebellum occurred in 5 of the calves. In some of these areas there was focal necrosis and demyelination accompanied by moderate numbers of macrophages and a few lymphocytes. Overlying meninges were thickened by fibrosis and an infiltration of plasma cells, lymphocytes and macrophages.

Other organs: The epithelium lining the interlobular ducts of the parotid gland in Calf 7 revealed moderate squamous metaplasia in some areas, and goblet cells were markedly reduced in number or absent. Focal accumulations of mononuclear cells, predominantly lymphocytes, infiltrated the adjacent interlobular tissues. In the majority of animals, a mild subacute interstitial pneumonia was noticeable. Changes in other organs were unremarkable, except for a mild focal lymphocytic interstitial nephritis in 2 calves.

Chemical pathology

Plasma retinol and β-carotene levels of 15 heifers from Farm 2 are given in Table 2. The retinol levels, ranging between 0,16 and 0,97 μmol/1, were markedly low in all but 2 of the animals. The levels

TABLE 2 Plasma retinol and β-carotene levels of 15 heifers from Farm 2 and the fate of their progeny

Heifer No.	Retinol (μmol/ℓ)	β-carotene (μmol/ℓ)	Fate of progeny
1	0,64	2,72	Blind (Calf 7; Table 1)
2	0,95	1,14	Blind (Calf 8; Table 1)
3	0,16	0,19	Blind
4	0,28	0,28	Stillbirth
5	0,97	5,14	Stillbirth
6	0,29	0,39	Stillbirth
7	0,30	0,35	Stillbirth
8	0,25	0,38	Normal
9	0,24	0,24	Normal
10	0,28	0,39	Normal
11	0,29	0,52	Normal
12	0,24	0,35	Normal
13	0,30	0,49	Normal
14	0,30	0,36	Normal
15	0,38	0,91	Not pregnant

Normal retinol value = 0,88–2,10 μmol/ℓ (Booth, Reid & Clark, 1987)

Optimum β-carotene value = 2,79 μmol/ℓ (Blood, Radostits & Henderson, 1983)

of β-carotene were between 0,19 and 5,14 μmol/l and, except in 1 animal, were very low.

Virology

Antibodies in the sera of the calves and heifers against the viruses of RVF, WSD, AD, BT and BVD-MD were generally absent or the titres were very low (<1:10).

Discussion

Based on the history, clinical signs and pathological findings, a diagnosis of congenital hypovitaminosis A was made in the calves. The lowplasma retinol levels in 13 out of the 15 heifers and low β-carotene values in the majority of these animals were also indicative of a vitamin A deficiency. In addition, pupillary dilation and corneal opacity, noticed in some of these heifers, have also been noted by other workers in cattle suffering from a deficiency of vitamin A (Barnett *et al.*, 1970).

Several factors could have contributed to vitamin A deficiency in the heifers. Brewer's grain, which contains no β-carotene or potential vitamin A activity (National Research Council, 1978), was the major ingredient of the ration on Farm 1. The potential vitamin A activity is also very low in sorghum grain and wheat straw (National Research Council, 1978). In addition, the heifers had no free access to natural veld or pastures during gestation and vitamin A or its equivalents were not supplemented. Adverse storage conditions on Farm 2 of the sorghum grain during the summer months, particularly in periods of excessive heat and light (Miller, 1979), may have caused some destruction of the already low levels of β-carotene. Although the animals received hay *ad libitum*, the β-carotene content in hay is usually only a small proportion of that in green grass (Miller, 1979). The pregnant heifers on this farm were not allowed to graze veld or pastures, and the single injection of vitamin A was not sufficient to meet their requirements.

Blindness with dilated pupils, nystagmus, weakness and incoordination observed in the calves in this study correspond with clinical signs reported in calves that were born from vitamin A deficient dams (Crocker, 1919 cited by De Schweinitz & De Long, 1934; De Schweinitz & De Long, 1934; Moore *et al.*, 1935).

In the calf, elevated cerebrospinal fluid (CSF) pressure is an early change associated with vitamin A deficiency (Eaton, 1969). The increased pressure has been attributed to impaired resorption of CSF (Calhoun, Hurt, Eaton, Rousseau & Hall, 1967) caused by biochemical and structural alterations of arachnoid granulations and villi (Cousins, Eaton, Rousseau & Hall, 1969; Hayes, McCombs & Faherty, 1971). Furthermore, there is a correlation between the extent of the deficiency and the elevation of the CSF pressure (Mills, Nielsen, Rousseau, Woelfel & Eaton, 1967). Cerebrospinal fluid pressures were not measured in our study, but the dilated lateral ventricles in the 8 calves most probably resulted from an increased CSF pressure.

In 4 of the 8 calves studied, there was a reduction in size and dorsoventral narrowing of the optic canal which resulted in severe constriction of the optic nerve. Crocker in 1919 (cited by De Schweinitz & De Long, 1934) originally described blindness in new-born calves resulting from stenosis of the optic canal with compression on the optic nerves. Subsequently, similar lesions have been reported in naturally occurring and experimentally induced hypovitaminosis A in calves (De Schweinitz & De Long, 1934; Moore *et al.*, 1935; Wetzel & Moore, 1940; Abrams *et al.*, 1961; Spratling *et al.*, 1965; Hayes *et al.*, 1968; Barnett *et al.*, 1970), and in pigs (Palludan, 1961).

Thickened occipital and sphenoid bones, doming of the frontal and parietal bones and compression of the brain have been produced experimentally in vitamin A deficient calves (Blakemore, Ottaway, Sellers, Eden & Moore, 1957; Hayes *et al.*, 1968). Bone lesions associated with compression of the brain and herniation of the cerebellum were also reported in vitamin A-deficient puppies (Mellanby, 1941), lion cubs (Bartsch, Imes & Smit, 1975) and piglets (Palludan, 1961). In piglets, a variety of congenital anomalies including microphthalmia, heart defects, diaphragmatic hernia, genital hypoplasia, displaced and malformed kidneys and cleft palate may accompany the bone lesions (Palludan, 1961).

The pathogenesis of the bone lesions appears to be related to defective remodelling of bone during growth, and is characterized by reduced resorption in the presence of continued bone formation (Hayes *et al.*, 1968; Davis, Krook & Warner, 1970). During remodelling of the sphenoid bone in the calf, there is a downward growth of the dorsal portion or bone plate of the optic canal. Bone is laid down on the inner surface, and resorbed on the outer surface of the bone plate. To accommodate for the optic nerve, the lateral and ventral bone plates must grow outward and downward, respectively. This requires bone resorption on their inner surfaces and bone formation on their outer surfaces. With hypovitaminosis A, the downward movement of the dorsal bone plate continues, but bone resorption from the inner surfaces of the lateral and ventral bone plates is retarded. This results in the optic canal being narrowed dorsoventrally (Hayes *et al.*, 1968; Davis *et al.*, 1970). In the 4 calves examined, lesions in the bone plates ventral and lateral to the optic nerves were similar to those reported by Davis *et al.*, (1970), indicating a decrease in the rate of resorption of bone, particularly osteolytic resorption.

Thickening of the dura mater overlying the sphenoid bone and at the entrance of the optic canal near the optic chiasma noticeable in 4 of the calves has been produced experimentally in calves fed a diet

deficient in vitamin A (Hayes *et al.*, 1968; Eaton, 1969; Gallina, Helmboldt, Frier, Nielson & Eaton, 1970). It was postulated that the altered contour of the optic canal and an increased CSF pressure in the subarachnoid space may result in compression of dural blood vessels and impaired circulation followed by fibrosis (Hayes *et al.*, 1968).

Combined compression of the altered bone plates and thickened dura mater causes varying degrees of vascular occlusion and ischaemic necrosis of the nerve as it passes through the optic canal. The main blood vessels supplying the nerve are located on its medial side. Necrosis therefor initially develops in the lateral portion of the nerve most distant from the medial vascular supply and eventually the enitre nerve becomes necrotic and fibrotic (Hayes *et al.*, 1968). Similar changes were seen in the calves described in this study.

Papilloedema associated with hypovitaminosis A presumably results from an increased CSF pressure (Moore & Sykes, 1940). It has been reported in calves (De Schweinitz & De Long, 1934; Moore; 1939; Spratling *et al.*, 1965; Nielsen, Mills, Woelfel & Eaton, 1966) and adult cattle (Divers *et al.*, 1986; Booth *et al.*, 1987). According to Barnett *et al.* (1970), it is the first objective clinical sign of value in the diagnosis of vitamin A deficiency in cattle. Papilloedema was not a consistent finding in the calves described in this report and is in agreement with the findings reported previously (Nielsen *et al.* 1966; Mills *et al.*, 1967). However, in 4 of the calves lesions of the optic disc were characterized by gliosis, and according to Hogan & Zimmerman (1962) these changes may result from longstanding papilloedema.

In the calves studied, atrophy and gliosis of the inner retinal layers were attributed to necrosis and loss of nerve fibres in the optic nerve. Similar lesions were observed in new-born calves which suffered from hypovitaminosis A (De Schweinitz *et al.*, 1934). Cohrs (1955) described atrophy and gliosis of the ganglion cell layer in affected adult cattle and suggested that the ganglion cells were those primarily affected.

Retinal dysplasia, evident in 3 of the calves examined, has been observed in piglets born from vitamin A-deficient dams (Palludan, 1961), but this is the first report on its occurrence in new-born calves. Apart from the rosette formation, the dysplastic lesions closely resembled the degenerative retinal lesions described in experimentally induced hypovitaminosis A in calves (Barnett *et al.*, 1970) and the naturally occurring disease in adult cattle (Cohrs, 1955; Booth *et al.*, 1987).

Congenital blindness in calves, accompanied by retinal dysplasia, optic neuritis and atrophy of the optic nerve, have been induced with the virus of BVD-MD (Bistner, Rubin & Saunders, 1970; Scott, *et al.*, 1973; Wilcock, 1983). In these animals retinal dysplasia is always associated with cerebellar hypoplasia, but lesions of the optic canal are absent.

Squamous metaplasia of the parotid duct epithelium is considered pathognomonic in vitamin A-deficient calves (Jungherr, Helmboldt & Eaton, 1950). It is not a consistent lesion and the severity and extent of metaplasia is correlated with the degree and duration of the deficiency (Nielsen, Mills, Rousseau & Woelfel, 1966). The epithelial changes would seem to be unrelated to the occurrence of lesions in the skeletal or nervous system.

After hypovitaminosis A was diagnosed, vitamin A was added to the existing rations on both farms ($2{,}5 \times 10^6$ 1.U./1 000 kg). No clinical signs indicative of a vitamin A-deficiency have since been reported.

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