VITAMIN A DEFICIENCY IN THE CAPTIVE AFRICAN LION CUB *PANTHERA LEO* (LINNAEUS, 1758)

R. C. BARTSCH([1]), G. D. IMES, Jr.([2]) and J. P. J. SMIT([3])

ABSTRACT

BARTSCH, R. C., IMES, G. D. Jr., and SMIT, J. P. J. Vitamin A deficiency in the captive African lion cub, *Panthera leo* (Linnaeus, 1758). *Onderstepoort. J. vet. Res* 42 (2), 43-54 (1975).

Dietary, breeding and clinical histories and pathological findings are presented from 2 confirmed and 5 presumed cases of vitamin A deficiency in immature African lions. Five of the 7 animals were born in the wild while 2 were born in captivity. All animals were fed lean red meat sprinkled with a vitamin/mineral supplement. Salient clinical signs were incoordination, "star gazing", blindness and intermittent convulsions. Pathological lesions seen in 4 animals included severe thickening of the cranial bones, with consequent marked compression of the brain and partial herniation of the cerebellum. Vascular damage in the cerebellum and ensuing haemorrhages, resulting in acute increases of an already high intracranial pressure, were thought to be the cause of some of the clinical signs, particularly convulsions rather than direct pressure-necrosis and atrophy of nervous tissue.

INTRODUCTION

In the past feeding of wild carnivores in captivity has been largely unsatisfactory and responsible for the production of several of the classical nutritional deficiencies, judging by the number of reports on the subject (Halloran, 1955). The feeding of all red-meat diets to large carnivores is perpetuated partially by zoo economics. Equally important is the pleasure derived by the public from watching a large predator devour red meat. In recent years, however, nutritional advances have proved that various vitamins and minerals are either deficient or entirely lacking in all red-meat diets (Price, 1970). These findings have encouraged the development of commercial preparation of more balanced wild carnivore diets. Many zoological parks, however, still use all red-meat diets. Recently some zoos have resorted to the addition of a vitamin/mineral powder supplement, sprinkled on the meat fed to their captive carnivores.

Four lion cubs from the Zoological Park of Paris died with a syndrome called "star gazing" in reference to their continuous staring into the sky (Perrin-Raybaud, Guillon & Wyers, 1973). The cubs ranged in age from 4–19 months. Symptoms of "star gazing", incoordination, opisthotonus and frequent epileptiform convulsions preceded death. According to these authors the lesions were similar to those of vitamin A deficiency of certain other species. Although vitamin A analyses were not undertaken in these instances, a presumptive diagnosis of vitamin A deficiency was strengthened when supplementation of the diet of pregnant dams and cubs at the zoo apparently prevented further cases. Vitamin A deficiency was also incriminated in 2 other lion cubs, 15 and 17 months old, with clinical signs of incoordination, nystagmus and opisthotonus (Tuch & Pohlenz, 1973).

The purpose of this communication is to report 2 confirmed and 5 presumed cases of vitamin A deficiency in captive lion cubs. The symptomatology and pathology are compared to those previously reported in lion cubs and other animal species.

CASE REPORT

History

Over a period of 2½ years 9 lion cubs between 2 and 12 months of age were received at the National Zoological Gardens, Pretoria. Three animals were born in captivity and 6 were free-living before their capture. The approximate ages of the cubs on arrival, their origin and fates are summarized in Table 1.

With the exception of those from the Kalahari Gemsbok Park, the cubs arrived at the zoo in excellent condition and with good appetites. The former were in poor condition but soon gained in mass.

Seven of the cubs developed similar nervous symptoms after a period of about 4 months in the zoo and 6 subsequently died, of which 4 were necropsied. The 7th, a female cub, was treated and improved clinically. One female of the remaining 2 died acutely with violent convulsions of sudden onset without previous symptoms. The remaining cub which was 12 months old and the oldest and most developed when received, never became ill.

TABLE 1 Summary of the history of the 9 cubs

Date received	No.	Sex	Age	Origin	Fate	Post Mortem No.
28/2/70..	2	M	6 mths...	Cape Town Zoo....................	Died: 13 mths old.................	—
		F	6 mths...	Cape Town Zoo....................	Died: 13 mths old without previous symptoms......................	—
18/11/71.	2	M	8 wks...	Kaokoveld of South West Africa.....	Died: 10 mths old.................	1
		F	8 wks...	Kaokoveld of South West Africa.....	Died: 11 mths old.................	2
3/3/72...	4	M	12 mths..	Kalahari Gemsbok Park............	Still alive.........................	—
		F	9 mths...	Kalahari Gemsbok Park............	Died: 16 mths old.................	3
		F	4 mths...	Kalahari Gemsbok Park............	Recovered after treatment Died: ± 3 yrs of age from dystocia...........	—
		F	2 mths...	Kalahari Gemsbok Park............	Died: 9 mths old.................	—
24/8/72..	1	M	9 mths...	Cape Town Zoo....................	Euthanized: 13 mths old...........	4

([1]) Section of Pathology, Veterinary Research Institute, Onderstepoort

Present Address: Department of Veterinary Pathology, College of Veterinary Medicine, Washington State University, Pullman, Washington, U.S.A.

([2]) Major, USAF, VC, Zoonotic Pathology Division, Armed Forces Institute of Pathology, Washington, D.C., U.S.A.

Presently stationed in the Section of Pathology, Veterinary Research Institute, Onderstepoort

([3]) National Zoological Gardens, P.O. Box 754, Pretoria

Clinical findings

The first clinical sign was disturbed equilibrium consisting of an unsteady and swaying gait. A fixed staring expression and apparent blindness was often observed. The animals walked into strange objects placed in their paths. Pupillary light reflexes and patellar reflexes appeared normal. Motor activity was severely depressed and there was marked apathy. However, several animals were occasionally irritable and restless. Anorexia was not observed but most animals had diminished appetites.

At a later stage tilting of the head and "star gazing" became evident in most cases and 2 cubs developed severe *convergent strabismus*. Sporadic convulsions and shivering were constant late manifestations. However, the animals invariably died during the night and death was not observed. A period of approximately 2 months elapsed between the onset of clinical signs and death.

Diet

The lion cubs were fed excellent quality beef containing bones. This was obtained from carcasses retained because of *Cysticercus bovis* infestation and treated by freezing for 14 days. The small cubs were occasionally fed whole chickens or rabbits for 1–2 months after their arrival.

A vitamin/mineral supplement (Table 2), adapted from that recommended for the domestic cat (Siegmund, 1967), was sprinkled onto the meat at the rate of 2,4 kg of supplement/145 kg of meat (based on a 182,0 kg carcass). Depending on their age, cubs were fed 1–4,5 kg of this preparation 6 days a week and fasted on the 7th day. It was estimated that a fully grown lion would receive up to 9 000 IU of vitamin A daily from the supplement.

Treatment

A 6-month-old female cub, which had severe clinical signs of approximately 1 month's duration, was treated 3 times with a vitamin A preparation containing 150 000 IU/ml vitamin A. Two ml were administered 3 times: initially, 14 days later and finally after another month. In addition she received a diet containing approximately 50 000 IU of vitamin A daily. Improvement was obvious after 1 week and continued gradually until all signs disappeared 2 months after the commencement of treatment. Subsequently this animal died from dystocia at approximately 3 years of age.

TABLE 2 Vitamin/Mineral supplement powder

Monocalcium phosphate	42,3	kg
Limestone powder	62,3	kg
Salt	57,3	kg
Magnesium sulphate	50,0	kg
Choline chloride	7,5	kg
Vitamin A (500 000 IU/g)	30	g
Vitamin D$_3$ (400 000 IU/g)	2,5	g
Vitamin E (25 %)	610	g
Vitamin B$_{12}$	160	g
Vitamin B$_1$	2,5	g
Vitamin B$_2$	6,0	g
Vitamin B$_6$	3,0	g
Folic acid	0,5	g
Pantothenic acid	10	g
Niacin	33	g
Iron sulphate	870	g
Copper sulphate	100	g
Cobalt sulphate	40	g
Manganese sulphate	50	g
Zinc oxide	20	g
Potassium iodide	7,5	g

Necropsy findings

Four lion cubs were available for post-mortem examination (Table 1). Lions 1 and 3 were badly decomposed. However, Lions 2 and 4 were necropsied very soon after death. All 4 animals were in fair to good general condition, fat being plentiful in the body depots.

Few macroscopic lesions other than those in the skeletal and nervous systems were noticed in Cases 1 and 3. The parathyroids of Case 3 appeared enlarged and were 4 mm in diameter. In addition the costochondral junctions were enlarged and resembled a rachitic rosary. However, the consistency of the bones of Animal 3 appeared normal. Mild diffuse pulmonary congestion and petechiae and ecchymoses of the diaphragmatic lobes were observed in Lions 2 and 4. In addition there were petechiae and ecchymoses of the parietal pleura of the diaphragm in Lion 2. The eyes and contiguous tissues were examined in 3 cases but no gross abnormalities were observed.

Except for the enlarged costochondral junctions of Case 3, gross pathological changes of the skeleton were noticed only in the bones of the head. The degree of abnormality varied only slightly between the 4 cases. The most obvious lesion was the severe thickening of the *osseus tentorium cerebelli*. Closer inspection of the skulls, after sagittal sectioning, revealed an increase in thickness of all the bones composing the brain case. The relative thickening of the cranial bones of Cubs 1 and 4 is compared with the skull of an adult lion from the Kalahari Gemsbok Park in Fig. 1 & 2. The occipital bones, especially in the area below the nuchal crest and dorsal to the foramen magnum, were severely thickened compared to those of the adult lion. Although the parietal bones appear to be of equal thickness in the figures, the adult animal had a prominent sagittal mid-line crest. In the cubs there was no such crest and the increased thickness was due to a uniform thickening of the parietal bones. Examination of Fig. 1 & 2 also reveals marked thickening of the sphenoid bones of the cubs. Comparison of the skulls also reveals a diminished size in the *sella turcica* of the cubs and decreased diameters of the proximal openings of the foramina of the optic, auditory and hypoglossal nerves.

The mandibles of the lion cubs were thickened in all respects and disproportionately bulky compared to the length of the zygomatic processes. The mandibles of Lion 1 were compared with a museum specimen of those of a slightly older lion cub which originated from the Kruger National Park (Fig. 3). On cursory inspection the mandibles of Lion 1 were found to be disproportionately thick, poorly streamlined and very bulky. The height from the ventral surface to the dorsal surface of the mandibles at points A, B and C were measured using a pair of calipers. Thus, the mandible of Lion 1 was 4,2 cm at A, 4,3 cm at B and 3,8 cm at C compared to 3,9 cm at A, 3,7 cm at B and 3,4 cm at C. The thickness from the medial to lateral aspect was 2,1 cm at B and 3,4 cm at C in the mandible of Lion 1 compared to 1,8 cm at B and 1,9 cm at C in the case of the museum specimen. The dry mass of the mandibles of Lion 1 was 237,7 g compared to 215,0 g for the mandibles of the museum specimen. Therefore, the mandibles of Lion 1 were larger and heavier than those of the museum specimen.
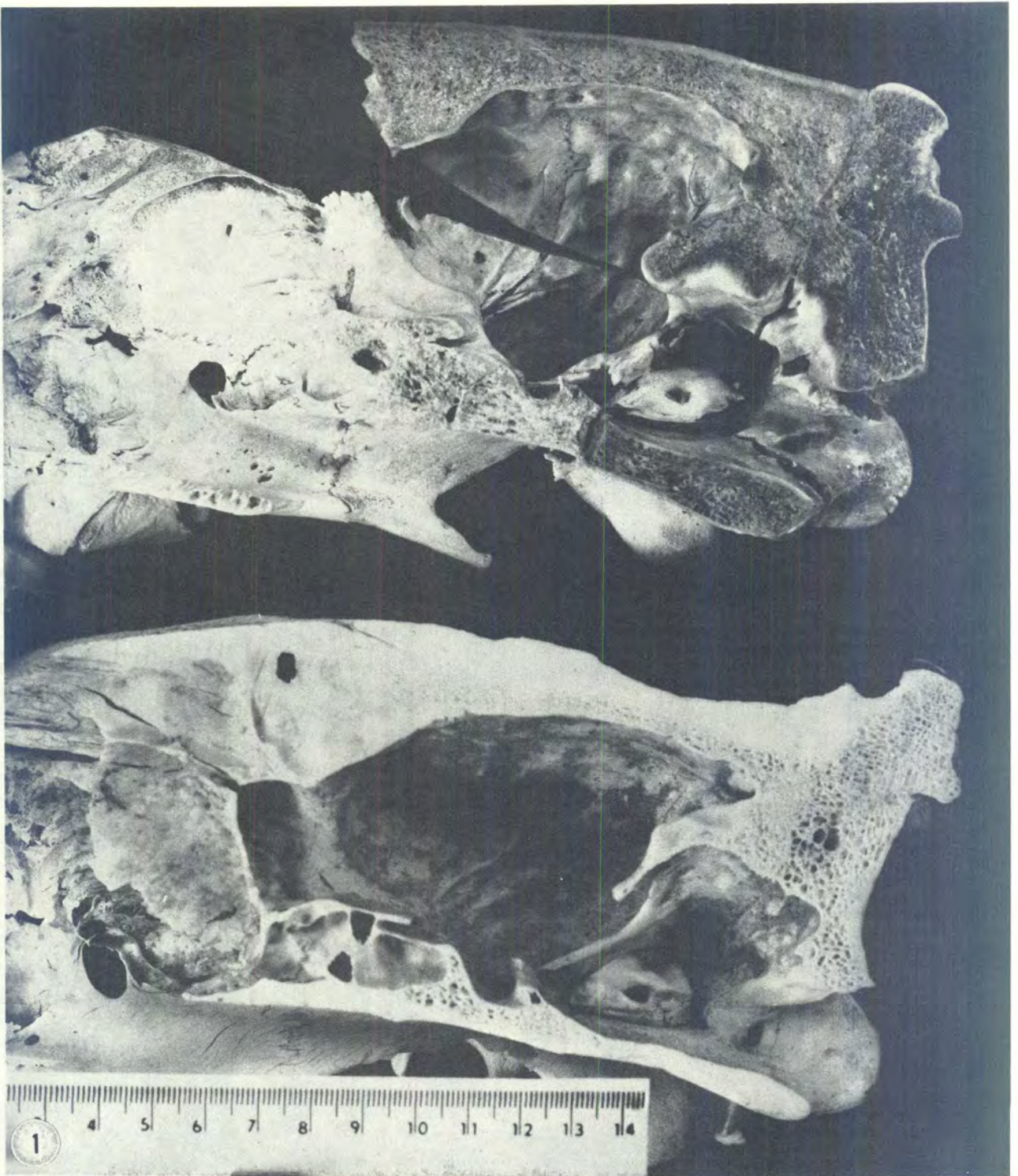
FIG. 1 Comparison of sagittal mid-line section of vitamin A deficient Cub 1 (top) with that of an adult wild lion (bottom). The bones of the posterior cranial vault of the lion cub are much thicker than those of the adult
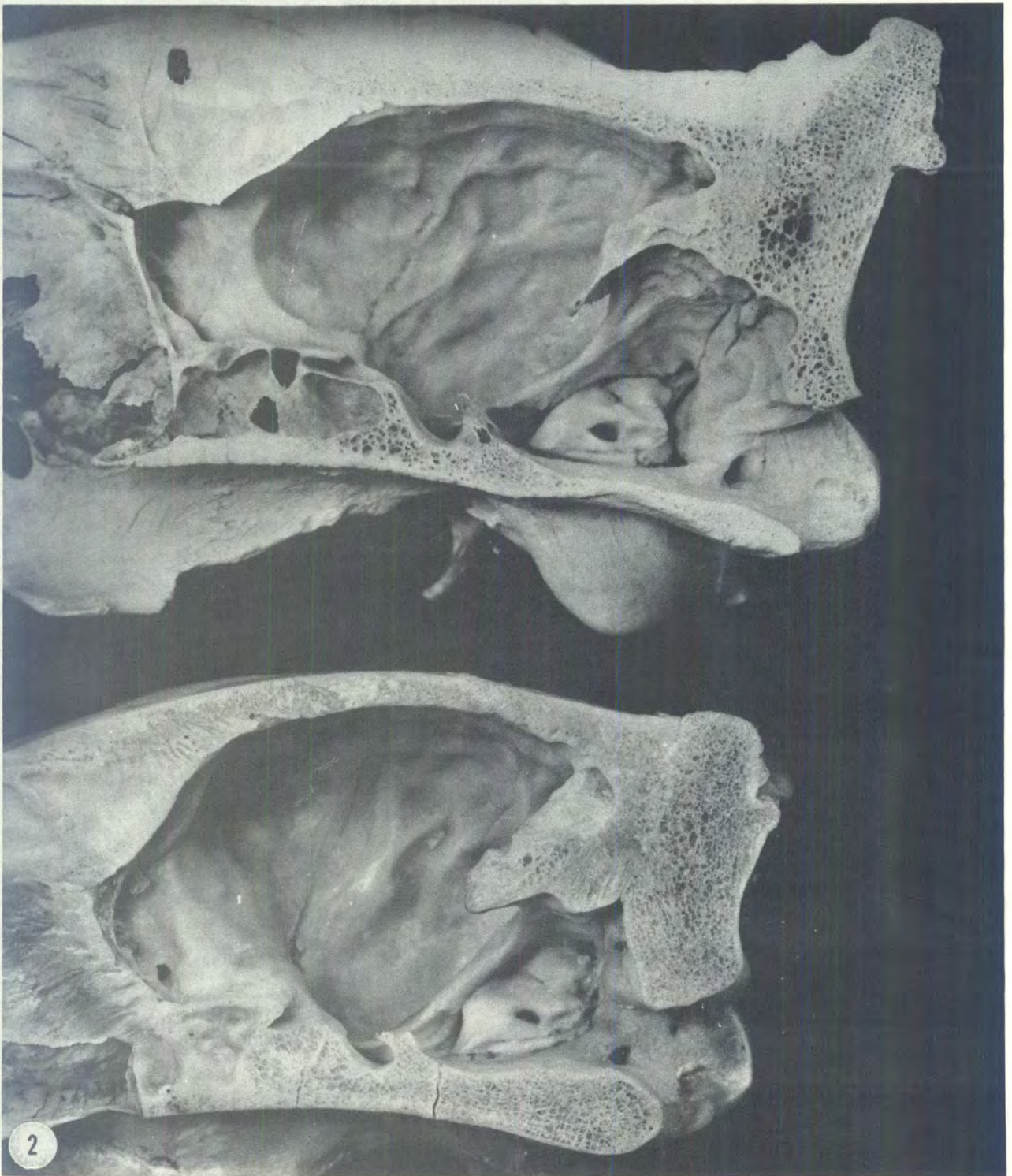
FIG. 2 Comparison of thickened cranial bones of Cub 4 (bottom) with those of the normal adult lion. Thickening of the *osseus tentortium cerebelli* and occipital and sphenoid bones is striking
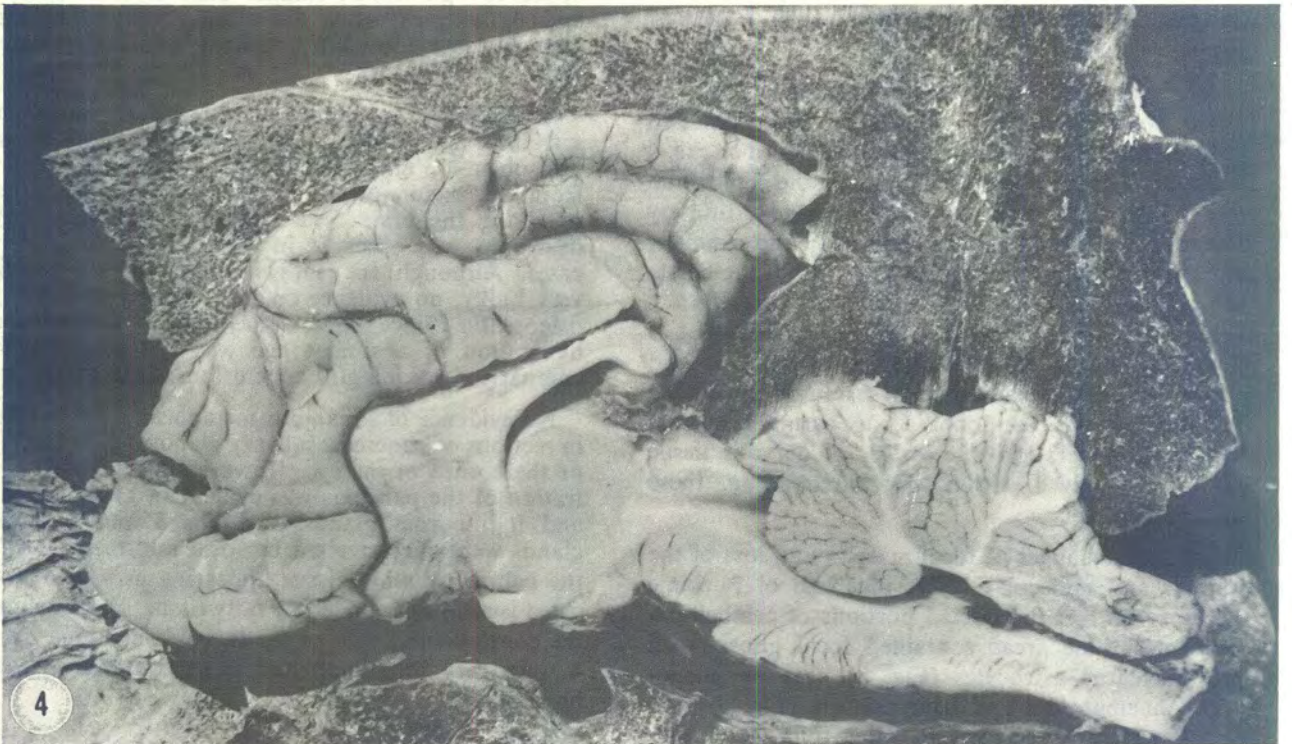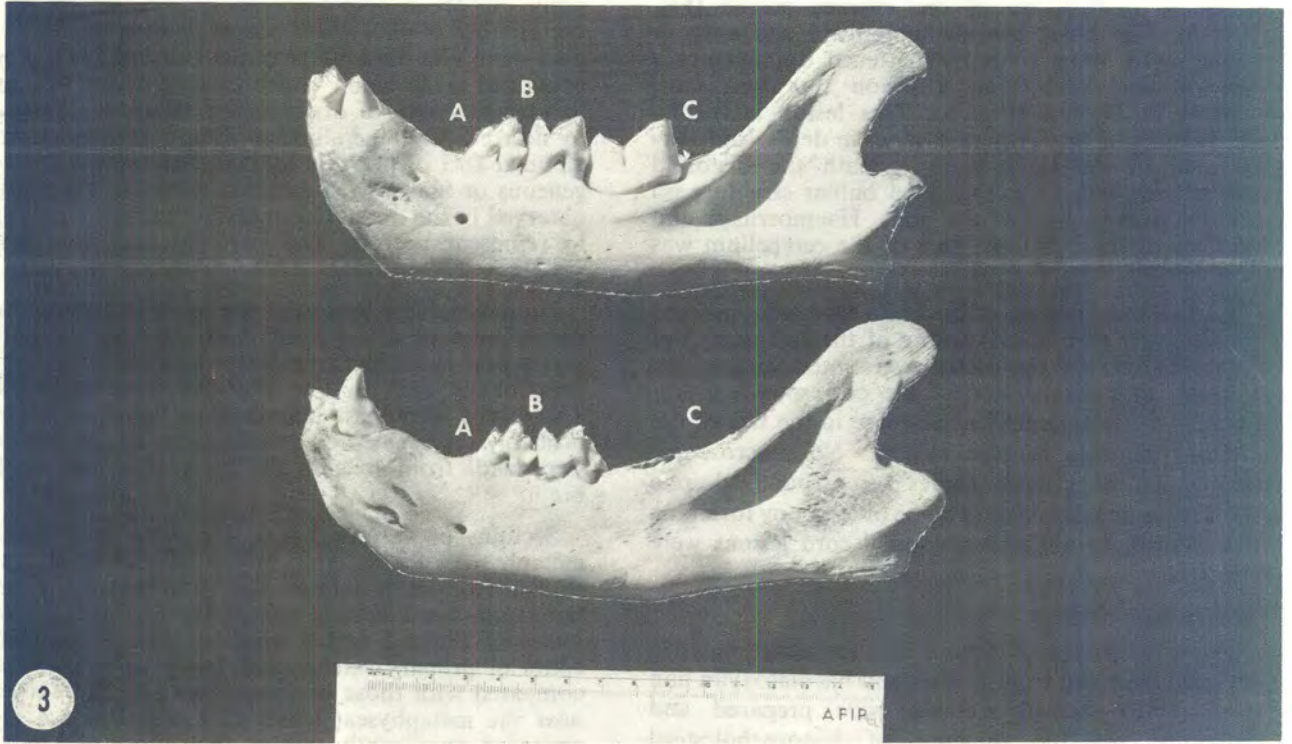
FIG. 3 Comparison of thickened and poorly remodelled mandible of Cub 1 (bottom) with that of a slightly older wild lion cub (top). See text for measurements

FIG. 4 Sagittal mid-line section of cranium and brain of Cub 1. The relationship between the thickened bones and dorso-ventrally compressed cerebellum, brain stem and herniated cerebellum is evident

The most obvious lesion in the brain was herniation, haemorrhage and necrosis of the posterior part of the *vermis cerebelli* (Fig. 4, 5 & 6). The hemispheres of the cerebellum of all cases were flattened dorsoventrally, when a sagittal section was examined, with complete obliteration of the *cisterna magna* (Fig. 4 & 5). The pons, medulla oblongata and anterior spinal cord were similarly flattened dorsoventrally beneath the cerebellum, a lesion that was most evident in Case 4 (Fig. 5). This lesion is further illustrated in Fig. 6 where a concave depression may be seen in the brain stem beneath the distorted cerebellum, with an exaggerated bulbar structure on the anterior portion of the pons. Haemorrhage and necrosis of the herniated part of the cerebellum was also evident (Fig. 4 & 6).

Further examination of the brain revealed a marked compression and overcrowding of the cerebrum and diencephalon (Fig. 5). By transverse sectioning of the 4 brains and comparison of the corresponding sections, a severe symmetrical decrease in the size of the lateral ventricles became evident. No macroscopic lesions of the cranial nerves were found, despite the diminished diameter of some of the bony foramina (see above). In addition no spinal cord lesions were observed.

Microscopic findings

A wide variety of tissues was collected in 10% buffered formalin from 3 cases and haematoxylin and eosin (HE) stained sections were prepared and examined for the presence of histopathological changes. Special stains were used when necessary (see below).

Microscopic lesions of the central nervous system (CNS) were primarily confined to the herniated portions of the cerebellum and spinal cord in all 4 lion cubs. The most evident lesions of the cerebellum were acute focal punctate haemorrhages diffusely disseminated throughout the molecular and granular layers and white tracts of some folia within the herniated portions. These haemorrhagic foci were characterized by centrally located arterioles and capillaries in varying stages of degeneration, thrombosis and fibrinoid necrosis, leading to a residuum consisting of homogeneous acidophilic appearing material (Fig. 7). Degeneration or necrosis of nervous tissue was only observed within, not surrounding, these haemorrhagic foci.

Less acute changes of focal malacia and loss of the granular and molecular layers plus loss of Purkinje cells were evident in affected portions of cerebellum. Frequently these areas contained focal gliosis with multi-nucleated astrocytes (Fig. 8), free or phagocytized haematoidin and haemosiderin (Fig. 9), and foci of mature fibrous tissue. Some folia were compressed to the extent of appearing pointed but were without evidence of degenerative changes or atrophy. There was focal thickening of the overlying meninges due to infiltration of plasmacytes, lymphocytes and large mononuclear lymphoid cells. Moreover, occasional foci of meningeal fibroplasia (Fig. 10) and submeningeal haemorrhages, congestion and oedema were encountered.

Wallerian degeneration of fibres of the ventral spinal tracts was observed in sections of the anterior spinal cord (Fig. 12). Luxol fast blue staining revealed demyelination in these areas and many reactive astrocytes with vesicular nuclei and deeply acidophilic cytoplasm were observed. A marked increase in the number of glial fibres was evident using Holzer's glial stain. The dura mater of the anterior spinal cord contained many blood vessels that were occluded and in various stages of degeneration from hyalinization to necrosis to mineralization (Fig. 11). Linear and globular foci of necrotic looking, acidophilic, homogeneous or mineralized material were also frequently observed in the dura. This material was also thought to represent necrotic and partially resorbed blood vessels.

No microscopic lesions of the optic or oculomotor nerves were observed. Cells with eosinophilic cytoplasm and small dark centrally located nuclei were occasionally seen in one acoustic nerve (Fig. 13). These cells were best identified as "glial cells" but probably represented oligodendroglia, as the sections were made from areas of the nerves proximal to the brain.

Sections of various bones, including long bones, metaphyses of ribs and bones of the skull were studied from each animal. The structure of the long bones appeared normal except for the metaphyseal plates of Lions 2 and 4 which contained elongated zones of primary calcification and ossification when compared with those of Lions 1 and 3. The cortices near the metaphyseal plates of Lions 2 and 4 also appeared significantly thinner than those of Lions 1 and 3, with excessive fibroblastic activity, conspicuously large Howship's lacunae and active osteoclasis.

The skull bones examined included the mandible, maxilla, frontal bone, *osseus tentorium cerebelli* and basisphenoid, and 2 portions of occipital bone, 1 from the region of the nuchal crest and the other overlying the brain. No evidence of fibrous osteodystrophy was observed in the skull bones of the 4 cases. Although the subperiosteal bones appeared very bulky, no evidence could be found of excessive osteoplasia. Since bone tissue from a normal free-living lion of a similar age was not available for comparison meaningful conclusions were impossible.

No evidence of squamous metaplasia was observed in sections of pancreas, salivary glands, trachea, lungs or the cornea of the eye. However, severe fatty infiltration of the pancreas was evident in Lions 2 and 4 and the thyroid glands of Lions 3 and 4. These glands were characterized by focal infiltration of fat, the parenchymatous tissue appearing as well demarcated islands surrounded by fatty tissue. Furthermore, the parafollicular cells of the thyroids in Lions 2 and 4 were very prominent and were considered to be hyperplastic.

Vitamin A analysis

Vitamin A analysis was performed on fresh frozen liver as described by Moore (1957).

Levels from Lions 3 and 4 were too low to detect i.e. less than 0,5 IU of vitamin A/g on a wet basis. A fresh frozen specimen from a wild lion, approximately 2 years old, obtained for comparison, contained 5 400 IU of vitamin A/g.
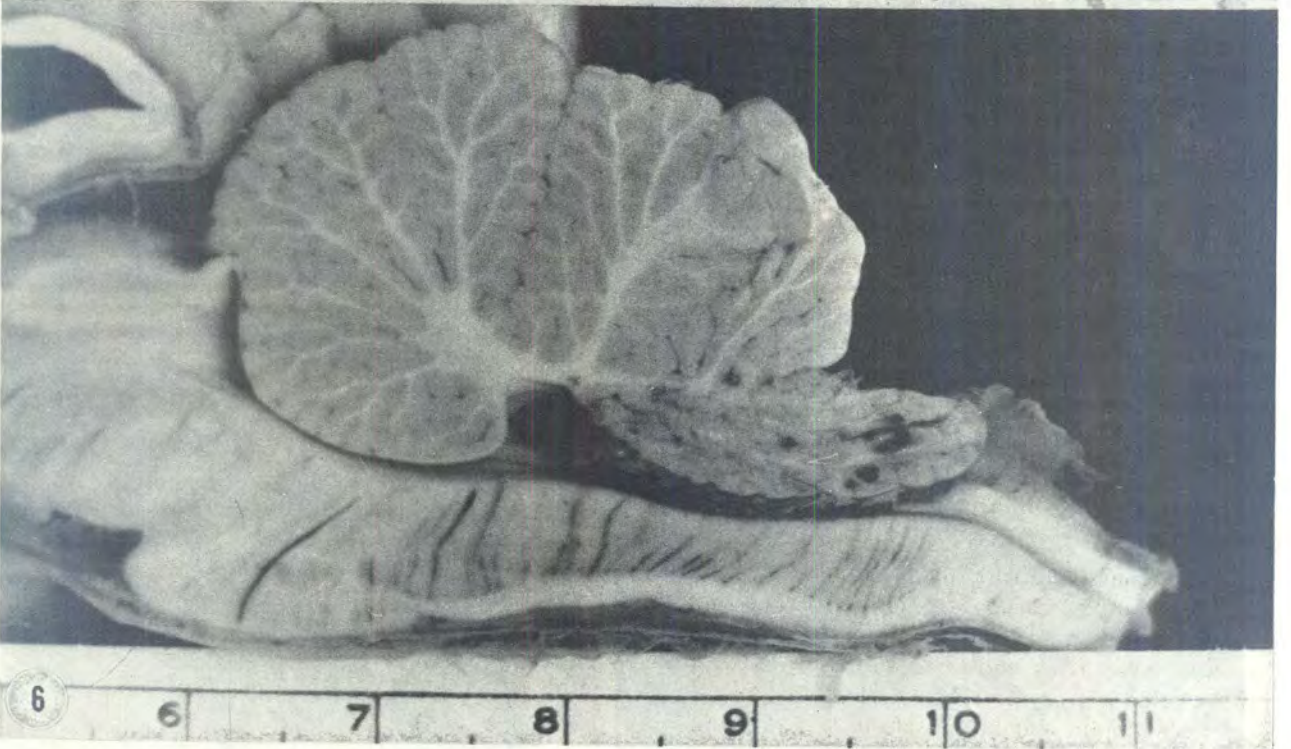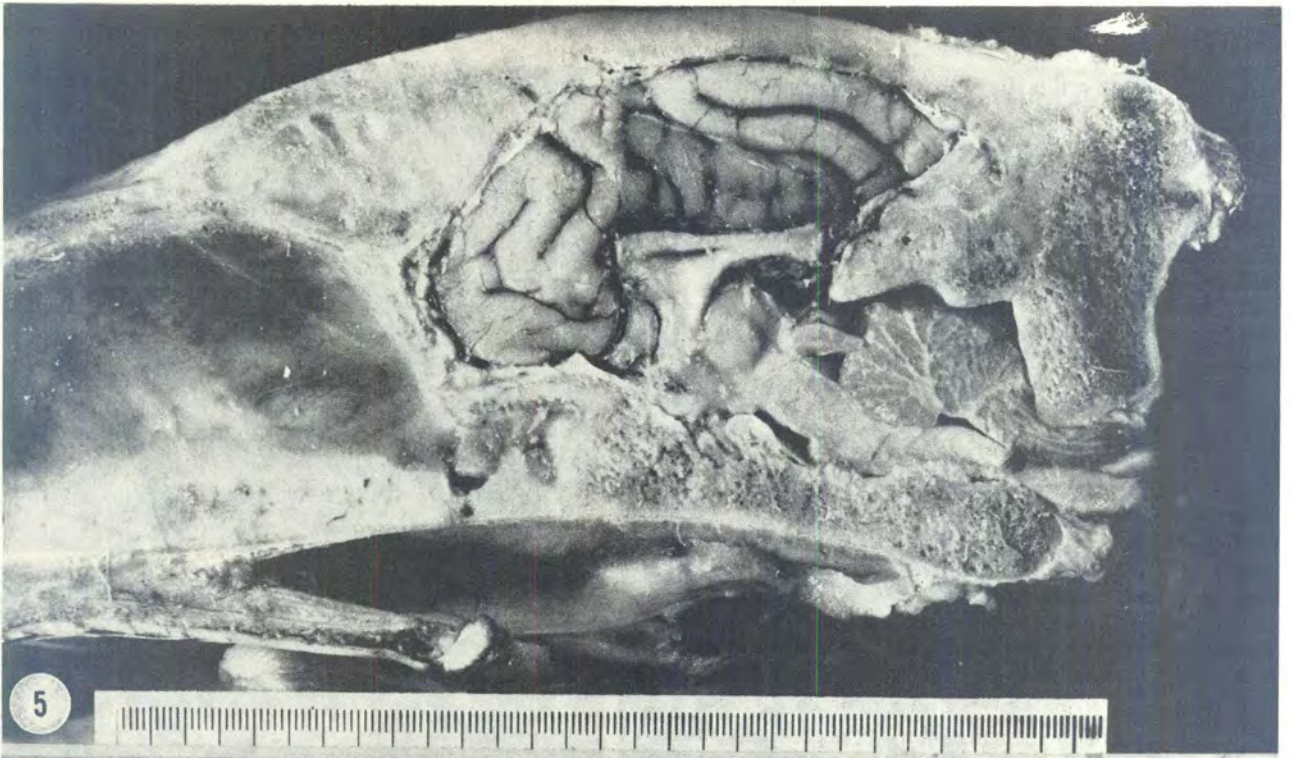
FIG. 5 Sagittal mid-line section of cranium and brain of Cub 4. Notice the overcrowded appearance of the cerebrum and partial obliteration of the lateral ventricles. The brain stem beneath the cerebellum has been severely compressed and the *vermis cerebelli* has herniated into the foramen magnum, obliterating the cisterna magna

FIG. 6 Sagittal mid-line section of the brain of Cub 3 demonstrating the haemorrhages in the herniated portion and dorso-ventral flattening of the remaining cerebellum and brain stem beneath with an abnormal bulbar structure on the anterior pons
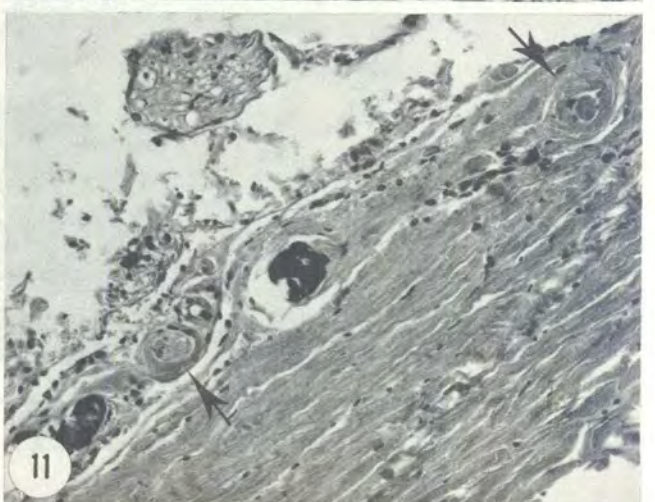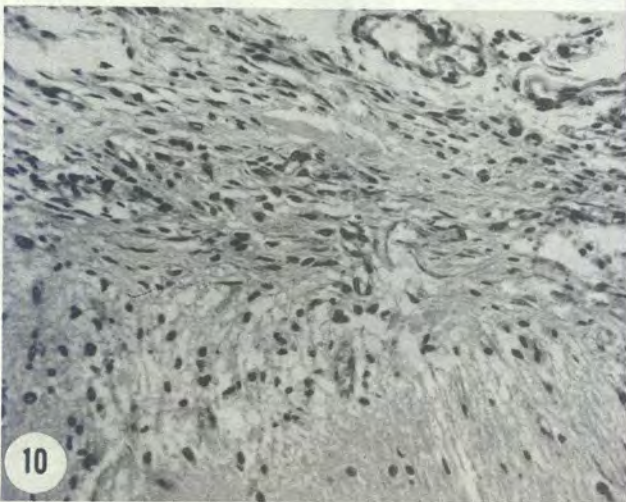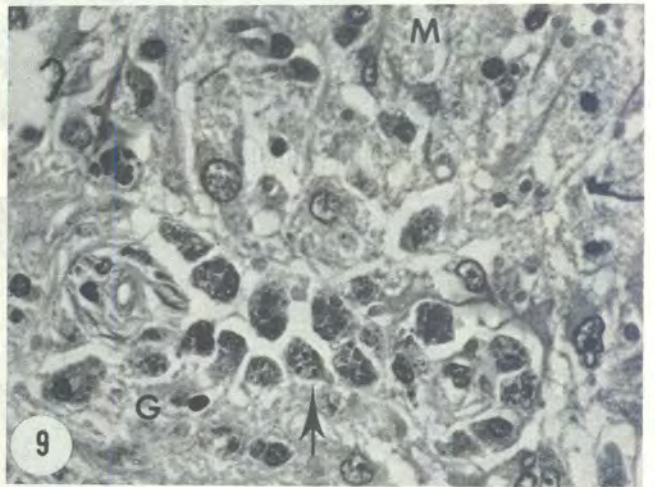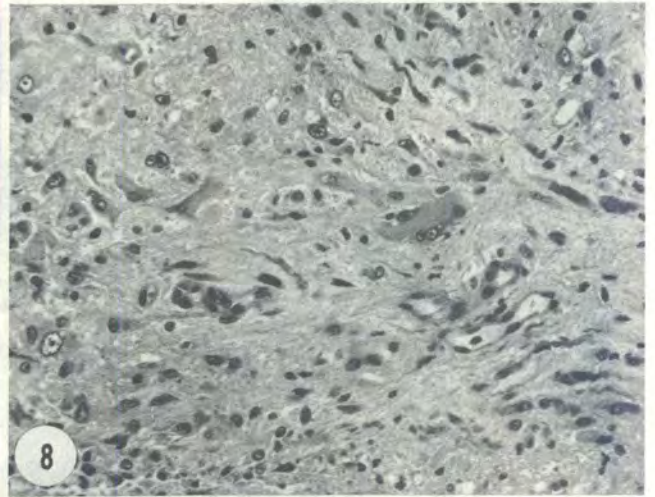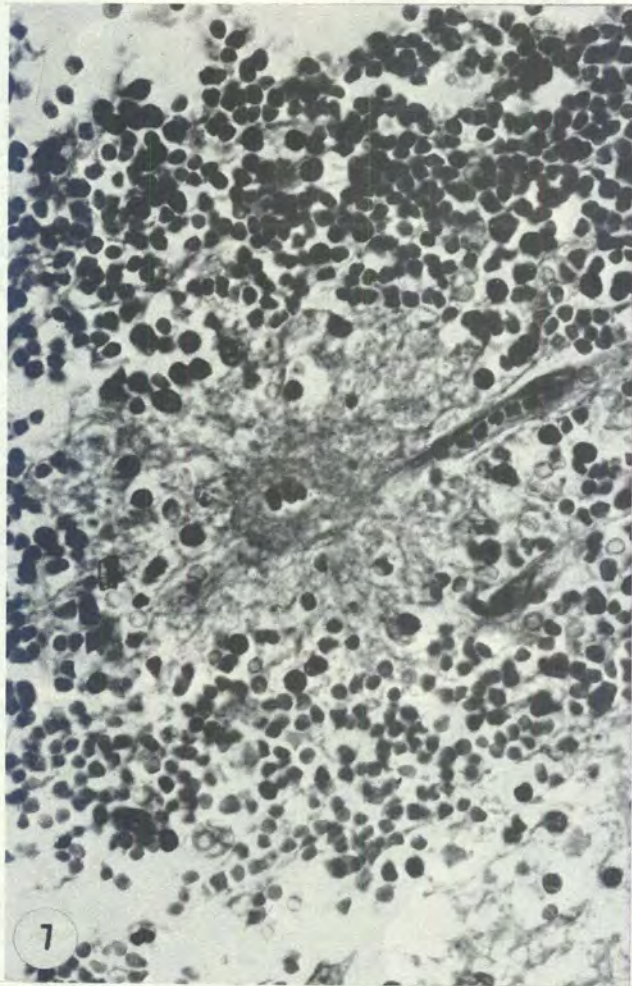
FIG. 7 Recent haemorrhage in cerebellum. Capillary showing necrosis and thickening of wall with fibrinoid material. H E × 500

FIG. 8 Focal gliosis in white tract of cerebellar folium. Reactive astrocytes and astrocytic giant cell. H E × 200

FIG. 9 Site of old haemorrhage and focal loss of Purkinje cells in cerebellar folium (M=molecular layer; G=granular layer). Aggregation of haemosiderin bearing gitter cells (arrow). H E × 500

FIG. 10 Focal fibrous thickening of leptomeninges in cerebellar folium. H E × 200

FIG. 11 Dura mater of anterior spinal cord. Occlusion of blood vessels in the inner aspect of the dura mater with homogeneous eosinophilic material (arrows) and mineralization of some vessels. H E × 200
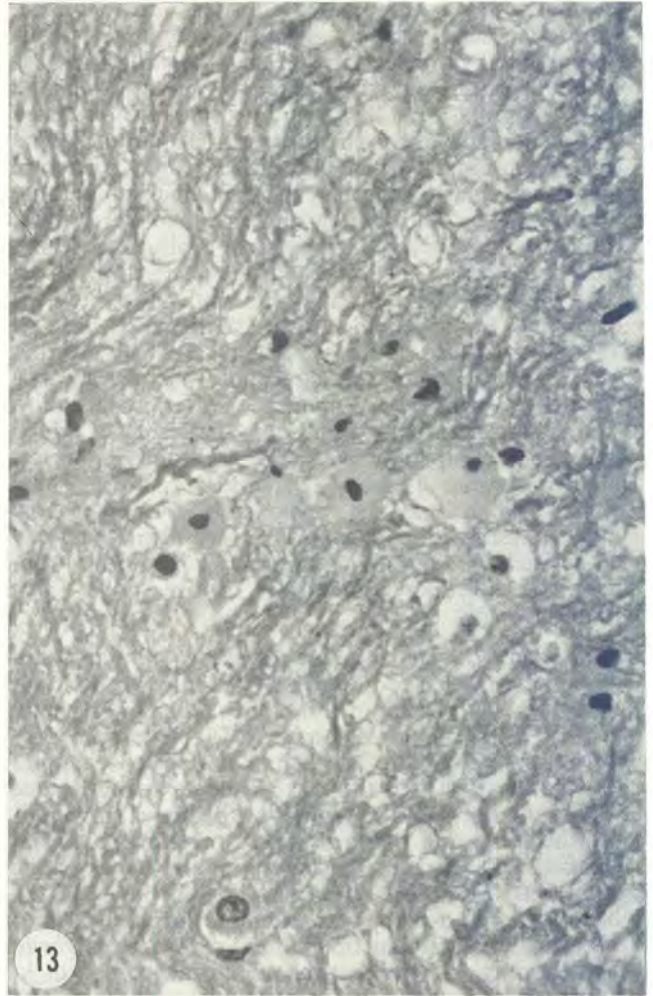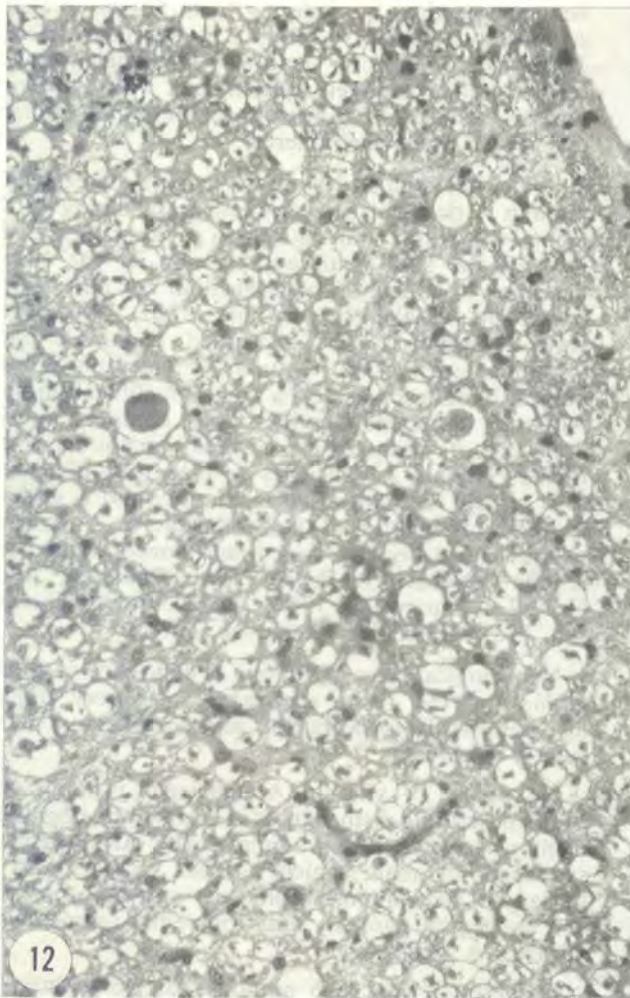
FIG. 12 Wallerian degeneration of ventral spinal tract in anterior spinal cord. Swollen axons and demyelination H E × 200

FIG. 13 Acoustic nerve: Abnormal cells which have small dark nuclei and a large amount of homogeneous eosinophilic cytoplasm. Probably reactive oligodendroglial cells. H E × 500

DISCUSSION

The minute quantities of vitamin A in the livers of Lions 3 and 4 justified a diagnosis of vitamin A deficiency when compared with the level in the liver of a 2-year-old wild lion. Since the same clinical symptoms and skull deformation were seen in Lions 1 and 2 there is little doubt that they were also deficient in vitamin A. Based on the microscopic appearance of the metaphyses and C-cell hyperplasia in the thyroids of Lions 2 and 4 it appeared that their vitamin A deficiency was complicated by fibrous osteodystrophy.

The identical clinical symptoms seen in 3 other cubs that were not available for post-mortem examination is highly suggestive that they also suffered from a deficiency of vitamin A. This supposition is further substantiated by the fact that when 1 of these cubs was placed on vitamin A therapy she recovered. Necropsy of this animal at an age of 3 years revealed no gross or microscopic lesions referable to vitamin A deficiency. It was tempting to speculate that a narrowed or malformed pelvis had predisposed to the fatal dystocia. However, the pelvis appeared normal in every respect, though no pelvis from a free-living lioness was available for comparison.

Vitamin A deficiency in captive African lions has been observed previously. Stillbirths, neonatal deaths and multiple anomalies in lion cubs are suspected to be manifestations of vitamin A deficiency. In the Rotterdam Zoo 32 lion cubs were either stillborn or died within 14 days during an 18-month period (Van Bemmel, Zwart & Peters, 1962; Krediet & Zwart, 1964). Evidence incriminating a deficiency in vitamin A was the improvement in breeding of adults and viability of cubs after vitamin A supplementation. Likewise, Heywood (1967) reported anaemic appearing, weak-born lion cubs and frequent stillbirths in the Chester Zoo. Vitamin A was absent in the livers of several stillborn cases and an average of only 3,7 IU vitamin A/g of liver was found in 7 lion cubs. The liver of the dam of some of these cubs contained only 8 IU vitamin A/g.

Multiple congenital anomalies were found in the lion cubs mentioned in the above reports. Cardiac anomalies were prominent: Persistent ductus arteriosus, ventricular septal defects, persistent right aortic arch and segmental aplasia of the pulmonary arterial tree (Krediet & Zwart, 1964; Heywood, 1967). Heywood (1967) also reported pulmonary dysplasia and hypoplasia in these lion cubs.

Maternal deficiency of vitamin A is known to have a teratogenic effect in rats, swine and cattle (Jubb & Kennedy, 1970). Anomalies are perhaps more marked in stillborn or neonatally dead piglets and include hypotrichosis, subcutaneous cysts, dwarfed ears,

polydactylism and contracted legs, cleft palate, ventricular septal defects, persistent ductus arteriosus pulmonary hypoplasia and aplasia, partial diaphragmatic closure and diaphragmatic hernia, hepatic cysts, hypoplasia of the large intestine and displaced malformed and polycystic kidneys. Genital anomalies like hypoplasia, hermaphroditism and segmental aplasia are also reported, as are microphthalmia, hydrocephalus and protrusion of spinal cord tissue into the intervertebral foramina (Palludan, 1961). Microphthalmia, accompanied by constriction of the optic nerves due to narrowed optic foramina, is prominent in rats and calves (Wolbach & Bessey, 1941; Blakemore, Ottaway, Sellers, Eden & Moore, 1957). Productivity of pregnant female animals deficient in vitamin A may also be diminished due to dystrophic changes in the reproductive tract which may be incompatible with the gametocytes or implanted zygote (Jubb & Kennedy, 1970). These effects which may be responsible for embryonic deaths, resorption and abortion, are also frequently associated with hypovitaminosis A in various non-domestic species, particularly captive lions (Van Bemmel et al., 1962).

The very distinctive gross lesions of cranial bones and nervous tissue described in this report and observed by others in lion cubs (Perrin-Raybaud et al., 1973; Tuch & Pohlenz, 1973) have been produced experimentally in vitamin A deficient puppies (Mellanby, 1941). In these experiments an imbalance was found between the growth of the bones surrounding the brain and the brain itself, resulting in partial cerebellar herniation. Thickening of the bones of the skull was less severe anteriorly but all bones of the head were affected to some extent. Other bone lesions observed were calcifications of the *tentorium cerebelli*, hypertrophy of the petrous temporal bone, thickening of the cribriform plate, thickened vertebrae (resulting in decreased diameter of the vertebral canal) and a less pronounced thickening of the pelvic bones and femurs. Lesions of the brain included degeneration, especially of cranial nerves 1, 2, 5 and 8, flattening of the dorsum of the cerebellum and compression of the pons and medulla oblongata. Pressure on these areas of the brain resulted in diminution in size of the 4th ventricle and aqueduct of Sylvius. Thus the pathological lesions of experimental vitamin A deficiency in puppies are nearly identical to those described in lion cubs.

The lesions reported previously (Perrin-Raybaud et al., 1973; Tuch & Pohlenz, 1973) in lion cubs suffering from suspected vitamin A deficiency were essentially the same as those observed in the present cases. However, Perrin-Raybaud et al. (1973) also observed hydrocephalus, syringomyelia, thickened and bulky vertebrae and fragile teeth with thin enamel. In addition to the spinal lesions, lordosis and kyphosis were observed clinically. Changes in the vertebral column were not evident in the present cases, nor was hydrocephalus observed. In fact a marked decrease in the size of the lateral ventricles was seen in 2 of the animals.

Perrin-Raybaud et al. (1973) observed excessive ossification of the *osseus tentorium cerebelli* but indicated that this was a normal finding in Felidae. However, comparison of this structure in the normal wild lion with those of the vitamin A deficient animals (Fig. 1 & 2) illustrates the excessive overgrowth of the bony partition. At least 2 of the lion cubs described

here appeared to be suffering from fibrous osteodystrophy in addition to vitamin A deficiency. Considering the precarious method of balancing an all red-meat diet, by merely sprinkling it with a vitamin/mineral powder, it is not surprising that multiple deficiencies were encountered.

Somewhat similar lesions have been described in vitamin A deficient calves. There was doming of the frontal bone area and thickening of the bones at the base of the skull with compression of the brain; flattening or coning of the cerebellum was particularly prominent (Blakemore et al., 1957). Moreover, calves characteristically presented narrowed optic foramina and twisted, tortuous or constricted optic nerves; blindness was also a common clinical finding. Although apparent blindness was common in the lion cubs, its pathological basis could not be determined. Vitamin A deficiency in pigs, rats, quail and fowl closely resembles that in the dog and is characterized by herniation of the cerebellum or other areas of the central nervous system and concomitant bone lesions (Wolbach & Bessey, 1941; Palludan, 1961; Howell & Thompson, 1967; Howell, Pitt & Thompson, 1969; Howell & Thompson, 1970).

Neurological signs of vitamin A deficiency in young animals of the above species are also very similar and consist of ataxia, paresis and convulsions, particularly in calves.

No report of vitamin A deficiency in man was found describing disturbances in cranial bone development as seen in lower animals. The Arnold-Chiari syndrome of man, which consists primarily of a prolapsed cerebellum, myelocoele and spina bifida, is a congenital anomaly and apparently unrelated to vitamin A deficiency.

Domestic kittens, 3–6 months old, fed vitamin A deficient diets experimentally (Gershoff, Andrus, Hegsted & Lentini, 1957) failed to develop clinical signs or lesions noted in the lion cubs. However, kittens developed ataxia (thought to be the result of muscle weakness) and prominent squamous metaplasia of the epithelia of the conjunctiva, trachea, bronchi, ducts of the salivary glands and uterus. Their failure to develop the more serious nervous syndrome may reflect a slower rate of growth in the domestic cat compared to lions and this may have prevented development of the cranial lesions. Or the kittens may have had adequate hepatic reserves of vitamin A prior to the experiment which tended to protect them during a more rapid growth period early in the experiment. It is also an interesting consideration that the oldest of the 9 lion cubs in this report was spared from the vitamin A deficiency syndrome.

Captive felids of various species fed diets containing 100 IU/day were found to have liver vitamin A reserves of only 8–10 IU/g of liver (Heywood, 1967), but no overt clinical signs of deficiency were noted. It was concluded that this level was apparently sub-normal because when the vitamin A content of the diet was increased to 200 IU/kg/day the condition and breeding performance of the animals improved substantially. The kidney vitamin A levels of these captive felids were usually negligible (Heywood, 1967). The low levels are explainable on the basis of the observed low hepatic reserves, especially when compared to the hepatic reserves of the wild lion sampled in this study. It would have been interesting to know the level of vitamin A stored in the kidneys of this wild lion cub.

It has been known for some time that vitamin A deficiency causes squamous metaplasia of epithelia in domestic animals (Helmboldt, Jungherr, Eaton & Moore, 1953; Jubb & Kennedy, 1970). Squamous metaplasia of the epithelium of the parotid duct system has been considered the pathognomonic lesion in calves (Helmboldt, *et al.*, 1953). However, Wolbach & Bessey (1941) have stated that the epithelial changes are entirely unrelated to the occurrence of lesions in the bone or nervous system. In addition squamous metaplasia was not described by Perrin-Raybaud *et al.* (1973) or Tuch & Pohlenz (1973) in their suspected vitamin A deficient lions and no evidence of metaplasia was found in the present cases.

Papilloedema and incoordination related to increased cerebrospinal fluid (CSF) pressure have been described in experimental vitamin A deficient animals (Moore & Sykes, 1940; Jubb & Kennedy, 1970). The increased CSF pressure was not related to bone malformation of the skull and could be lowered to normal levels by the addition of vitamin A. It has now been shown that increased pressure is caused by under absorption of CSF, which has been postulated to be brought about by changes in the epithelium of the arachnoid villi by Davson and also Calhoun, Hurt, Eaton, Rousseau & Hall (according to Eaton, 1969). Hayes (1969) commented that the highly differentiated cells of the arachnoid epithelium appeared to be reduced to a keratinized cell type. The development of ataxia in kittens already discussed (Gershoff *et al.*, 1957), which was thought to be due to muscular weakness, may have been caused by increased pressure of CSF. This was not determined in the present cases. However, the fact that 1 female cub started to improve dramatically a week after vitamin A therapy was begun suggests that her severe incoordination was related to high CSF pressure.

Occlusive vascular lesions in small vessels of the leptomeninges and dura mater over the brain were first described in calves by Hayes, Nielsen & Eaton (1968). Similar changes were seen in the dura mater of the most anterior portion of the cervical spinal cord of the cubs discussed in this paper.

In the absence of osseous tissue from normal lion cubs, comparative microscopic studies could not be undertaken in this investigation. The basic cause of increased thickness, especially of bones of the cranium, has not been completely elucidated. Earlier studies in dogs suggested that vitamin A deficiency precipitated both osteoblastic and osteoclastic activity, causing thickened, poorly remodelled bones due to a shift from compact to cancellous bone (Mellanby, 1941). Wolbach & Bessey (1941) felt that the thickened bones were the result of growth of new periosteal bone. Later work on chicks (Howell & Thompson, 1967), quail (Howell & Thompson, 1970) and calves (Gallina, Helmboldt, Frier, Nielsen & Eaton, 1970) supported these findings. Gallina *et al.* (1970) hypothesized that vitamin A deficiency altered the metabolism of the periosteum, resulting in an increased production of bone. Hayes *et al.* (1968) observed a reduction in bone resorption while formation continued in the periosteum of sphenoid bones. They offered 2 explanations, 1 related to lowered oxygen tension brought about by decreased circulation and the other to a failure of differentiation of the mesenchymal cell from the osteoblast to the osteoclast. Davis, Krook & Warner

(1970) suggested that the thickened bones were related to decreased resorption caused by faulty lysosomal proteases responsible for hydrolysis of bone matrix during osteolysis.

Most authors have explained nervous symptoms and lesions as being secondary to compression of the cranial vault (Mellanby, 1941; Wolbach & Bessey, 1941; Blakemore *et al.*, 1957; Gitter, 1962; Howell & Thompson, 1967, 1970) and increased CSF pressure (Moore & Sykes, 1940; Jubb & Kennedy, 1970). Mellanby (1941), Blakemore *et al.* (1957) and Hayes *et al.* (1968) clearly described degenerative inflammatory lesions in cranial and/or spinal nerves brought about by defective configuration of nerve canals through bone and by a general pressure increase. Wallerian degeneration of the spinal cord related to compression pressure has been reported in pigs (Palludan, 1961), fowl and quail (Howell & Thompson, 1967, 1970) and lions (Tuch & Pohlenz, 1973). It was also seen in the cubs of the present report. The pathological changes in the brain and their significance have not received much attention. Gitter (1962) found acute haemorrhages in the cerebellum, which were not related to necrosis of nerve tissue, and multifocal non-suppurative meningitis in the cerebrum of swine. Tuch & Pohlenz (1973) observed haemorrhagic infarction, but also described degeneration and loss of Purkinje cells and reduction of the granular layer not related to haemorrhages, in the cerebellum of lions. Both acute and subacute lesions were observed in the cerebella of the lion cubs considered in this report.

Acute lesions consisted of focal cerebellar and cerebellar meningeal haemorrhages which were not accompanied by necrosis of nervous tissue, except immediately adjacent to haemorrhagic vessels in the cerebellum. Acute haemorrhages were not considered agonal in nature because the capillaries and arterioles within haemorrhagic foci were invariably necrotic and/ or thrombosed. Subacute lesions in the cerebellum obviously represented organizing haemorrhagic foci. They were focal and contained large amounts of haematoidin and haemosiderin. Therefore, vascular degeneration of terminal vessels appeared to be the primary lesion in the brain, accounting for the haemorrhages and ensuing small foci of necrosis. This deduction was substantiated by the total absence of diffuse necrosis or atrophy of nervous tissue, as would be expected if the primary aetiology was increased intracranial pressure causing mechanical damage or generalized ischaemia resulting from compression of larger vessels. Indeed, many herniated folia were compressed to such an extent that they were pointed, but their components appeared normal.

Perhaps the gradual increase in intracranial pressure, and the resulting caudal displacement of the cerebellum, interfere with blood flow or occlude the capillaries and arterioles, leading to thrombosis, necrosis and haemorrhage, and represent a progressively developing lesion. The acute increases in pressure elicited by these haemorrhages are probably critical, considering the progressive bony compression and assumed elevated CSF pressure, and may be the stimulus for the intermittent convulsive seizures and clinical exacerbations observed. The vascular lesions are thought to have played a major role in the pathogenesis of the vitamin A deficiency syndrome in the lion cubs studied in this investigation.

REFERENCES

BLAKEMORE, F., OTTAWAY, C. W., SELLERS, K. C., EDEN, E. & MOORE, T., 1957. The effects of a diet deficient in vitamin A on the development of the skull, optic nerves and brain of cattle. *J. comp. Path. Ther.*, 67, 277–288.

DAVIS, T. E., KROOK. L. & WARNER, R. G., 1970. Bone resorption in hypovitaminosis A. *Cornell vet.*, 60, 90–119.

EATON, H. D., 1969. Chronic bovine hypo- and hypervitaminosis A and cerebrospinal fluid pressure. *Am. J. clin. Nutr.*, 22, 1070–1080.

GALLINA, A. M., HELMBOLDT, C. F., FRIER, H. I., NIELSEN, S. W. & EATON, H. D., 1970. Bone growth in the hypovitaminotic A calf. *J. Nutr.*, 100, 129–142.

GERSHOFF, S. N., ANDRUS, S. B., HEGSTED, D. M. & LENTINI, E. A., 1957. Vitamin A deficiency in cats. *Lab. Invest.*, 6, 227–240.

GITTER, M., 1962. Unusual cerebellar conditions in pigs. Part 1. Cerebellar herniation associated with vitamin A deficiency. *Vet. Rec.*, 74, 1150–1152.

HALLORAN, PATRICIA O., 1955. A bibliography of references to diseases of wild mammals and birds. *Am. J. vet. Res.*, 16, Suppl. 2, 1–465.

HAYES, K. C., 1969. Comments. *Am. J. clin. Nutr.*, 22, 1081–1084.

HAYES, K. C., NIELSEN, S. W. & EATON, H. D., 1968. Pathogenesis of the optic nerve lesion in vitamin A-deficient calves. *Arch. Ophthal., New York.*, 80, 777–787.

HELMBOLDT, C. F., JUNGHERR, E. L., EATON, H. D. & MOORE, L. A., 1953. The pathology of experimental hypovitaminosis A in young dairy animals. *Am. J. vet. Res.*, 14, 343–354.

HEYWOOD, R., 1967. Vitamin A in the liver and kidney of some Felidae. *Br. vet. J.*, 123, 390–396.

HOWELL, J. McC. & THOMPSON, J. N., 1967. Lesions associated with the development of ataxia in vitamin A-deficient chicks. *Br. J. Nutr.*, 21, 741–750.

HOWELL, J. McC., PITT, G. A. & THOMPSON, J. N., 1969. The development of lesions in vitamin A deficient adult fowl. *Br. J. exp. Path.*, 50, 181–186.

HOWELL, J. McC. & THOMPSON, J. N., 1970. Lesions in nervous tissue and bone in ataxic vitamin A deficient quail. *Acta neuropathol.* 16, 285–292.

JUBB, K. V. F. & KENNEDY, P. C., 1970. Pathology of domestic animals, New York & London; 2, 2nd ed.; Academic Press.

KREDIET, P. & ZWART, P., 1964. Congenital anomalies of the heart and the arterial trunks in lion cubs. *Tijdschr. Diergeneesk.*, 89, Suppl., 32–45.

MELLANBY, E., 1941. Skeletal changes affecting the nervous system produced in young dogs by diets deficient in vitamin A. *J. Physiol.*, 99, 467–486.

MOORE, T., 1957. Vitamin A. Amsterdam, London, New York: Elsevier Publishing Co.

MOORE, L. A. & SYKES, J. F., 1940. Cerebrospinal fluid pressure and vitamin A deficiency. *Am. J. Physiol.*, 130, 684–689.

PALLUDAN, B., 1961. The teratogenic effect of vitamin-A deficiency in pigs. *Acta vet. scand.*, 2, 32–59.

PERRIN-RAYBAUD, F., GUILLON, J. C. & WYERS, M., 1973. Contribution à l'étude de la "maladie des etoiles" du lion a propos de 4 observations. *Recl Méd. vét. Éc. Alfort*, 149, 739–752.

PRICE, D. A., 1970. Dogs need more than meat. Editorial. *J. Am. vet. med. Ass.* 156, 681–685.

SIEGMUND, O. H., 1967. The Merck Veterinary Manual. Rahway, New Jersey: Merck & Co., Inc.

TUCH, K. & POHLENZ, J., 1973. Partielle cerebellarhernie beim löwen (*Panthera leo* L.). Patologische befunde am kleinhirn und am schädelskellett. *Vet. Path.*, 10, 299–306.

VAN BEMMEL, A. C. V., ZWART, P. & PETERS, J. C., 1962. Report on births and deaths occurring in the gardens of the Royal Rotterdam Zoo during the years 1959 and 1960. *Tijdschr. Diergeneesk.*, 87, 826–836.

WOLBACH, S. B. & BESSEY, D. A., 1941. Vitamin A deficiency and the nervous system. *Archs Path.*, 32, 689–722.