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Seasonal corneal oedema in small ruminants and camelids in New Zealand: case investigations in sheep and goats

H Hunt [a], D Green [b], S Doohan [c], B Vaatstra [d], J Makin [e] and P Price [f]

[a]Tāwharau Ora – School of Veterinary Science, Massey University, Palmerston North, New Zealand; [b]Ministry for Primary Industries, Upper Hutt, New Zealand; [c]AgResearch Limited, Grasslands Research Centre, Palmerston North, New Zealand; [d]Awanui Veterinary, Palmerston North, New Zealand; [e]Warkworth Veterinary Services Ltd., Auckland, New Zealand; [f]Totally Vets, Feilding, New Zealand

ABSTRACT

Case history: A seasonal syndrome, presenting as corneal oedema and distinct from infectious keratoconjunctivitis, has been reported in sheep, goats, and camelids in New Zealand. This study details the diagnostic investigation on two properties, of multiple cases of corneal oedema in small ruminants. Outbreak 1 occurred in a mob of sheep in April/May 2023 in the Manawatū region, with 27/52 sheep affected. Outbreak 2 occurred in a group of farmed goats in February/March 2024 in the Auckland region, with 4/5 goats affected.

Clinical findings: A spectrum of corneal abnormalities, including focal and diffuse corneal oedema and bullous keratopathy/corneal hydrops, were observed in both the sheep and goats. All animals had normal menace responses and pupillary light reflexes, and there was no associated blepharospasm, epiphora or ocular discharge, except in five sheep that developed secondary ulcerative keratitis. These five sheep had severe ulceration or corneal perforation necessitating euthanasia, while the other affected sheep all recovered within 5 months. The corneal oedema in all goats improved over the following 6 months, but one required a thermokeratoplasty procedure to aid resolution of the oedema and the other three goats had residual focal oedema that did not appreciably affect vision.

Diagnosis: It is proposed that a primary corneal endothelial dysfunction was the cause of the oedema, but the aetiopathogenesis is not well understood.

Clinical relevance: This is the first peer-reviewed description of this presentation in New Zealand. In contrast to other causes of corneal oedema in ruminants, seasonal corneal oedema is, in some cases, self-limiting with minimal impacts on production and welfare. However, secondary ulceration and corneal perforation may occur, which is painful and may lead to deep infections and permanent visual deficits. Topical antibiotic therapy does not appear to aid in the resolution of the oedema.

Abbreviations: MPI: Ministry for Primary Industries

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KEYWORDS
Bullous keratopathy; corneal oedema; endothelial dysfunction; sheep; goat; seasonal; ophthalmology

Introduction

The seasonal occurrence of corneal oedema in the absence of uveitis is an unusual clinical disorder in small ruminants and camelids in New Zealand, which was first recognised in llamas in 2009 (Liefting 2009). Cases occur in late summer and autumn, between the months of February to May, and through personal communication with veterinarians, the authors (PP and HH) are aware of 14 small block/lifestyle properties in the North Island where seasonal corneal oedema has been reported between 2018 and 2024. Affected species have included sheep, goats, alpacas, and llamas of a variety of ages. The morbidity varies between properties but often 50% or more of the animals within a particular mob or flock are affected.

The initial presentation is a focal-to-diffuse, unilateral, or bilateral, corneal oedema with intact (fluorescein negative) corneal epithelium (Figure 1). The increase in corneal opacity is not primarily accompanied by blepharospasm, ocular discharge, nor epiphora, which are commonly associated with other diseases affecting the cornea in farmed animals, such as keratoconjunctivitis caused by *Moraxella* spp., *Mycoplasma* spp., *Chlamydia* spp., *Listeria* spp. (McMullen and Passler 2020). Affected animals are systemically well with no other abnormalities on physical examination, in contrast to disease caused by viruses from the herpesviral or orbiviral genera. In some animals, seasonal corneal oedema may progress to bullous keratopathy/corneal hydrops, resulting in secondary ulcerative keratitis and associated discomfort. A variety of anti-inflammatory and antimicrobial treatments have been used, and so far, none of these have made a clear impact on the progression

CONTACT H Hunt h.hunt@massey.ac.nz

of the disease. The corneal pathology seems to resolve over weeks to months and animals are not systemically unwell.

This corneal disease is distinct from the currently recognised ulcerative corneal diseases in these species and is most consistent with a primary endothelial dysfunction with secondary corneal oedema. This clinical study outlines the clinical and laboratory findings from two outbreaks in New Zealand of corneal oedema and bullous keratopathy consistent with this syndrome, one in a mob of sheep in the Manawatū District, and one in a goat herd in Auckland. In these two outbreaks, more extensive diagnostic investigations were performed than in previously reported cases, as the sheep were part of an unrelated research trial, and the goats were on the same property as imported wildlife species (including giraffe and zebra), prompting selected exotic disease testing by the Ministry for Primary Industries (MPI). These additional investigations facilitate the discussion of the potential pathogeneses of this disease (including a possible link with sporidesmin toxicity) and future directions for research. The cases were naturally occurring clinical cases, and all testing was performed as part of the diagnostic investigation rather than for research purposes, therefore ethical approval was not required.

Outbreak 1

Case history

In mid-April 2023, a veterinarian from a practice servicing the affected farm was called to examine a mob of 18–20-month-old Romney-cross wethers (mean weight 60 kg) in the Manawatū region. Ocular examinations performed by this veterinarian revealed acute, blue opacification of the cornea (corneal oedema) in 27/52 (52%) sheep in the mob. The mob was intensively managed and involved in a vaccine research trial, however there were equal numbers of affected animals in both the treatment and control groups. In the weeks prior to and during the outbreak, the sheep were grazing ryegrass (*Lolium perenne*) dominant pastures, with average pasture covers of 2,200 kg DM/ha.

The corneal oedema was not associated with blepharospasm, conjunctival hyperaemia or ocular discharge and some animals had a notably convex distortion of the corneal curvature. The affected animals did not display behaviour consistent with discomfort or malaise, such as isolation or reduced appetite. Following this initial veterinary visit, treatment of sheep with corneal oedema consisted of spraying the eyes with a compounded topical 1% oxytetracycline spray comprising 100 mg/mL commercial oxytetracycline (Engemycin; MSD Animal Health, Upper Hutt, NZ) diluted with 50:50 glycerine and distilled water once daily for 3 days, using a handheld trigger spray bottle. The sheep were checked daily and no change in the ocular appearance was noted by the farm staff during this treatment or in the following 7 days.

Weekly sporidesmin toxicity risk surveillance and regular facial eczema prophylaxis were carried out on the farm from early January to late May each year (summer/autumn). On the paddocks that the mob had grazed over the previous 3 weeks, the *Pithomyces chartarum* spore counts, performed using the method described by Smith *et al.* (1987), had been 15,000 spores/g of pasture or below. This is considered low, as generally it is recommended that facial eczema prophylaxis is started at counts of 30,000 spores/g of pasture, and higher counts present a higher risk (Cuttance *et al.* 2016). However, one paddock reached 50,000 spores/g of pasture during the same week the corneal oedema was initially identified, and 110,000 spores/g of pasture in the week following the detection of corneal oedema. Seven weeks prior to detection of corneal oedema the sheep had been administered a slow-release intraruminal zinc bolus containing 67 g ZnO (Time Capsule; Agritrade, Hamilton, NZ) for 6 weeks of facial eczema prophylaxis in adult sheep.

Clinical findings

Fourteen days after the initial veterinary visit, the corneal oedema had progressed to ulceration in 5/27 affected sheep and the remaining cases had not improved or resolved, so an ophthalmic residency-trained veterinarian (PP) visited the property on 5 May 2023 and performed full ophthalmic examinations on five affected sheep, chosen to represent the range of severity of corneal lesions, as well as two unaffected sheep in the same mob. Ocular examinations included menace response and pupillary light reflex evaluation, slit lamp biomicroscopy (Kowa SL-17; Kowa Co. Ltd., Tokyo, Japan), tonometry (Tonovet Plus – equine setting; Icare, Vantaa, Finland) and fluorescein staining. Binocular indirect ophthalmoscopy (Scanoptics SO-2700; Adelaide, Australia) with a 20-dioptre handheld lens (Scanoptics) was performed where the ocular media permitted observation of the fundus. A spectrum of corneal disease was identified, and eyes were affected asymmetrically within the same animal. All sheep had normal menace responses and pupillary light reflexes. Of the five affected sheep, two presented with focal oedema, located in the lateral-paraxial cornea and sparing the medial and peripheral aspects (Figure 1a), while diffuse oedema was present in the other three sheep (Figure 1b). In the most severely oedematous regions, the corneal stroma was markedly expanded, with bullae formation and convex distortion of the corneal curvature (Figure 1c). Generally, the corneal oedema restricted

evaluation of the internal ocular structures partially or totally. In animals with focal disease, evaluation of aqueous flare and the iris was possible and no signs of anterior uveitis such as miosis, aqueous flare or rubeosis iridis were detected. Fundic examination was normal in the unaffected animals and in the one affected animal where the corneal clarity permitted fundic examination. Two eyes in two different affected sheep were ulcerated with stromal loss, conjunctival hyperaemia, epiphora and blepharospasm, and neovascularisation was present in one eye. One cornea had evidence of healing ulceration (Figure 1d). Tonometry measurements of 12–19 mm Hg were obtained on normal corneas and on regions of normal cornea in affected eyes, which were within the range of normal intraocular pressure measurements (7–20 mm Hg, median 11 mm Hg) reported in sheep with a similar instrument by Peche and Eule (2018). Measurements taken on oedematous corneas were lower at 5–11 mm Hg, but the presence of marked corneal oedema suggests these are an inaccurate estimation of the true intraocular pressure.

Laboratory and pathological findings

During the initial veterinary visit in April and prior to any treatment, sterile swabs of the palpebral conjunctiva were taken from 10 randomly selected affected sheep and submitted to a commercial diagnostic laboratory (Awanui Veterinary, Palmerston North, New Zealand) for aerobic bacterial culture and PCR testing for *Mycoplasma conjunctivae, Chlamydia* spp., *Moraxella bovis*, *Moraxella bovoculi*, *and Moraxella ovis*. Nine of the 10 swabs were positive on the combined *Moraxella bovoculi/ovis* PCR (the test does not differentiate between these species), and all other results were negative (Table 1).

A complete blood count was performed on one mildly affected sheep and two severely affected sheep. Mild mature neutrophilia was present in the two severely affected sheep, and one also had mild eosinophilia. All blood count parameters were normal in the mildly affected sheep, and none of the three sheep sampled had abnormalities in red cell indices or fibrinogen. Serum gamma-glutamyl

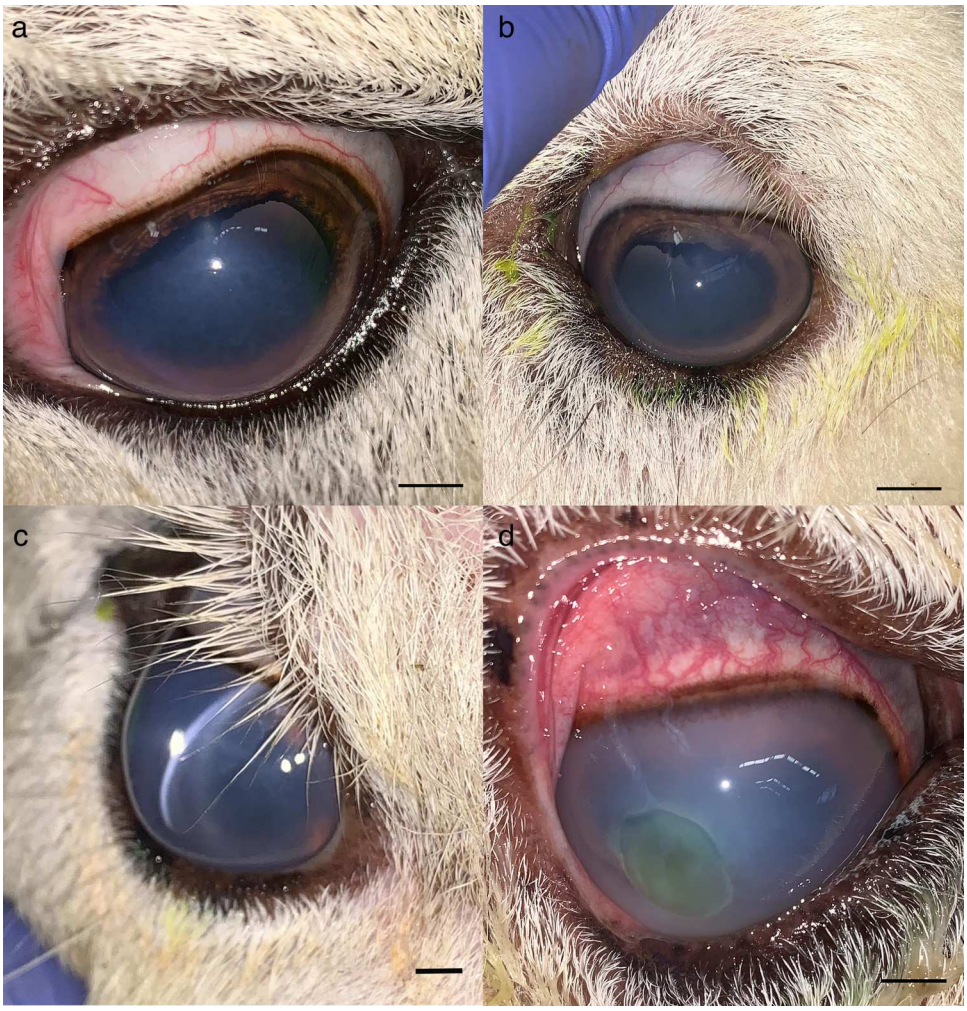

Figure 1. Photograph of eyes of sheep affected with seasonal corneal oedema on a farm in New Zealand (Outbreak 1). Oedema varied from focal (a) to diffuse (b). The expanded corneal stroma leads to divergence of a slit lamp beam (c). Secondary corneal ulceration with focal stromal loss, early limbal-based neovascularisation and conjunctival hyperaemia was apparent in five eyes (d). Bars = 5 mm.

Table 1. Results of laboratory testing on conjunctival swabs taken from 10 sheep with seasonal corneal oedema[a] in New Zealand (Outbreak 1).

Test[b]	Results
Mycoplasma conjunctivae PCR	Not detected
Chlamydia spp. PCR	Not detected
Moraxella bovis PCR	Not detected
Moraxella bovoculi/ovis PCR	Detected in 9/10 samples
Aerobic bacterial culture	No significant isolates

[a]All sheep had corneal oedema at the time of sample collection.
[b]Testing performed by Awanui Veterinary, Auckland and Palmerston North, NZ.

transferase and glutamate dehydrogenase activity were within normal reference intervals in these three sheep; full serum biochemistry was not performed.

Both eyes from two affected sheep (sheep A and B) in this mob were available for histological examination after the sheep were euthanised on 17 May 2023 due to welfare concerns associated with corneal ulceration. All four eyes showed variable corneal oedema, characterised by separation of corneal fibres by clear space, along with vascular proliferation in the peripheral cornea accompanied by small numbers of mature lymphocytes, plasma cells, and occasional eosinophils and macrophages (Figure 2a). A focal area of the cornea directly adjacent to Descemet's membrane in sheep A was vacuolated (Figure 2b). Sheep B had a central corneal perforation and iris prolapse in the right eye, associated with neutrophilic inflammation (not pictured). In sheep B, there were aggregates of neutrophils within the trabecular meshwork but none of the eyes examined had histological evidence of underlying uveitis, vasculitis, or infectious organisms in the sections examined.

Treatment and outcome

The five sheep with blepharospasm due to secondary ulceration were treated with a single SC injection of meloxicam (Metacam 20 mg/mL Solution for Injection; Boehringer Ingelheim Animal Health NZ, Manukau City, NZ) at a dose of 1 mg/kg and their eyes were treated topically with a further application of compounded 1% oxytetracycline spray (as detailed in the case history section), twice daily for 3 days. Three of the most severely affected sheep with unilateral ulcers were treated with temporary nictitating membrane flaps, using nylon metric size 4.0 suture (Rivermid; Riverpoint, Portland, OR, USA), in conjunction with a SC injection of 20 mg/kg oxytetracycline (Bivatop; Boehringer Ingelheim Animal Health NZ) and SC injection of meloxicam as described above. The oxytetracycline and meloxicam injections were repeated once, 3 days later, in these three sheep. No perceived decline or improvement was noted when the third eyelid flap was removed between 5 and 7 days later for each

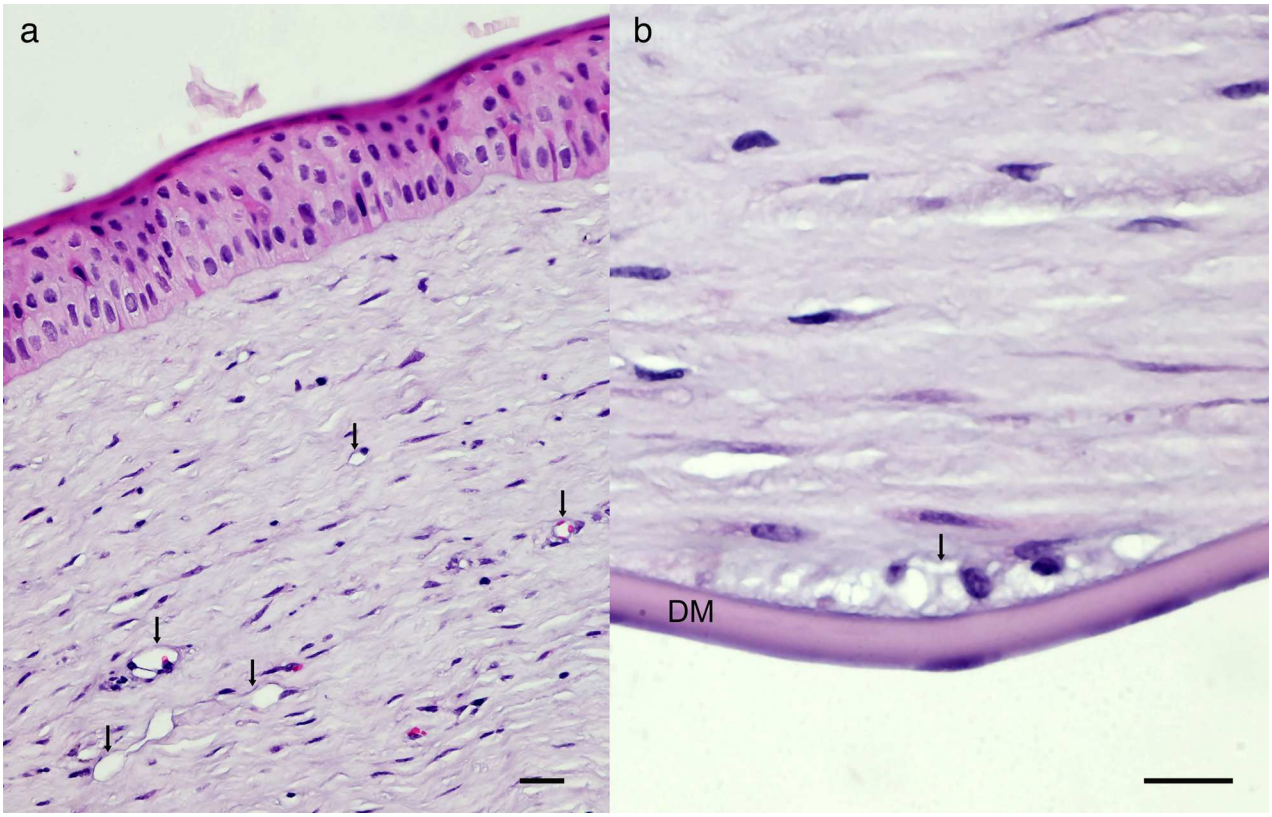

Figure 2. Photomicrographs of histological sections from the cornea of an 18-month-old wether (Sheep A) diagnosed with seasonal corneal oedema and showing increased corneal opacity. (a) Superficial aspect of the peripheral cornea, showing separation between corneal collagen fibres (mild oedema) and proliferation of small blood vessels (arrows) surrounded by small numbers of mixed inflammatory cells. (b) Deep aspect of the central cornea, showing vacuolation of the cornea (arrow) adjacent to Descemet's membrane (DM). H&E; bars = 25 µm.

sheep. Over the following 4 weeks, a total of five sheep, including the two for which histologic findings were described above, were euthanised due to severe or persistent corneal ulcers associated with blepharospasm and compromising animal welfare.

Subsequently, over 2 weeks, 10 further sheep, spread throughout three large mobs of mixed-aged or cull ewes on the same farm, were identified with corneal disease. Some were affected predominantly with corneal oedema, while others had advanced ulcerative keratitis with extensive stromal loss or perforation and iris prolapse. When two of these sheep were euthanised for welfare reasons, one eye from each was collected for histologic examination. Similar to sheep A and B described above, there was variable corneal oedema accompanied by peripheral vascularisation and mild mixed inflammation within the cornea. One of these sheep had a focal area of corneal ulceration associated with small numbers of neutrophils, but there was no evidence of underlying uveitis, vasculitis, or infectious disease.

Five months following the first examination, all surviving affected sheep from the initial wether mob were re-examined with illumination by the same residency-trained veterinary ophthalmologist. The oedema seen at the initial visit (Figure 3a) had resolved and corneas ranged from perfect to good clarity with subtle-moderate vascularisation and fibrosis (Figure 3b). One animal that had initially presented with severe disease had significant corneal fibrosis and vascularisation in the ventral cornea. All animals were able to see and had no detectable discomfort.

Outbreak 2

Case history

Over a 3-week period starting in mid-February 2024, 4/5 adult goats in a mixed-age, non-breeding herd in the Auckland region of New Zealand developed bilateral corneal oedema. No blepharospasm, epiphora or ocular discharge were reported, and the animals were bright and alert. Sheep and deer in neighbouring paddocks were unaffected, but in the previous year, 6/150 alpaca on the property developed corneal oedema. The cases in the alpaca resolved spontaneously and no diagnostic testing was performed. No corneal oedema was observed in the alpacas at the time the goats were affected in 2024. There were also imported exotic animals, including giraffe and zebra, on the property, and these were unaffected.

P. chartarum spore counts were not routinely performed on this farm, but spore counts conducted in mid-March (3 weeks after the first case occurred) revealed 60,000 spores/g.

Clinical findings

On 26 February and approximately 1 week after the first goat developed corneal oedema, the goats were first examined by a veterinarian (JM) and a single corneal swab taken from the affected goat. Subsequently, as the oedema did not improve, and three other goats developed similar clinical signs, the veterinarian visited the property again on March 17. Full ophthalmic examinations were not performed in this outbreak due to the geographical distance from a veterinary ophthalmologist. At the second visit, the four affected goats all had bilateral corneal oedema which, as in the sheep, often spared the peripheral and medial aspects of the cornea (Figure 4a, b). The corneal epithelium was intact in the affected goats, with no stain uptake when fluorescein dye was topically applied. A small amount of nasal discharge was present in the affected goats.

Laboratory findings

The corneal swab taken at the initial visit on 26 February, was tested for *Mycoplasma conjunctivae*, *Moraxella*

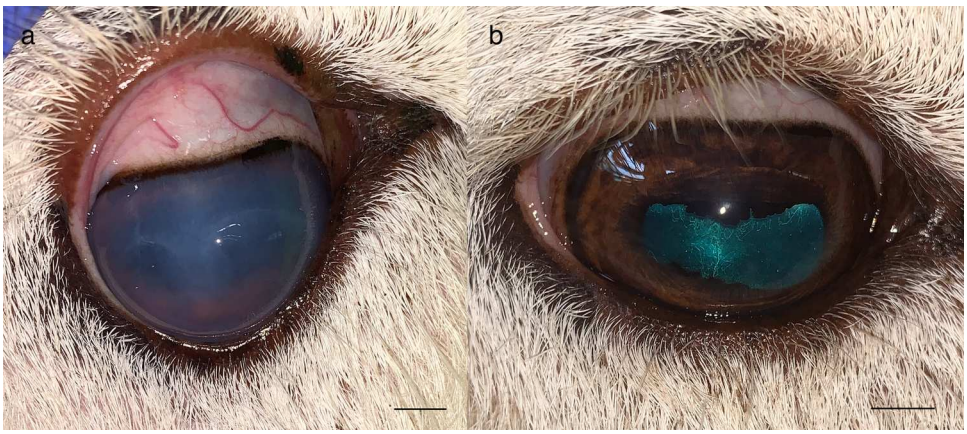

Figure 3. Photographs of the eye of an 18-month-old wether diagnosed with seasonal corneal oedema and taken 5 months apart. (a) On initial presentation, there was diffuse corneal oedema with bullae formation. (b) Five months later, the eye had regained corneal clarity with ghost vascularisation visible on retro-illumination. Bars = 5 mm.

Figure 4. Photograph of the eye of a goat affected with seasonal corneal oedema on a farm in New Zealand (Outbreak 2). The clinical appearance is similar to the sheep in Outbreak 1, with focal oedema in some goats (dorsally in A) and more diffuse oedema in others (B). Bars = 5 mm.

sp., and *Chlamydophila pecorum* by PCR at a commercial veterinary diagnostic laboratory (Awanui Veterinary, Auckland and Palmerston North, NZ), with negative results (Table 2). As there were imported wildlife species on the property, MPI was notified about the corneal oedema in the goats and recommended further laboratory testing due to the potential for an exotic disease incursion. Subsequently, corneal and nasal swabs from three of the four affected goats, and EDTA blood and plain serum tubes (BD Vacutainers; Becton Dickinson, Franklin Lakes, NJ, USA) from all five goats on the property, were collected at the second visit on March 17 and submitted to MPI for further testing at the Animal Health Laboratory (Wallaceville, NZ). Very light growths of mixed bacterial species were obtained from the three corneal swabs (Table 2), and fungal culture isolated *P. chartarum* in Goat 2 and *Cladosporium* sp. in Goat 3. Antibody ELISA tests for *Chlamydia abortus* and bluetongue virus on serum, and PCR testing for bluetongue virus, chlamydia, and generic herpesvirus on blood, nasal and corneal swabs were all negative. No ocular histology was performed in this outbreak as enucleation or euthanasia were not indicated in these cases.

Treatment and outcome

After the second visit, the affected goats were treated with topical cloxacillin (Orbenin Eye Ointment; Zoetis, Auckland, NZ) every 48 hours for several weeks, which did not result in any clinical improvement. One of the affected goats had a persistent bilateral corneal oedema so approximately 3 months after the onset of the oedema, a thermokeratoplasty procedure as

Table 2. Laboratory tests and results, from samples taken from four goats with seasonal corneal oedema and one unaffected herdmate in New Zealand (Outbreak 2).

Test	Number of goats tested[a]	Samples	Results
Mycoplasma conjunctivae PCR[b]	1	Corneal swab	Not detected
Moraxella bovis PCR[b]	1	Corneal swab	Not detected
Chlamydia spp. PCR[c]	3	Corneal swab	Not detected
Chlamydia abortus/Chlamdia psittaci antibody ELISA[c]	5	Serum	Negative
Aerobic bacterial culture[c]	3	Corneal swab	Very light growth of *Pantoea eucrina*, *Mobilicoccus* sp. (Goat 1), *Paenibacillus* sp., *Microbacterium* sp. (Goat 2), and *Streptomyces* sp. (Goats 2 and 3)
Fungal culture[c]	3	Corneal swab	No fungi isolated (Goat 1) *Pithomyces chartarum* isolated (Goat 2) *Cladosporium* sp. isolated (Goat 3)
Bluetongue virus competitive antibody ELISA[c]	5	Serum	Negative
Bluetongue virus PCR[c]	5	EDTA blood (5) Nasal swab (3) Corneal swab (3)	Not detected
Herpesvirus generic PCR[c]	5	EDTA blood (5) Nasal swab (3) Corneal swab (3)	Not detected

[a]Serum and EDTA blood were only collected from the unaffected herdmate for ELISA and PCR testing.
[b]Testing performed by Awanui Veterinary, Auckland and Palmerston North, NZ.
[c]Testing performed by Animal Health Laboratory, Ministry for Primary Industries, Wallaceville, NZ. Bacterial isolates were identified by Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry and 16s rRNA gene sequencing. Fungal isolates were identified by colony morphology, microscopic morphology, and fungal ITS gene sequencing.

described by Michau *et al.* (2003), followed by bilateral temporary tarsorrhaphy was performed under general anaesthesia by one of the authors (JM), and the oedema largely resolved after this. In the other three affected goats, the corneal oedema improved without any further treatment or interventions, but some persistent residual focal oedema remained 6 months after the initial presentation, with no apparent impact on vision.

Discussion

The sheep and goats in these outbreaks were initially presented for veterinary examination because of increased corneal opacity, rather than blepharospasm, ocular discharge and epiphora, which are commonly associated with other diseases affecting the cornea in farmed animals. In corneal oedema, the organised arrangement of collagen fibrils within the cornea is disrupted by fluid accumulation, resulting in light diffraction and an opaque, blue appearance (Hendrix *et al.* 2021) instead of the normal transparent structure. Corneal oedema can arise from loss of epithelium or endothelial dysfunction, with the latter resulting in more severe oedema than loss of corneal epithelium (Maurice and Giardini 1951).

In the sheep and goat cases described here, as well as the other anecdotal cases the authors are aware of, it is proposed that the oedema is due to corneal endothelial dysfunction rather than epithelial loss. This is based on the early clinical signs of corneal oedema without ulceration, as well as the marked stromal expansion and bullous keratopathy that occurs in these animals. Bullous keratopathy is rarely reported in small ruminants and camelids, although bilateral bullous keratopathy in a septic calf has been documented (Bonelli *et al.* 2023). In dogs, bullous keratopathy is most commonly associated with primary endothelial dystrophy or endothelial degeneration (Michau *et al.* 2003) and in cats and horses it may be associated with breaks in Descemet's membrane or *Pseudomonas* spp. infection (Utter and Wotman 2009; O'Leary *et al.* 2022). In the small number of cases in Outbreak 1 where ocular histology was performed on affected sheep, Descemet's membrane was intact (other than in Case B, where there was corneal perforation due to ulceration), and there was no evidence of a primary bacterial infection, further supporting corneal endothelial dysfunction as a cause of the oedema and bullous keratopathy.

The sudden onset of corneal oedema in multiple animals on a farm suggests an infectious aetiology or a toxic effect from a common exposure, with both systemic and topical routes of entry possible. If a topical route is the mechanism, this would suggest that the compound or organism penetrates the intact corneal epithelium and preferentially affects the corneal endothelium, or that the epithelial pathology is not visible or is unobserved/transient. A compound or toxin that alters the function of Na^+/K^+-ATPase pumps could be a plausible candidate, as in health the corneal endothelium actively removes fluid from the cornea through the action of Na^+/K^+-ATPase pumps (Hendrix *et al.* 2021). It is of interest that *P. chartarum* was cultured from a corneal swab from an affected goat as it has been suggested that after ingestion, the toxin (sporidesmin) produced by this fungus causes biliary pathology through disruption of Na^+/K^+-ATPase pumps (Jordan 2020). *P. chartarum* and the sporidesmin it produces are the cause of facial eczema, a syndrome of hepatotoxicity and photosensitisation in ruminants and camelids, and fungal spore counts are highest in late summer and autumn in the North Island of New Zealand (Phillips *et al.* 2023), which is consistent with the seasonality and geographic occurrence of the corneal oedema cases. In Outbreak 1, the *P. chartarum* spore counts on pasture reached a maximum of 50,000 spores/g in the weeks leading up to the onset of cases, while in Outbreak 2, spore counting was not routinely performed, although counts 3 weeks after the onset of signs were 60,000 spores/g. Generally, counts greater than 30,000/g are considered potentially toxic for animals ingesting the spores (Boyd 2016), but spore counts can vary significantly between aliquots, samples and within a paddock (Cuttance *et al.* 2017), and thresholds for topical toxicity may be lower as purified sporidesmin is reported to cause severe irritation upon contact with the eyes (Miles *et al.* 1992). None of the animals in this report had evidence of hepatopathy and photosensitisation usually associated with sporidesmin toxicity, and the three sheep that had serum biochemical testing performed had normal serum liver enzyme activities (gamma-glutamyl transferase and glutamate dehydrogenase). This could reflect topical exposure rather than ingestion of spores, and, as part of a facial eczema prophylaxis programme, the sheep had been previously treated with zinc to mitigate the effect of ingested sporidesmin (Boyd 2016).

It is possible that the culture of *P. chartarum* from the goat corneal swab could be a result of transient colonisation of the cornea rather than the cause of the oedema, but interestingly, there have been cases reported previously of corneal oedema in camelids where *P. chartarum* has also been cultured. In April 2009, three llamas on a property in South Auckland, New Zealand developed corneal oedema after grazing paddocks with high spore counts, and a heavy growth of *P. chartarum* was isolated from conjunctival swabs in all affected animals (Liefting 2009). Furthermore, a direct action of sporidesmin on the rostral nasal cavity of sheep has been proposed (De las Heras *et al.* 2022), suggesting that topical toxicity is possible. Topical exposure would be consistent

with the observed sparing of the lateral and medial aspects of the cornea, as it is the central part of the cornea that is closest to the pasture when animals are grazing. In human medicine, there are also examples of topical corneal toxicity causing corneal oedema, with case reports of acute corneal endothelial toxicity when people touch their eyes after handling milkweed (*Asclepias* sp.). These plants have sap that contains high levels of cardiac glycosides that inhibit Na^+/K-ATPase pumps (Heersink and Syed 2022). Systemic exposure to a toxin or drug resulting in corneal oedema is also possible, as demonstrated by the example of phenothiazine-induced corneal disease in ruminants. Oedema can develop in the parts of the cornea exposed to light after administration of either single high doses or repeated low doses of phenothiazine anthelmintics (Bistner *et al.* 1981), but this is considered unlikely in the present cases, given there was no history of recent drug administration in either outbreak and phenothiazine-derived anthelmintics and fungicide sprays are no longer commercially available in New Zealand. In addition, the oedema was not bilaterally symmetrical whereas this is the norm in phenothiazine and other systemic toxicity cases.

Anterior uveitis as a cause of endothelial dysfunction is considered a less likely pathogenesis for seasonal corneal oedema, as although there was histologic evidence of uveitis in two of the six globes examined in this study, these sheep also had corneal ulceration or perforation. Malignant catarrhal fever causes corneal oedema, anterior uveitis and keratoconjunctivitis in association with high mortality in cattle due to alcelaphine herpesvirus I and ovine herpesvirus 2 (Zemljič *et al.* 2012). Natural infection with ovine herpes virus 2 is not associated with clinical disease in sheep, however a syndrome like malignant catarrhal fever has been demonstrated after experimental inoculation (Li *et al.* 2005). When intraocular structures could be evaluated, the sheep and goat cases reported here did not have clinical evidence of uveitis, nor was there any indication of systemic disease, and the goats were negative for exotic viruses known to affect blood vessels (herpes and bluetongue). In addition, a systemic infection or hypersensitivity with immune complex deposition in the corneal endothelium would usually be expected to cause diffuse and bilateral corneal oedema (Curtis and Barnett 1983), whereas animals in the present study often presented with unilateral or focal oedema.

Infectious keratoconjunctivitis, commonly termed "pinkeye", was also considered as a possible cause of seasonal corneal oedema, as it can lead to cytotoxic damage of the epithelium or neovascularisation of the cornea, both of which can lead to an influx of fluid into the corneal stroma. Seasonal corneal oedema is present without keratoconjunctivitis and ulceration in the initial stages of disease, but there is some overlap clinically with classic infectious keratoconjunctivitis. Furthermore, corneal oedema may progress to formation and rupture of corneal bullae, and secondary infection may ensue, so infectious keratoconjunctivitis and seasonal oedema may be clinically indistinguishable in the latter stages. In sheep and goats, *Mycoplasma conjunctivae* and *Chlamydia pecorum* are important causes of infectious keratoconjunctivitis (Nietfeld 2001), and these were not detected in any of the samples from affected sheep and goats that were tested in this study. *Moraxella bovis* is the most important cause of keratoconjunctivitis in cattle (Postma *et al.* 2008), but in sheep and goats *Moraxella* spp. can be part of the normal conjunctival flora (Bonelli *et al.* 2013; Meekins *et al.* 2017). The presence of *Moraxella bovoculi/ovis* in 9/10 of the conjunctival swabs taken from sheep in Outbreak 1 is therefore likely to be incidental, however opportunistic infection following epithelial damage could occur in cases with corneal ulceration. The bacteria isolated from the caprine corneal swabs are commonly associated with soil, plant, and faecal material (Walterson and Stavrinides 2015; Grady *et al.* 2016). While these bacteria are occasionally reported as a cause of nosocomial infections in humans (Alonso-Echanove *et al.* 2001; Walterson and Stavrinides 2015; Grady *et al.* 2016), they are unlikely to be significant here given there was only very light growth and no observable response to topical antibiotic treatment in the goats, although antibiotic sensitivity testing was not performed on the isolates. *Cladosporium* sp. fungi were also isolated from one goat corneal swab, but these are reported as part of the normal conjunctival mycoflora of sheep (Bonelli *et al.* 2013). It has been reported as a cause of keratitis in humans (Cheng *et al.* 2015), but colonisation of the cornea is usually preceded by epithelial damage and cases are sporadic and rare, so this is considered to be an unlikely cause of seasonal corneal oedema.

In the sheep and goat cases described here, topical antibiotic and systemic anti-inflammatory treatment did not appear to hasten the resolution of corneal oedema. As the cause of the disease is currently unknown it is not possible to make specific treatment recommendations, but some general principles are outlined here. Topical anti-inflammatory therapy (corticosteroid or non-steroidal drugs) to treat potential corneal endothelial inflammation could be considered for fluorescein-negative cases, particularly those that are not at high risk of corneal ulceration. However, there is a paucity of information on the use of these medications in these species and none are registered for use in food-producing animals in New Zealand. If animals are treated with topical anti-inflammatories, close monitoring for corneal ulceration is advisable as these medications may increase the risk of keratomalacia in the presence of corneal ulceration (Brown

et al. 1970; Rigas *et al.* 2020). Topical hypertonic saline may reduce corneal oedema (Chow and Chan 2021), but frequent application is unlikely to be practical in farming situations. In cases with secondary corneal ulceration, topical antibiotics should be used, and systemic analgesia administered. Ophthalmic antibiotic ointments containing cloxacillin, such as Orbenin eye ointment, or topical powders containing oxytetracycline, such as Terramycin Pinkeye Powder (both manufactured by Zoetis NZ Ltd.) are licenced for use in sheep, but there are no registered antibiotics for topical ocular use in goats and camelids in New Zealand. Animals with marked bullous keratopathy could benefit from tamponade provided by a nictitating membrane flap or temporary tarsorrhaphy, as employed in cats and horses with acute bullous keratopathy (Pederson *et al.* 2016; Burn 2023). An alternative intervention to reduce corneal bullae is a corneal thermokeratoplasty using a low-temperature, handheld thermocautery probe (Michau *et al.* 2003). Animals with deep or perforated corneal ulcers may benefit from corneal grafting surgery (Lacerda *et al.* 2017). Failing that, enucleation could be considered. However, the practicality of different treatment options for animals who develop complications from corneal oedema may vary depending on whether the animal is on a lifestyle block or is part of a commercial flock, where ongoing ocular problems could be a reason to cull.

Future investigations into seasonal corneal oedema should include nationwide collation of data from affected animals to characterise the epidemiology of the disease. Practitioners should consider submitting corneal or conjunctival swabs from cases, as well as parallel swabs from clinically normal in contact control animals, for fungal culture to further characterise the potential involvement of *P. chartarum*. Imaging techniques such as *in vivo* confocal microscopy and optical coherence tomography could help to characterise the corneal changes, particularly those affecting the endothelium, but may be impractical in farmed species and unavailable in the veterinary sector in New Zealand. To investigate possible topical sporidesmin corneal toxicity, *ex vivo* trials could be used to establish Na^+/K^+-ATPase pump activity on corneas harvested at slaughter before and after spore inoculation. *In vivo* inoculation of corneas with spores from *P. chartarum* could also be considered but has a higher animal welfare cost.

Clinicians should be aware of seasonal corneal oedema in small ruminants and camelids on both lifestyle and farming properties and should differentiate this disease from the more widely known infectious keratoconjunctivitis, due to the primary corneal oedema with lack of ulceration in the early stages of disease. The pathogenesis is currently unknown but could be the result of endothelial dysfunction. Corneal oedema may be self-limiting or progress to bullous keratopathy and corneal ulceration and threaten vision and welfare. More research is required to establish the aetiopathogenesis, prognosis and treatment options.

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ORCID

H Hunt http://orcid.org/0000-0001-7810-0560
D Green http://orcid.org/0000-0003-4276-7886
S Doohan http://orcid.org/0000-0001-9057-649X
B Vaatstra http://orcid.org/0009-0007-7564-1039
P Price http://orcid.org/0000-0002-9610-1214

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