Causes of Quantitative Deficiency

Keratoconjunctivitis sicca (KCS) results from a deficiency of the precorneal tear film in which either an inadequate quantity or deficient quality of tears are produced.

The precorneal tear film is composed of 3 layers:
- Inner mucin layer: adheres the tear film to the cornea
- Middle aqueous layer: provides corneal nutrition and waste removal
- Outer lipid layer: prevents evaporation of the tear film

Quantitative deficiency involves the aqueous layer, which is produced by the orbital and nictitating membrane (NM) lacrimal glands.

Qualitative deficiency involves the mucin layer, which is produced by conjunctival goblet cells, or the lipid layer, which is produced by meibomian glands.

Other causes include:
- Trauma to the eye or orbit
- Congenital lacrimal gland hypoplasia or aplasia
- Neurogenic deficiency (loss of sensory innervation from cranial nerve V or loss of parasympathetic innervation via cranial nerve VII)
- Drug-induced
  - Temporary caused by atropine, sedation, local anesthesia, or general anesthesia
  - Permanent or temporary because of systemic sulfonamide or etodolac administration
• Lack of correction or surgical removal of prolapsed NM gland
• Local irradiation
• Endocrine diseases (eg, diabetes mellitus, hypothyroidism, hyperadrenocorticism)
• Canine distemper virus infection
• Chronic blepharoconjunctivitis

Causes of Qualitative Deficiency
► Chronic blepharitis, blepharoconjunctivitis, or meibomianitis
► Immune-mediated diseases targeting mucocutaneous junctions (eg, bullous pemphigoid, systemic lupus erythematosus)

Signalment
► Predisposed breeds for presumptive immune-mediated KCS include:
  • Cavalier King Charles spaniel, English bulldog, Lhasa apso, shih tzu, West Highland white terrier, American cocker spaniel, Pekingese, Boston terrier, miniature schnauzer, Samoyed
► Predisposed breeds for lacrimal gland hypoplasia/aplasia:1,2
  • Chinese crested, Yorkshire terrier, Bedlington terrier, pug

Deficient quantity of tears leads to hypertonicity of tears with subsequent dehydration and hypoxia of the ocular surface.

Pathophysiology
► Deficient quantity of tears leads to hypertonicity of tears with subsequent dehydration and hypoxia of the ocular surface.1
► Deficient tear quality leads to destabilization of the tear film with subsequent evaporative loss.
► Deficient tear quality also hinders the smooth movement of eyelids over the ocular surface; this creates irritation and decreases clearance of metabolites.1
► Inflammation of the conjunctiva and cornea can predispose a patient to secondary bacterial conjunctivitis in association with breakdown of protective barriers.
► Ocular surface pigmentation, vascularization, and fibrosis result from chronic irritation associated with insufficient protection of the ocular surface.

Clinical Signs
► Conjunctival hyperemia and mucoid-to-mucopurulent (in the presence of secondary bacterial infection) ocular discharge are present in early stages.
► Lackluster ocular surface caused by patchy and incongruous precorneal tear film in early stages (Figure 1, previous page) can be seen.
► Corneal vascularization, fibrosis, and pigmentation are noted in later stages (Figure 2, next page).
► Corneal ulceration may be present (Figure 1, previous page).
► Immune-mediated, drug-induced, canine distemper virus-associated, and endocrine-associated conditions generally cause bilateral disease.
► Congenital, neurogenic, irradiation-induced, and surgically induced conditions may be unilateral or bilateral.

DIAGNOSIS
► Diagnosis of quantitative tear film deficiency is made via Schirmer tear test (STT), which measures basal and reflex production of the aqueous component:1
  • Normal: 15 mm wetting/minute
  • Early KCS: 11-14 mm wetting/minute
  • Moderate KCS: 6-10 mm wetting/minute
  • Severe KCS: <5 mm wetting/minute
► The presence of coinciding clinical signs, particularly in the early stages, is important in the diagnosis of KCS.
TEAR FILM BREAK-UP TIME TEST

After application of fluorescein stain to the corneal surface, the eyelids are held open and the uniformity of distribution of the fluorescein is visualized. The break-up time is the time at which dark spots appear within the fluorescein, indicating dispersion of the underlying tear film.

A normal result in dogs is 20 seconds. The appearance of dark spots prior to 20 seconds is suggestive of a qualitative tear film deficiency.

TREATMENT

Medical

Treatment of quantitative and qualitative tear film deficiencies requires the use of lacrimomimetics, with the specific type determined by the underlying cause.

As most cases of KCS in dogs are presumed to be immune-mediated, calcineurin inhibitors are most effective for decreasing the T cell infiltration of the lacrimal glands that inhibits lacrimal secretions.³⁴

- Cyclosporine is commercially available as 0.2% ointment and is also available compounded to solutions with concentrations as high as 2%.³⁴

Diagnosis of qualitative tear deficiency is more difficult, as the STT is normal but clinical signs consistent with KCS are present.

- Visual observation should be performed for lackluster, incomplete tear film.
- Severe generalized eyelid margin inflammation may be present.
- A tear film break-up time test (see Tear Film Break-Up Time Test) may confirm a mucin deficiency that leads to poor adherence of the tear film to the ocular surface.
- Rose bengal staining can identify mucin and albumin deficiencies on the ocular surface.

Rose bengal staining can identify mucin and albumin deficiencies on the ocular surface.

Right eye of a 14-year-old spayed English bulldog, demonstrating conjunctival hyperemia, superficial corneal vascularization, and diffuse corneal edema associated with KCS. The tear film is appropriate (note the fluorescein stain accumulating in the lacrimal lake) because of response to topical therapy; however, the ocular surface inflammation remains.

Left eye of the same dog. Mucoid discharge and conjunctival hyperemia are demonstrated. Moderate corneal pigmentation is present axially, along with superficial vascularization and corneal edema and fibrosis (grayish appearance surrounding the dark pigment). The tear film is visibly appropriate in this eye as well because of a response to topical therapy, but the chronicity of tear film deficiency is evident in association with the described changes. The irregular yellow shape near the dorsomedial limbus is a reflection of the overhead lighting in the tear film.
• Tacrolimus is available as compounded preparations (0.02% to 0.03%).
• Administration is generally 1 drop of solution (or 1/4 inch strip of ointment), 2 to 3 times daily for the remainder of the patient’s life, for both cyclosporine and tacrolimus.

Neurogenic causes of KCS require cholinergic agonists to provide direct parasympathetic stimulation to the lacrimal glands, which is effective when functional glandular tissue remains.
• Pilocarpine ophthalmic solution (1% to 2%) can be administered orally.
• Administration starts at 1 drop/10 kg body weight twice daily and gradually increases by 1 drop/day every 5 to 7 days until improvement is noted.
• The oral route of administration predisposes to systemic effects of parasympathetic stimulation (eg, vomiting, excessive salivation, urination, defecation), which necessitates decreasing the daily dosage to the highest level that does not cause adverse effects.
• As an alternative, topical dilute pilocarpine (0.125%) can be administered.
  – However, this may cause significant ocular irritation and is less likely to result in increased tear production.
• Some cases of neurogenic KCS may be self-limiting, allowing discontinuation of therapy.

All cases of tear film deficiency benefit from lacrilmimetic agents (tear supplements or artificial tears) that mimic tear film.
• Formulations contain molecules with physicochemical properties that improve adherence to and coverage of the cornea by the tear film.
  – Improve eyelid movement
  – Improve clearance of metabolites
  – Improve patient comfort
• Common ingredients include hyaluronate, methylcellulose, hydroxypropyl methylcellulose, and polyvinyl alcohol
  – Many commercial, over-the-counter options are available.

In some cases, tear film deficiency may lead to ocular surface inflammation that is significant enough to necessitate short-term administration of topical corticosteroids in combination with an antibiotic (to address potential coinciding secondary bacterial infection).
• Dexamethasone with neomycin and polymyxin B 2 to 3 times daily for 2 to 3 weeks is generally sufficient.

Surgery
• Surgical transposition of the parotid salivary duct to the conjunctival fornix can improve signs by redirecting salivary secretions to the ocular surface.
• Referral to a veterinary ophthalmologist is advised.
• Short- and long-term complication rate is 50%, including (but not limited to) intolerance to saliva, ocular surface mineral deposition, progression of corneal pigmentation, recurrent and recalcitrant ulcerations, and excessive salivation and facial wetting.

Client Education
• Treatment is lifelong.
• Recurrence or development of new signs warrants repeat evaluation.
  • May indicate reduced responsiveness to current treatment regimen
  • May indicate development of new (and potentially unrelated) ophthalmic condition
**FOLLOW-UP**

- Evaluation of STT and clinical signs should occur within 1 month of initiation of treatment with lacrimostimulants.
  - Some cases will not respond completely within 1 month; treatment for an additional 2 to 4 weeks before diagnosing a treatment failure may be appropriate.
- If no improvement occurs, or if improvement is followed by deterioration over time, increase the concentration of cyclosporine or substitute tacrolimus, and increase frequency of lacrimomimetic therapy.
- Tear film deficiencies require regular (every 6 to 12 months) monitoring to ensure continued appropriate response to therapy.
- Uncontrolled KCS results in progressive clinical signs and vision compromise.

**IN GENERAL**

**Relative Cost**

- $ per month, lifelong
  - Topical lacrimogenic
  - Topical lacrimomimetic
  - Follow-up examination every 6 to 12 months once condition has stabilized

- With judicious care and regular monitoring, prognosis for retaining vision and comfort is good, providing the condition is recognized early (ie, prior to onset of significant corneal pigmentation, vascularization, and fibrosis).

**COST KEY**

- $ = up to $100
- $$ = $101–$250
- $$$ = $251–$500
- $$$$ = $501–$1000
- $$$$$ = more than $1000

See page 94 for references.

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