PESQUISA VETERINÁRIA BRASILEIRA
Brazilian Journal of Veterinary Research
ISSN 0100-736X (Print)
ISSN 1678-5150 (Online)

Pesq. Vet. Bras. 43:e07249, 2023
DOI: 10.1590/1678-5150-PVB-7249

Original Article
Livestock Diseases

Vitamin A deficiency as a cause of blindness in feedlot calves[1]

Rayane C. Pupin[2]*, Larissa L. Souza[3], Thaisa X. Silva[3], Helena Carolina F. Fonseca[3], Eduarda A.S. Silva[3], Danilo C. Gomes[2], Marcelo Augusto de Araújo[4] and Ricardo Antônio A. Lemos[2]

ABSTRACT.- Pupin R.C., Souza L.L., Silva T.X., Fonseca H.C.F., Silva E.A.S., Gomes D.C., Araújo M.A. & Lemos R.A.A. 2023. **Vitamin A deficiency as a cause of blindness in feedlot calves.** *Pesquisa Veterinária Brasileira 43:e07249, 2023*. Laboratório de Anatomia Patológica, Faculdade de Medicina Veterinária e Zootecnia, Universidade Federal de Mato Grosso do Sul, Av. Senador Felinto Muller 2443, Campo Grande, MS 79074-460, Brazil. E-mail: rayane.pupin@ufms.br

Vitamin A is an essential micronutrient to reproduction, development, normal growth, and function of the nervous system and vision, especially in growing animals. Hypovitaminosis A can affect any of these functions. The aim of this study was to describe the epidemiology, clinical signs, pathological aspects, and diagnostic approach in an outbreak of blindness in feedlot calves fed only grain. Five of 57 ten-month-old calves became blind after eight months at the feedlot. Clinical signs were mydriasis, absent pupillary and menace reflexes, bilaterally. Hypovitaminosis A was suspected and subsequently confirmed by low serum levels of vitamin A. One calf was euthanized and necropsied, and no gross findings were present. Histopathological lesions were restricted to the retina and characterized by degeneration and atrophy of the photoreceptor layer and some retinal scars. The calves were treated with intramuscular vitamin A injection at a dose of 5,000 international units (IU) per kilogram of body weight (kg BW) every 60 days until slaughter. Affected calves did not recover visual capacity, but no other cases occurred.

INDEX TERMS: Vitamin A, blindness, hypovitaminosis A, photoreceptor, retinal atrophy, rhodopsin, calf, cattle.

RESUMO.- [**Deficiência de vitamina A como causa de cegueira em bezerros confinados**] - Vitamina A é um micronutriente essencial para reprodução, desenvolvimento, crescimento normal, além de participar do funcionamento do sistema nervoso central e visão, especialmente em animais em crescimento. Hipovitaminose A pode afetar qualquer uma dessas funções. O objetivo desse artigo é descrever a epidemiologia, sinais clínicos, aspectos patológicos e abordagem diagnóstica em um surto de cegueira em bezerros confinados alimentados apenas com grãos. De 57 bezerros de dez meses de idade, cinco ficaram cegos após oito meses no confinamento. Os sinais clínicos eram midríase, ausência de reflexo pupilar a luz e de ameaça, bilateralmente. Suspeitou-se de hipovitaminose A, que foi subsequentemente confirmada pelos baixos níveis séricos de vitamina A. Um bezerro foi eutanasiado e necropsiado, e alterações macroscópicas não foram encontradas. Lesões histopatológicas estavam restritas a retina e caracterizavam-se por degeneração e atrofia da camada de fotorreceptores, além de cicatrizes na retina. Os bezerros foram tratados com injeção intramuscular de vitamina A, na dose de 5.000 unidades internacionais (UI) por quilograma de peso vivo (Kg PV) a cada 60 dias, até o dia do abate. Os bezerros afetados não recuperaram a capacidade visual, mas novos casos não ocorreram.

TERMOS DE INDEXAÇÃO: Vitamina A, cegueira, hipovitaminose A, fotorreceptores, atrofia retinal, rodopsina, bezerro.

[1] Received on February 13, 2023.
Accepted for publication on April 20, 2023.

[2] Laboratório de Anatomia Patológica, Faculdade de Medicina Veterinária e Zootecnia (FAMEZ), Universidade Federal do Mato Grosso do Sul (UFMS), Av. Senador Felinto Muller 2443, Campo Grande, MS 79074-460, Brazil. *Corresponding author: rayane.pupin@ufms.br

[3] Professional Residency Program in Veterinary Medicine, Faculdade de Medicina Veterinária e Zootecnia (FAMEZ), Universidade Federal do Mato Grosso do Sul (UFMS), Av. Senador Felinto Muller 2443, Campo Grande, MS 79074-460, Brazil.

[4] Departamento de Clínica Médica e Cirúrgica de Grandes Animais, Faculdade de Medicina Veterinária e Zootecnia (FAMEZ), Universidade Federal do Mato Grosso do Sul (UFMS), Av. Senador Felinto Muller 2443, Campo Grande, MS 79074-460, Brazil.

INTRODUCTION

Vitamin A refers to a group of fat-soluble retinoids, including retinol, retinal, and retinyl esters, whose main functions are the synthesis of rhodopsin (a visual pigment present in rods), bone development, maintenance of mucous membranes and epithelial cells, and reproductive and immune functions (Moore 1961, Zeoula & Geron 2006, Dewell 2014, McGill et al. 2019). Ruminants are unable to produce vitamin A, so it must be obtained from dietary sources, mainly green pastures, such as those containing β-carotene, which is hydrolyzed by pancreatic enzymes and then stored in the liver (Craig et al. 2016, Sajovic et al. 2022) until needed, when it is released into the blood as retinol, after being converted into the active form – retinoic acid (McGill et al. 2019).

Vitamin A deficiency is described in cattle, swine fed only grain and dry hay for months or even years and is associated with different clinical signs. Defective bone modeling can cause narrowing and compression of the brain and spinal cord. Teeth abnormalities are described in rodents, such as low-quality dentin. Reproductive disorders include abortions, stillbirths, congenital blindness, carpus enlargement, hydrocephalus, optic nerve degeneration, and retinal dysplasia (Dewell 2014, Craig et al. 2016, Constable et al. 2017). Dermatological disorders in cattle include scaling dermatitis associated with squamous metaplasia in different epithelia (Mauldin & Peters-Kennedy 2016). Ocular lesions can be caused by optic nerve atrophy due to the narrowing of the optic foramen or degeneration of photoreceptors and retinal scars (Wilcock & Njaa 2016).

Diagnosis is based on epidemiological findings, clinical signs, and anatomopathological aspects and confirmed by vitamin A serum levels (Donkersgoed & Clark 1988, Hill et al. 2009, Kang et al. 2017, Parker et al. 2017). This paper describes the epidemiology, clinical and pathological aspects, and a diagnostic approach in a blindness outbreak affecting feedlot calves.

MATERIALS AND METHODS

Historical and epidemiological data were obtained from the farm's keeper and veterinarian. Blood samples were collected from two calves – one sick and one healthy – in tubes containing a coagulation activator to evaluate vitamin A levels. One sick calve was euthanized and submitted to necropsy, when fragments of all organs and both eyes were collected and fixed in 10% formalin, routinely processed for histology, and stained with hematoxylin and eosin (HE).

RESULTS

An outbreak of blindness occurred in feedlot calves affecting five of 57 animals of ten months of age (morbidity 8,77%). These calves were weaned two days after birth. They received milk replacers until they were two months old when they started to feed an adaptative diet composed only of pelleted grain submitted to and special process that, according to the manufacturer, improves the use of the corn. At three months old, the commercial product was changed to the final diet, in a total grain system, without access to green forage. They didn't receive any mineral supplementation besides commercial products. Affected calves circled constantly and showed bilateral blindness, mydriasis (Fig.1), absence of pupillary reflex and menace response. No other abnormalities were found.

A preliminary diagnosis of vitamin A deficiency was made, and animals were moved from the feedlot to a paddock to feed green forage.

The healthy calf had a serum level of vitamin A of 45μg/mL, and the sick one of 10μg/mL. At necropsy, no gross lesions were found. Histopathologic lesions were restricted to the retina in both eyes. There was retinal atrophy or even disappearance of the outer nuclear layer – where the nuclei of the photoreceptors are found – and the outer plexiform layer (Fig.2). In some spots, lesions were most severe and affected the inner nuclear and plexiform layers (Fig.3). Furthermore, there was choroid and retinal fusion in some places.

All calves were treated with intramuscular injection of vitamin A (Monovin A, Laboratory Bravet LTDA), at a dose of 5000 international units (IU) per kilogram of body weight (kg BW), every 60 days until the day of slaughter.

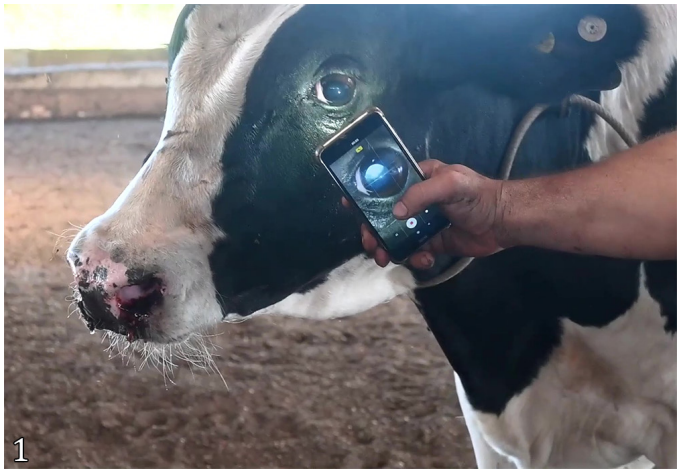

Fig.1. Hypovitaminosis A in feedlot calves. A sick calf showing mydriasis and absence of pupillary reflex.

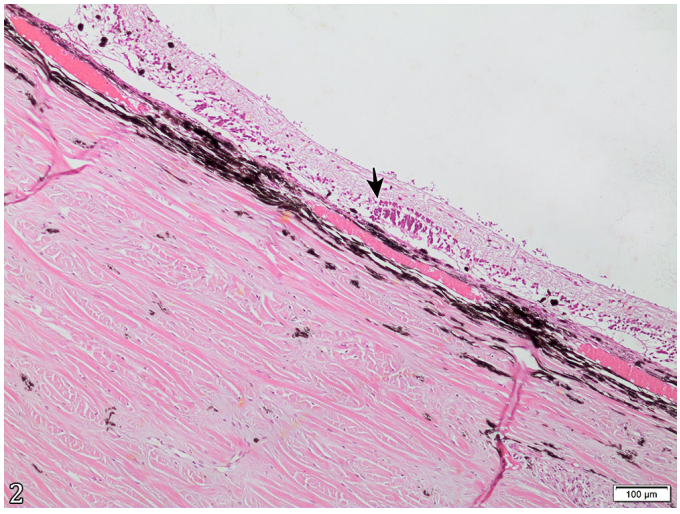

Fig.2. Hypovitaminosis A in feedlot calves. There are multiple spots of retinal degeneration and atrophy, especially in the outer nuclear and plexiform layers. Remnants of the outer nuclear layer are sparse (arrow). HE, obj.10x.

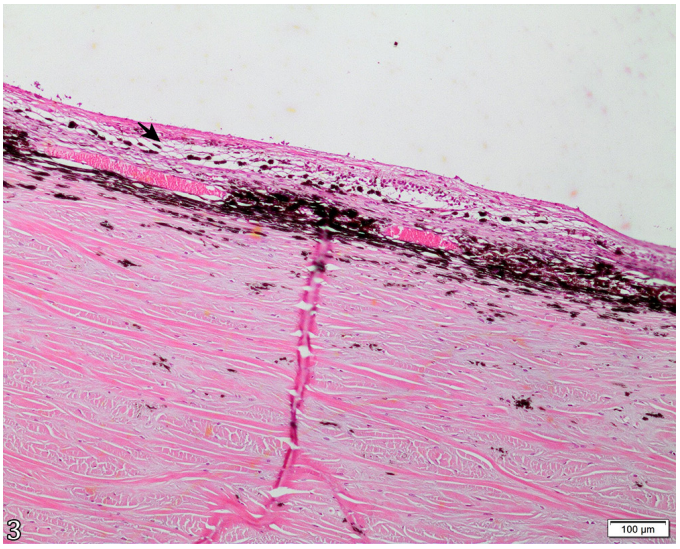

Fig.3. Hypovitaminosis A in feedlot calves. In the most affected areas of the retina, there is diffuse atrophy and disappear of inner nuclear and plexiform layers, and the atrophic retina is fused with the choroid (arrow). HE, obj.10x.

DISCUSSION

The diagnosis of hypovitaminosis A was based on the epidemiology, clinical signs, and histopathological findings and confirmed by a serum vitamin A lower than normal values in calves – 25 to 35µg/dL (Kohlmeier & Burroughs 1970). There was no occurrence of new cases after calves had been moved from the feedlot to a paddock to fed green forage and after one vitamin A parenteral injection. Different levels of serum vitamin A are associated with clinical signs, having already been described as less than 7µg/dL, 12µg/dL, 20µg/dL (Swanson et al. 2000, Yoon et al. 2003) and as low as 0.317µg/dL and 0.481µg/dL (Kang et al. 2017).

The retinal lesions in the necropsied calf suggested that the blindness was caused by photoreceptor degeneration – especially rods – due to rhodopsin deficiency, which is synthesized from vitamin A. Light causes physicochemical changes in rhodopsin and then electrical changes in photoreceptor membranes. Therefore, vitamin A deficiency causes rhodopsin deficiency and no neuronal transmission from photoreceptors (Wilcock & Njaa 2016, Sajovic et al. 2022). Histopathological findings were multifocal to diffuse photoreceptor atrophy, first in the outer rod layer, causing night blindness (Wilcock & Njaa 2016, Sajovic et al. 2022), which is usually undetected (Moore 1961, Donkersgoed & Clark 1988) until it evolves into day blindness because of diffuse photoreceptor atrophy, loss of the outer nuclear layer, and even full retinal atrophy with scars in the choroid and retina (Donkersgoed & Clark 1988, Wilcock & Njaa 2016, Labelle 2017).

Blindness was described in two weaned calves with hypovitaminosis A, but in these, there was just bilateral optic disk swelling (papilledema), identified through indirect ophthalmoscopy examination (Kang et al. 2017). Papilledema results from increases in cerebrospinal fluid pressure because of reduced absorption in the arachnoid villi and thickened connective tissue in the dura mater (Donkersgoed & Clark 1988, Constable et al. 2017). This increase caused optic disk changes after 6-12 weeks of hypovitaminosis A (Blakemore et al. 1957, Donkersgoed & Clark 1988), and it was not seen in this animal, similar to previously described (Yoon et al. 2003). This was probably because papilledema is the first detectable lesion and usually occurs before blindness starts (Yoon et al. 2003). If treatment is not initiated, it can evolve into retinal atrophy (Blakemore et al. 1957), as probably occurred in the animal evaluated here.

Optic nerve lesions and cranial bone thickening were not found in the necropsied calf. In Canada, blindness and neurological disorders were described in 19-month-old cattle associated with optic nerve damage characterized by extensive necrosis and gitter cells (malacia). These lesions were associated with nerve compression secondary to remodeling failure at the level of the optic foramen (Parker et al. 2017).

The calves affected were young – 10 months of age – like those previously described (Donkersgoed & Clark 1988, Kang et al. 2017). Young animals have greater vitamin A requirements and lower hepatic stores, more prone to hypovitaminosis A (Wilcock & Njaa 2016). Neonate calves from dams with low serum vitamin A can show ocular lesions, usually caused by optic nerve compression due to optic foramen stenosis (Van Der Lugt & Prozesky 1989, Wilcock & Njaa 2016). Besides the ocular lesions, cerebellum herniation, heart defects, palatine cleft (Hill et al. 2009), and hydrocephalus (Van Der Lugt & Prozesky 1989) were seen.

Because vitamin A is fat soluble, liver storage only occurs if daily ingestion is 3-5 times over the daily needs (Dewell 2014). Animals consuming green forages have a hepatic retinol reserve sufficient for six months to two years (Wilcock & Njaa 2016). Feedlot cattle fed high grain diets and silage is prone to hypovitaminosis A. Yellow corn has low carotenoid levels. In contrast, silage has high levels, but fermentation decreases the availability (Zeoula & Geron 2006) and most have high nitrate levels, which destroys carotene in the digestive tract (Dewell 2014).

Swine and poultry are the main livestock animals susceptible to hypovitaminosis A, then cattle, sheep, and horses. This susceptibility is related to the raising system used since the first two usually receive high-grain diets (Moore 1961). Prolonged feeding with dry pastures, poorly stored forage, or high grain diets predispose to hypovitaminosis A at 5-18 months (Donkersgoed & Clark 1988, Constable et al. 2017, Parker et al. 2017), but cases have been described in calves after 100 days (Blakemore et al. 1957). In this outbreak, calves were fed exclusively grain for eight months, enough time to deplete retinol hepatic reserves.

Clinical improvement was previously described (Donkersgoed & Clark 1988) after treatment with 2 million IU of vitamin A. Usually, the dose is 440 IU/kg BW, making better use of aqueous substances (Constable et al. 2017). In this outbreak, none of the five sick calves recovered after treatment. The visual dysfunction can be reversible if treated early (Labelle 2017), but prolonged deficiency results in permanent degeneration of the photoreceptors (Sajovic et al. 2022). The outer parts of the photoreceptors have a fast turnover and the highest metabolic rates, so if their inner portion remains viable, they can regenerate quickly (Labelle 2017). This explains why these animals did not recover their visual capacity because the photoreceptor nuclei were gone.

Prevention can be with liquid supplementation mixed into feed, mineral salt, or parenteral administration (Dewell 2014). Considering the daily needs of 40 IU/Kg BW, supplementation levels can reach 110 IU/kg BW/day (Constable et al. 2017). For weaning calves fed milk replacers, daily vitamin A ingestion should be 11000 IU/kg of dry matter (Swanson et al. 2000). An alternative method is the parenteral injection of 3000 to 6000 IU/kg BW every 60 days (Constable et al. 2017).

According to the clinical signs, the main differential diagnoses in this outbreak were polioencephalomalacia and closantel poisoning. The blindness in polioencephalomalacia is of brain origin, so other clinical signs and histopathological lesions are sufficient to differentiate. In closantel poisoning, retinal lesions are present as degeneration and loss of the photoreceptor layer, inner nuclear layer, and atrophy of the outer plexiform layer (Pohl et al. 2020), but information about the use of this product helps exclude this. Some infectious diseases can cause blindness, for example, infectious bovine keratoconjunctivitis, malignant catarrhal fever, and infectious bovine rhinotracheitis. The first is caused by *Moraxella bovis*, a gram-negative bacteria which causes edema and conjunctival hyperemia, evolving into corneal ulceration. The other two are systemic diseases caused by members of the Herpeviridae family and are associated with other clinical signs (Wilcock & Njaa 2016). *Pteridium aquilinum* poisoning is a potential cause of retinal degeneration in sheep in the United Kingdom because ptaquiloside results in photoreceptor degeneration and even retinal atrophy (Labelle 2017).

CONCLUSION

An outbreak of vitamin A deficiency was diagnosed based on clinical signs, epidemiological data and low serum levels of vitamin A. The main clinical sign was blindness, caused by retinal degeneration and atrophy. After the cases, all calves were treated, and no more cases occurred, but the sick ones did not recover. This condition can be an important cause of blindness in young animals, especially in feedlot cattle.

Acknowledgments.- The authors thanks Ingeborg M. Langohr, from the Department of Pathobiological Sciences and Louisiana Animal Disease Diagnostic Laboratory, for help with the histopathological evaluation, and to Bianca Larissa de Bortoli, veterinary practitioner from Campo Grande, Brazil, for her assistance with the physical examination of the calves. One of the authors (R.A.A.L.) has a research fellowship from the "Conselho Nacional de Desenvolvimento Científico e Tecnológico" (CNPq).

Conflict of interest statement.- The authors declare that there are no conflicts of interest.

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. Pathol. 67(3):277-288. <https://dx.doi.org/10.1016/S0368-1742(57)80027-7> <PMid:13449185>

Constable P.D., Hinchcliff K.W., Done S.H. & Grünberg W. 2017. Veterinary Medicine: a textbook of the diseases of cattle, horses, sheep, pigs, and goats. 11th ed. Elsevier, St. Louis, p.1314-1320.

Craig L.E., Dittmer K.E. & Thompson K.G. 2016. Bones and joints, p.82-84. In: Maxie M.G. (Ed.), Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. Vol.1. 6th ed. Elsevier, St. Louis. <https://dx.doi.org/10.1016/B978-0-7020-5317-7.00002-3>

Dewell G. 2014. Vitamin A deficiency in beef calves. Iowa State University – Extension and Outreach, Iowa. Available at <https://store.extension.iastate.edu/product/Vitamin-A-Deficiency-in-Beef-Calves> Accessed on: Jun. 1, 2022.

Donkersgoed J.V. & Clark E.G. 1988. Blindness caused by hypovitaminosis A in feedlot cattle. Can. Vet. J. 29(11):925-927. <PMid:17423169>

Hill B.D., Holroyd R.G. & Sullivan M. 2009. Clinical and pathological findings associated with congenital hypovitaminosis A in extensively grazed beef cattle. Aust. Vet. J. 87(3):94-98. <https://dx.doi.org/10.1111/j.1751-0813.2009.00398.x>

Kang S., Park C. & Seo K. 2017. Ocular abnormalities associated with hypovitaminosis A in Hamwoo calves: a report of two cases. J. Vet. Med. Sci. 79(10):1753-1756. <https://dx.doi.org/10.1292/jvms.17-0166> <PMid:28890472>

Kohlmeier R.H. & Burroughs W. 1970. Estimation of critical plasma and liver vitamin A levels in feedlot cattle with observations upon influences on body stores and daily dietary requirements. J. Anim. Sci. 30(6):1012-1018. <https://dx.doi.org/10.2527/jas1970.3061012x> <PMid:5422003>

Labelle P. 2017. The eye, p.1265-1318. In: Zachary J.F. (Ed.), Pathologic Basis of Veterinary Disease. 6th ed. Elsevier, St. Louis. <https://dx.doi.org/10.1016/B978-0-323-35775-3.00021-7>

Mauldin E.A. & Peters-Kennedy J. 2016. Integumentary system, p.581. In: Maxie M.G. (Ed.), Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. Vol.1. 6th ed. Elsevier, St. Louis. <https://dx.doi.org/10.1016/B978-0-7020-5317-7.00006-0>

McGill J.L., Kelly S.M., Guerra-Maupome M., Winkley E., Henningson J., Narasimhan B. & Sacco R.E. 2019. Vitamin A deficiency impairs the immune response to intranasal vaccination and RSV infection in neonatal calves. Scient. Rep. 9(1):15157. <https://dx.doi.org/10.1038/s41598-019-51684-x> <PMid:31641172>

Moore T. 1961. The pathology of vitamin A deficiency. Vitamins Hormones 18:499-514. <https://dx.doi.org/10.1016/S0083-6729(08)60877-8> <PMid:13772362>

Parker E.M., Gardiner C.P., Kessell A.E. & Parker A.J. 2017. Hypovitaminosis A in extensively grazed beef cattle. Aust. Vet. J. 95(3):80-84. <https://dx.doi.org/10.1111/avj.12560> <PMid:28239860>

Pohl C.B., Lorezentt M.P., Cecco B.S., Henker L.C., Panziera W. & Driemeier D. 2020. Accidental closantel poisoning in sheep in the state of Rio Grande do Sul. Acta Scient. Vet. 48(Supl.1):500. <https://dx.doi.org/10.22456/1679-9216.101078>

Sajovic J., Meglič A., Glavač D., Markelj Š., Hawlina M. & Fakin A. 2022. The role of vitamin A in retinal diseases. Int. J. Mol. Sci. 23(3):1014. <https://dx.doi.org/10.3390/ijms23031014> <PMid:35162940>

Swanson K.S., Merchen N.R., Erdman Jr. J.W., Drackley J.K., Orias F., Morin D.E. & Haddad M.F. 2000. Influence of dietary vitamin A content on serum and liver vitamin A concentrations and health in preruminant Holstein calves fed milk replacer. J. Dairy Sci. 83(9):2027-2036. <https://dx.doi.org/10.3168/jds.S0022-0302(00)75083-1> <PMid:11003235>

Van Der Lugt J.J. & Prozesky L. 1989. The pathology of blindness in newborn calves caused by hypovitaminosis A. Onderstepoort J. Vet. Res. 56(2):99-109. <PMid:2748139>

Wilcock B.P. & Njaa B.L. 2016. Special senses, p.407-508. In: Maxie M.G. (Ed.), Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. Vol.1. 6th ed. Elsevier, St. Louis. <https://dx.doi.org/10.1016/B978-0-7020-5317-7.00005-9>

Yoon S., Jeong S., Seo K., Kim J., Jean Y., Hwang E., Chung G. & Han H. 2003. Clinical, ophthalmological, and pathological findings of hypovitaminosis A in cattle. Korean J. Vet. Pathol. 7(1):17-21.

Zeoula L.M. & Geron L.J.V. 2006. Vitaminas, p.355-395. In: Berchielli T.T., Pires A.V. & Oliveira S.G. (Eds.), Nutrição de Ruminantes. Funep, Jaboticabal.