Acta Scientiae Veterinariae, 2024. 52(Suppl 1): 1009.

CASE REPORT
Pub. 1009

ISSN 1679-9216

Endothelial Dysfunction in a Bitch: Treatment with Superficial Keratectomy Combined with Conjunctival Advancement of the "Gundersen" and Modified "Gundersen" Types

Kamila Aguiar da Silva[1], Úrsula Chaves Guberman[2], Thaís Gomes Rocha[1] & Cristiane dos Santos Honsho[1]

ABSTRACT

***Background*:** Endothelial dysfunction affects small and elderly dogs and is similar to Fuchs' corneal endothelial dystrophy observed in humans. This condition can be hereditary or acquired and is progressive, potentially leading to corneal edema, bullous keratopathy and recurrent, indolent ulcers. The aim of this report is to describe a case of bilateral endothelial dysfunction treated by a superficial lamellar keratectomy followed by conjunctival advancement using both Gundersen and modified Gundersen techniques in a 8-year-old bitch Shih-tzu with corneal ulcer refractory to clinical treatment, and to describe the 17-month postoperative outcome.

***Case*:** A 8-year-old bitch Shih-tzu was referred for ophthalmological evaluation due to progressive ocular opacity without blindness, developed over 2 months. The patient was using an Elizabethan collar and was being treated for bilateral superficial corneal ulcers with antibiotic eye drops and lubricating gel. Ophthalmological examination revealed moderate mucous secretion and normal menace response, normal pupillary light reflexes (direct, consensual and dazzle). Both eyes presented corneal edema, more pronounced in the right eye. Tear production and intraocular pressure were normal, and bilateral superficial ulcers were noted in the paracentral region. The patient was diagnosed with endothelial dysfunction and bilateral corneal ulcers, and treatment with antibiotic and hyperosmotic eye drops, oral analgesics and maintenance of the protective collar was initiated. After 14 days, ocular secretion improved, but edema and ulceration persisted in both eyes. Dimethylpolysiloxane-based eye drops were added, and due to the low therapeutic response, bilateral conjunctival advancement using the Gundersen technique was recommended for the left eye and the modified Gundersen technique for the right eye, where corneal edema was more intense. The conjunctival flaps were sutured with monofilament nylon in a simple interrupted and continuous pattern and were removed after 31 days. During this period, antibiotic, hyperosmotic and lubricating eye drops were continued. Oral anti-inflammatory and analgesic medications were also administered. Four days postoperatively, with ulcer resolution in the left eye, prednisolone-based eye drops were added, and the same was done for the right eye on the 22nd day. On the 37th day postoperatively, antibiotic and anti-inflammatory eye drops were discontinued, maintaining the hyperosmotic agent and lubricant, and adding the topical immunomodulator. After 6 months, the owner reported clearer eyes with no signs of discomfort, ocular secretion, or tearing. In the follow-up, 17 months postoperatively, the dog had been off all medication for 3 months. Positive menace responses and movement tests were observed; bilateral ocular opacity and corneal pigmentation in the left eye were noted, with no episodes of corneal ulcer since the procedure.

***Discussion*:** Endothelial dystrophy has been reported in dogs of various breeds, including Shih-tzu. There is a greater predisposition in bitches and elderly dogs, as seen in this case. With the decline in endothelial function, the remaining cells are unable to maintain deturgescence, allowing fluid accumulation between the collagen lamellae, causing corneal thickening, loss of transparency, development of keratopathies and blindness secondary to edema. Corneal ulcers frequently recur in patients with endothelial dysfunction, are challenging to heal, and cause ocular discomfort and corneal pigmentation. Among the therapeutic options, superficial keratectomy combined with conjunctival advancement is an easily performed procedure that does not require donors, and offers the potential to reduce edema, the recurrence of corneal ulcers, and discomfort.

Keywords: dog, cornea, edema, conjunctival edema.

DOI: 10.22456/1679-9216.141350

Received: 30 August 2024 Accepted: 26 November 2024 Published: 23 December 2024

[1]Curso de Medicina Veterinária, Universidade Vila Velha (UVV), Vila Velha, ES, Brazil. [2]Instituto de Oftalmologia Veterinária (IOV), Vitória, ES. CORRESPONDENCE: C.S. Honsho [cristiane.honsho@uvv.br]. Curso de Medicina Veterinária - UVV. Av. Comissário José Dantas de Melo n. 21. Boa Vista II. CEP 29102-920 Vila Velha, ES, Brazil.

INTRODUCTION

The cornea is the primary barrier to the passage of light rays into the eye; thus, any morphological alteration that interferes with its transparency will compromise vision [1]. Corneal endothelial dysfunction is a progressive, hereditary disease that leads to stromal edema, potentially triggering bullous and/or ulcerative keratopathy that is difficult to heal [1,3,8]. This condition typically occurs bilaterally and is a non-inflammatory disease that predominantly affects small-breed dogs [19]. It resembles Fuchs' endothelial corneal dystrophy in humans, and its developmental mechanisms are similarly not well understood [2,6]. The condition is rare in felines [3], with diffuse corneal edema being the most common sign [16], which can begin in paracentral or temporal regions and progress to involve the entire cornea over months or years [8].

This case report aims to describe the use of conjunctival advancement (Gundersen and modified Gundersen techniques) and its 17-month postoperative outcome in resolving a case of bilateral endothelial dysfunction in a bitch, presenting with corneal edema and superficial ulceration unresponsive to initial clinical treatment.

CASE

A 8-year-old bitch Shih-tzu, weighing 7.8 kg, was referred for specialized ophthalmologic care due to progressive ocular opacity over a 2-month period, without blindness. The patient was receiving treatment for superficial corneal ulcers in both eyes, with moxifloxacin hydrochloride[1] [Vigamox® 0.3% eye drops - every 12 h], sodium hyaluronate[2] lubricating [Hylo® 0.15% gel - every 2 h], and was also wearing an Elizabethan collar.

Ophthalmologic examination revealed moderate mucous discharge bilaterally and positive menace response, as well as direct, consensual, and dazzle pupillary light reflexes. The right eye (Figure 1A) showed moderate to severe edema (++/+++), affecting 90% of the cornea. The left eye (Figure 1B) exhibited mild to moderate corneal edema (+/+++), affecting approximately 80% of the cornea, with pigmentation in the temporal region between 2 and 4 o'clock and in the nasal region between 7 and 9 o'clock. Schirmer tear test[3] results were 16 mm/min for the right eye and 17 mm/min for the left eye. Fluorescein[4] staining test showed superficial bilateral ulcers in the paracentral region between 2 and 3 o'clock in the left eye, and between 9 and 11 o'clock in the right eye. Intraocular pressure[4] [Tonovet plus®] was 15 mmHg for the right eye and 16 mmHg for the left eye. The patient was diagnosed with endothelial dysfunction and bilateral corneal ulcer.

Treatment was initiated bilaterally with moxifloxacin-based and hypertonic saline[5] solution [Hipertonic® 5% - eye drops], both administered 5 times daily. Oral administration of dipyrone sodium [25 mg/kg, every 12 h for 5 days] was prescribed, along with continuous use of an Elizabethan collar. After 14 days, there was an improvement in ocular discharge, with persistent edema and ulceration in both eyes. To the initial treatment regimen, dimethylpolysiloxane[5] [Dimethylpolysiloxane® - eye drops - every 6 h] was added. Due to inadequate clinical response, bilateral conjunctival advancement using the Gundersen technique [10] was recommended.

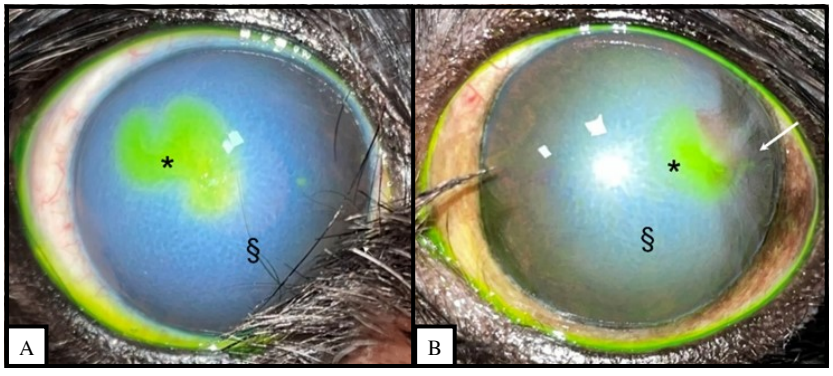

Figure 1. Photographic images of an 8-year-old Shih-tzu bitch with endothelial dystrophy. Note the bilateral fluorescein staining (*). A- Right eye shows diffuse corneal edema (§) with an intensity of ++/+++. B- Left eye shows corneal pigmentation in the temporal region (→) and corneal edema (§) with an intensity of +/+++.

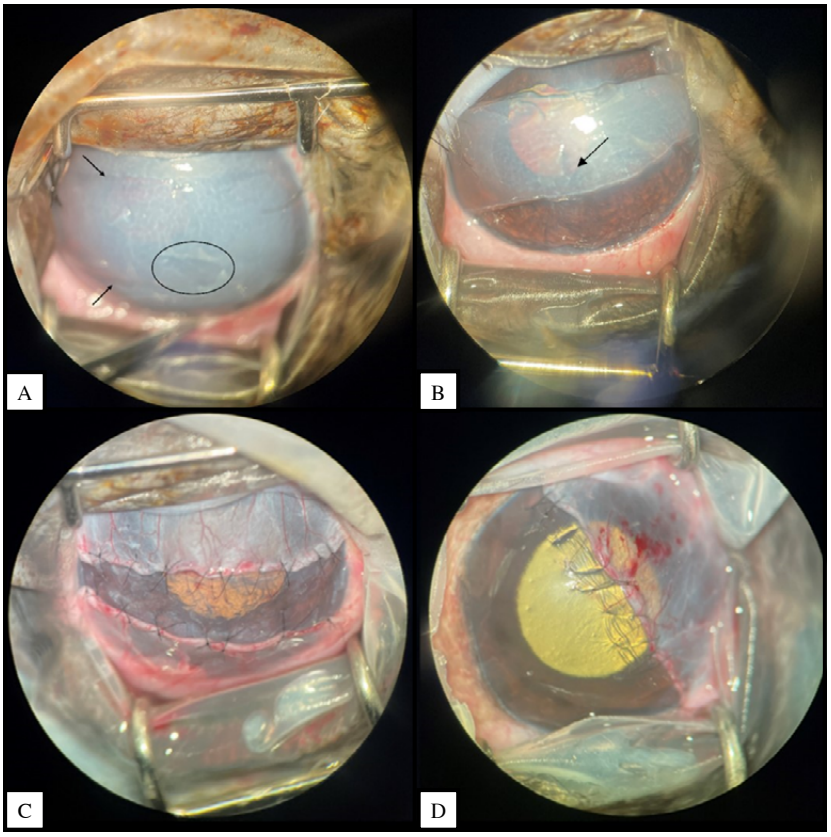

Figura 2. Photographic images of the right and left eyes of an 8-year-old Shih-tzu bitch during surgery. A, B, and C show the right eye. A- Arrows indicate horizontal lines demarcating a 6 mm width for the subsequent superficial keratectomy; the circle indicates the ulcerated area in the paracentral region. B- Visual aspect of the cornea shows the central strip after keratectomies, with the ulcer in the paracentral region indicated by (→). C- Conjunctival advancements are sutured in a simple interrupted and simple continuous pattern with 10/0 monofilament nylon suture. D- Left eye shows the cornea with a conjunctival graft in the temporal region, sutured in a simple continuous pattern with 10/0 monofilament nylon suture.

Following normal results from hematological (complete blood count), serum biochemical (urea, creatinine, proteins, and fractions concentrations, and ALT and ALP activities), and cardiological examinations, the Gundersen technique [10] was performed on the left eye, where edema was less intense and more concentrated in the temporal quadrants of the cornea. For the right eye, which exhibited diffuse and intense edema (++/+++), a modified Gundersen technique [6] was employed.

On the right eye, 2 horizontal lines 6 mm apart were marked on the cornea using a caliper (Figure 2A), followed by incisions with a 15 C blade, and lamellar keratectomy involving removal of corneal epithelium and significant portions of the stroma from the superior and inferior corneal areas, using an escalating blade (Figure 2B). Superficial lamellar keratectomy was performed axially, removing anterior epithelium and stroma. Subconjunctival saline solution was then applied to separate conjunctiva from Tenon's capsule, followed by conjunctival dissection using conjunctival scissors. Conjunctival flaps were sutured with 10/0 nylon in interrupted and continuous simple patterns (Figure 2C).

On the left eye, vertical corneal incision was made from 12 to 6 o'clock. Subsequently, superficial lamellar keratectomy was performed, followed by conjunctival advancement and suturing as described previously (Figure 2D).

Postoperatively, treatment was initiated with moxifloxacin and sodium hyaluronate[6] [Hyabak® 0.15% - eye drops], both administered 5 times daily. Oral anti-inflammatory prednisolone[7] was prescribed [Predsim® 5mg - 0.5 mg/kg/day for 7 days], along with dipyrone 5 days and the use of an Elizabethan collar. Weekly follow-ups were scheduled to monitor ocular progress.

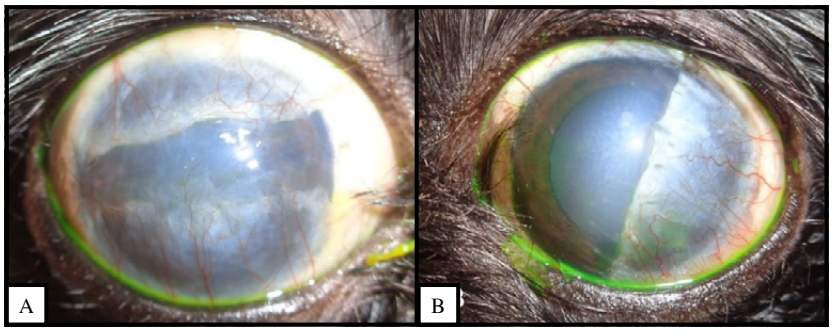

Figure 3. Photographic images of an 8-year-old Shih-tzu bitch with endothelial dysfunction, 37 days after undergoing a modified Gundersen and Gundersen graft. A- Right eye & B- Left eye, both show evident vascularization from the graft, a visible pupil, and the absence of an ulcer. In A and B, respectively, note the final appearance of the healing process.

On the 4th postoperative day, prednisolone[6] [Ster® 1% eye drops - twice daily] were added to the left eye's prescription. At 22 days post-surgery, the same prescription was extended to the right eye, along with bilateral use of hypertonic saline solution 5 times daily and immunomodulator tacrolimus[8] 0.03% once daily.

Sutures in both eyes were removed after 31 days (Figure 3), with the patient awake and corneal desensitization achieved using proxymetacaine[9] [Anestalcon® 0.5% - eye drops]. Moxifloxacin were discontinued at 37 days post-surgery, with tacrolimus 0.03% eye drops prescribed every 12 h and 5% sodium chloride every 8 h.

Six months post-procedure, the owner reported via telephone a clearer eye without discomfort, ocular discharge, or tearing. During a follow-up at 17 months post-surgery, the owner reported discontinuing topical medications on their own initiative at 3 months post-operatively. Ophthalmic examination revealed positive responses to menace and movement tests, bilateral ocular opacity (+/+++), corneal pigmentation in the upper quadrants of the left eye, and no episodes of corneal ulceration since the procedure (Figure 4).

DISCUSSION

In dogs, endothelial dysfunction has been described in breeds such as Boston Terrier, Dachshund, Chihuahua [1,3,6,8,13,14,16,19], German Shorthaired and Wirehaired Pointer [1,6], Boxer [3], Poodle and Shih-tzu [8]. There is a greater predisposition in bitches and the in elderly dogs, as observed in the patient in this report [1].

The corneal endothelium is an active layer responsible for transporting solutes and fluids from the cornea to the aqueous humor, maintaining corneal deturgescence essential for transparency [5]. As post-mitotic cells, corneal endothelial cells do not regenerate, and once they reach a critically low number, the remaining cells become incapable of maintaining deturgescence. This leads to fluid accumulation between

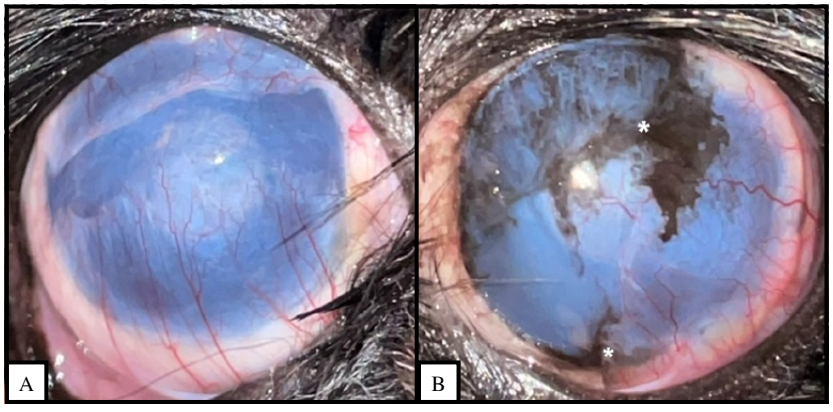

Figure 4. Photographic images of an 8-year-old Shih-tzu bitch with endothelial dysfunction, 17 months after undergoing a modified Gundersen graft in the right eye (A) and a Gundersen graft in the left eye (B). Note the diffuse corneal opacity (+/+++), evident vascularization from the graft, visible pupil, and absence of ulcers in both A & B. B- Pigmentation in the superior quadrants and the inferior perilimbal region.

collagen lamellae, causing corneal thickening, loss of transparency, and the development of keratopathies and secondary blindness due to edema [14,19]. Physiologically, endothelial cell loss increases with age, potentially impairing corneal transparency. It can also result from endothelial lesions post-intraocular surgeries, primary corneal diseases, uveitis, glaucoma, anterior lens luxation, diabetes mellitus, and endothelial dysfunction itself, the pathogenesis of which remains unclear [2]. In this patient's case, no other causes for endothelial dysfunction were identified beyond racial predisposition and age.

Corneal ulcers in animals with endothelial dysfunction recur due to excessive stromal hydration, resulting in epithelial edema and rupture of subepithelial cells, leading to bullous keratopathy and/or recurrent, indolent ulcers [5]. Chronicity may promote corneal pigment deposition, as observed in this case. Although bullous keratopathy can result from endothelial dysfunction, it was not observed in this patient [1,5,8].

The application of hypertonic solution on the corneal surface aims to remove excess intralamellar fluid, contingent upon intact epithelium. While it may reduce epithelial blistering extent, ocular irritation and tearing can dilute the product, reducing its effectiveness. In this case, standalone hypertonic therapy did not satisfactorily reduce corneal edema, prompting its combination with 5% saline solution and conjunctival advancement [4].

Topical hypertonic agents and antibiotics are recommended for resolving ulcers resulting from endothelial dysfunction but often fail to address corneal edema [1,5,13], as observed in this case. Surgical interventions such as thermokeratoplasty [2,13] and superficial keratectomy combined with conjunctival advancement [1,4,12,13,18] are therefore considered therapeutic options to improve clinical signs of endothelial dysfunction.

In this case, due to poor response to initial clinical treatment, Gundersen flap advancement was recommended as a viable surgical alternative to correct corneal edema, resolve corneal ulcers, and prevent recurrence. First reported by Gundersen in 1958 [10], the use of autologous conjunctiva eliminates the need for tissue donors and is easily performed [12], acting as a protective barrier providing blood supply, metabolic support, reducing ocular pain, irritability, and minimizing the need for topical medications [7]. Additionally, conjunctival flaps assist in maintaining corneal dehydration, providing an alternative route for fluid drainage via conjunctival vessels [12]; alternatively, fluid originally from the anterior chamber could follow the path of least resistance through the cornea [9]. As reported by Horikawa *et al*. [12] lamellar keratectomy was performed to reduce axial corneal stromal thickness, aiming to minimize the number of lamellae where edema could accumulate.

Penetrating keratoplasty remains the definitive treatment for severe endothelial dysfunction, providing a new source of corneal endothelial cells. However, it is costly, requires skilled professionals, appropriate surgical instruments, and, crucially, a donor [16]. In dogs, it is rarely employed for visual rehabilitation [13].

In this case, due to varying intensity of corneal edema between eyes, lamellar keratectomy and conjunctival advancement were chosen for the temporal cornea following Gundersen's technique [10], and for the left eye presenting more diffuse and intense edema, a modified technique [6] was employed. This technique creates an intact central corneal strip between 2 regions (superior and inferior) where superficial lamellar keratectomy and conjunctival advancement were performed. As reported by Giannikaki *et al*. [6], greater effectiveness was observed in reducing corneal edema in the left eye and consequently, corneal thickening.

Special attention was given to dissection of Tenon's capsule from the substantia propria, as its thickness increases conjunctival tissue tension, resulting in thicker scars that compromise corneal transparency [11]. Continuous simple monofilament nylon sutures were chosen for corneoconjunctival suturing due to their high elasticity, prolonged tensile strength, and low toxicity, minimizing vascular stimulation [15].

The use of corticosteroids for controlling scar inflammation is indicated, provided there is good epithelial coverage. Therefore, steroid use was initially instituted in the left eye and subsequently, at 22 days postoperatively, in the right eye, following a negative fluorescein staining test. Additionally, immunomodulators such as tacrolimus also possess anti-inflammatory properties, reducing corneal vascularization and pigmentation [17], which was achieved while the owner maintained its use.

In conclusion, Gundersen and modified Gundersen techniques proved effective in reducing low to moderate corneal edema, aiding in ulcer resolution,

preventing recurrence, reducing discomfort, and improving ocular transparency.

MANUFACTURERS

[1]Novartis Biosciences S.A. São Paulo, SP, Brazil.
[2]Pfizer, Laboratórios Ltda. Itapevi, SP, Brazil.
[3]Synn Vet. São Paulo, SP, Brazil.
[4]Icare Finland Oy. Vantaa, Finland.
[5]EyePharma. São Paulo, SP, Brazil.
[6]União Química Farmacêutica Nacional S.A. São Paulo, SP, Brazil.
[7]Brainfarma Indústria Química e Farmacêutica S.A. Anápolis, GO, Brazil.
[8]Drogavet Comércio de Produtos para Animais Ltda. Curitiba, PR, Brazil.
[9]Alcon Laboratórios do Brasil Ltda. São Paulo, SP, Brazil.

Declaration of interest. The author declares no conflicts of interest, and is solely responsible for the content and writing of the paper

REFERENCES

1 **Armour M.D., Askew T.E. & Eghrari A.O. 2019.** Endothelial keratoplasty for corneal endothelial dystrophy in a dog. *Veterinary Ophthalmology*. 22(4): 545-551. DOI: 10.1111/vop.12670.

2 **Boo G., Whittaker C.J.G., Caruso K.A., Moloney G., Hall E., Devasahayam R., Thomasy S. & Smith J.S. 2019.** Early postoperative results of Descemet's stripping endothelial keratoplasty in six dogs with corneal endothelial dystrophy. *Veterinary Ophthalmology*. 22(6): 879-890. DOI: 10.1111/vop.12666.

3 **Cooley P.L. & Dice P.F. 1990.** Corneal dystrophy in the dog and cat. *The Veterinary clinics of North America. Small Animal Practice*. 20(3): 681-692. DOI: 10.1016/s0195-5616(90)50057-1.

4 **Dower N.M.B., Amorim T.M., Ribeiro A.P., Dias A.F.L.R. & Souza V.R.F. 2020.** Edema de córnea severo em cão naturalmente infectado por *Leishmania* spp. *Acta Scientiae Veterinariae*. 48(Suppl 1): 525.

5 **Famose F. 2016.** Evaluation of accelerated corneal collagen cross-linking for the treatment of bullous keratopathy in eight dogs (10 eyes). *Veterinary Ophthalmology*. 19(3): 250-255. DOI: 10.1111/vop.12280.

6 **Giannikaki S., Escanilla N., Sturgess K. & Lowe R.C. 2020.** A modified technique of keratoleptynsis ("letter-box") for treatment of canine corneal edema associated with endothelial dysfunction. *Veterinary Ophthalmology*. 23(6): 930-942. DOI: 10.1111/vop.12823.

7 **Gibralter R.P. & Hawn V.S. 2022.** Conjunctival flaps for the treatment of advanced ocular surface disease - looking back and beyond. *Annals of Eye Science*. 7: 36. DOI: 10.21037/aes-22-36.

8 **Grahn B.H. & Peiffer R.L. 2021.** Veterinary Ophthalmic Pathology. In: Gelatt K.N. (Ed). *Veterinary Ophthalmology*. 6th edn. River Street: Hoboken, pp.479-563.

9 **Gundersen T. 1960.** Surgical Treatment of Bullous Keratopathy. *Archives of Ophthalmology*. 64(2): 260-267. DOI: 10.1001/archopht.1960.01840010262013.

10 **Gundersen T. 1958.** Conjunctival Flaps in the Treatment of Corneal Disease with Reference to a New Technique of Application. *Archives of Ophthalmology*. 60(5): 880-888. DOI: 10.1001/archopht.1958.00940080900008.

11 **Hartley C. & Hendrix D.V.H. 2021.** Diseases and surgery of the canine conjuntiva and nictitating membrane. In: Gelatt K.N. (Ed.). *Veterinary Ophthalmology*. 6th edn. River Street: Hoboken, pp.1059-1060.

12 **Horikawa T., Thomasy S.M., Stanley A.A., Calderon A.S., Li J., Linton L.L. & Murphy C.J. 2016.** Superficial Keratectomy and Conjunctival Advancement Hood Flap (SKCAHF) for the Management of Bullous Keratopathy: Validation in Dogs with Spontaneous Disease. *Cornea.* 35(10): 1295-1304. DOI: 10.1097/ICO.0000000000000966.

13 **Kim J., Ji D.B., Takiyama N., Bae J. & Kim M.S. 2019.** Corneal collagen cross-linking following superficial keratectomy as treatment for corneal endothelial cell dystrophy in dogs: Preliminary clinical study. *Veterinary Ophthalmology*. 22(4): 440-447. DOI: 10.1111/vop.12611.

14 **Leonard B.C., Kermanian C.S., Michalak S.R., Kass P.H., Hollingsworth S.R., Good K.L., Maggs D.J. & Thomasy S.M. 2021.** A Retrospective Study of Corneal Endothelial Dystrophy in Dogs (1991-2014). *Cornea*. 40(5): 578-583. DOI: 10.1097/ICO.0000000000002488.

15 **Melega M.V., Reis R., Lira R.P.C., Oliveira D.F., Arieta C.E.L. & Alves M. 2021.** Comparison Between Nylon and Polyglactin Sutures in Pediatric Cataract Surgery: A Randomized Controlled Clinical Trial. *Frontiers in Medicine*. 8: 700793. DOI: 10.3389/fmed.2021.700793.

16 **Michau T.M., Gilger B.C., Maggio F. & Davidson M.G. 2003.** Use of thermokeratoplasty for treatment of ulcerative keratitis and bullous keratopathy secondary to corneal endothelial disease in dogs: 13 cases (1994-2001). *Journal of the American Veterinary Medical Association*. 222(5): 607-612. DOI: 10.2460/javma.2003.222.607.

17 Rankin A.J. 2021. Anti-inflammatory and immunosuppresant drugs. In: Gelatt K.N. (Ed). *Veterinary Ophthalmology*. 6th edn. River Street: Hoboken, pp.349-478.

18 Scherrer N.M., Lassaline M. & Miller W.W. 2017. Corneal edema in four horses treated with a superficial keratectomy and Gundersen inlay flap. *Veterinary Ophthalmology*. 20(1): 65-72. DOI: 10.1111/vop.12342.

19 Shull O.R., Reilly C.M., Davis L.B., Murphy C.J. & Thomasy S.M. 2018. Phenotypic Characterization of Corneal Endothelial Dystrophy in German Shorthaired and Wirehaired Pointers Using *In Vivo* Advanced Corneal Imaging and Histopathology. *Cornea*. 37(1): 88-94. DOI: 10.1097/ICO.0000000000001431.