

## KCS and Acupuncture

Keratoconjunctivitis sicca (KCS or “dry eye”) is a major, potentially blinding, ocular disease in dogs. Animals with KCS exhibit ocular pain, conjunctival hyperemia and hypertrophy, thickened corneal epithelium, and a sticky mucoid to purulent ocular discharge. The disease arises from a simultaneous dysfunction of the lacrimal glands and the gland of the third eyelid.<sup>1</sup> The tear film has a deficient aqueous layer with increased osmolality, leading to conjunctival and corneal lesions. Chronic corneal inflammation can lead to ulceration, scarring, pigmentation and/or neovascularization which may eventually cause loss of vision.

Of the numerous causes of KCS, immune-mediated lacrimal adenitis is perhaps the most common. Drugs<sup>2 3</sup> and systemic disease (hypothyroidism, diabetes mellitus, hyperadrenocorticism, atopy, dysautonomia)<sup>4</sup> are implicated in the pathogenesis of KCS. Trauma to the eye, skull, or surrounding regions can damage the trigeminal or facial nerves; lacrimal nerve pathology may arise from distemper encephalitis.<sup>5</sup>

KCS affects approximately 2% of the canine population.<sup>6</sup> However, routine STT screening of 460 dogs among a survey population revealed a tear deficiency or actual KCS in 35% of dogs.<sup>7</sup> The diagnosis of KCS rests on a Schirmer tear test (STT) of <10 mm/min in conjunction with associated corneal and conjunctival lesions.<sup>8</sup> The clinical signs, pathogenesis, and histopathology of canine KCS closely resemble the dry eye condition in Sjögren’s syndrome (SS), a multisystemic autoimmune disease of humans.<sup>9</sup> As such, the study of dogs with KCS provides a useful animal model to explore treatments for humans. Interestingly, the use of cyclosporine (CsA) in KCS was first tried by veterinary

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<sup>1</sup> Izci C, Celik I, Alkan F, Ogurtan Z, Ceylan C, Sur E, and Ozkan Y. Histologic characteristics and local cellular immunity of the gland of the third eyelid after topical ophthalmic administration of 2% cyclosporine for treatment of dogs with keratoconjunctivitis sicca. *AJVR*. 2002;63(5):688-694.

<sup>2</sup> Majeed SK, Gopinath C and Heywood R. A report on drug-induced kerato-conjunctivitis sicca in dogs. *J Comp Path*. 1987;97:385-391.

<sup>3</sup> Carter R and Colitz CMH. The causes, diagnosis, and treatment of canine keratoconjunctivitis sicca. *Veterinary Medicine*. September 2002: 683-694.

<sup>4</sup> Kaswan R, Pappas Jr. C, Wall K, Hirsh SG. Survey of canine tear deficiency in veterinary practice. In Sullivan et al. (eds): *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2*. New York: Plenum Press, 1998. Pp. 931-939.

<sup>5</sup> Martin CL. Ocular manifestations of systemic disease in the dog. . In Gelatt KN (ed.): *Veterinary Ophthalmology*, 3<sup>rd</sup> edition. Philadelphia: Lippincott Williams & Wilkins. 1998;1401-1406.

<sup>6</sup> Kaswan RL and Salisbury MA. A new perspective on canine keratoconjunctivitis sicca: treatment with ophthalmic cyclosporine. *Vet Clin N Am, Small Anim Pract*. 1990;20:583-613.

<sup>7</sup> Kaswan R et al, 1998. Op. cit.

<sup>8</sup> Izci C et al. Op. cit.

<sup>9</sup> Gilger BC, Rose PD, Davidson MG, Roberts SM, and Miller T. Low-dose oral administration of interferon-alpha for the treatment of immune-mediated keratoconjunctivitis sicca in dogs. *Journal of Interferon and Cytokine Research*. 1999;19:901-905.

ophthalmologists in 1989, and only later by human ophthalmologists after noting its success in treating dogs.<sup>10</sup>

Topical ocular administration of cyclosporine works through immunosuppressive and direct lacrimogenic effects, effectively reversing dry eye by decreasing scarring and inflammation. Adverse effects involve periocular alopecia and irritation.<sup>11</sup> Significant systemic absorption and decreased lymphocyte function have been cited as a possible problem for small dogs (less than 10 kg) who would receive a proportionally higher CsA dose and those on concurrent immunosuppressive medications where the effects may be additive.<sup>12</sup> Cyclosporine is not curative; it must be continued life-long and requires frequent dosing. Some dogs may be unresponsive to CsA; dogs with very low or zero tear production have merely a 50% chance of showing increased tear production with CsA.<sup>13</sup> Oral drug options include interferon<sup>14</sup>, pilocarpine<sup>15</sup>, and the essential fatty acids linoleic acid (LA) and gamma-linolenic acid (GLA). Studies on LA and GLA for KCS demonstrated statistically significant changes in symptoms, lissamine green staining, and ocular surface inflammation, but not fluorescein break-up time (BUT) or the Schirmer tear test.<sup>16</sup> GLA is a precursor to prostaglandin E<sub>1</sub>, a potent anti-inflammatory agent. While recent drug treatment advances have provided several effective treatment options, some dogs fail to respond adequately to medication. When this happens, remaining options include punctal plugs<sup>17</sup> and parotid duct transposition. Punctal plugs may not be suitable for dogs with very low STT values and large breed dogs. The more common option is parotid duct transposition, which provides lubrication for the eyes and may prevent blindness, but which also may cause cicatrization and obstruction of the duct or papilla post-surgically, saliva overflow, deposition of crystalline salt material on ocular surface and eyelids, and sialolithiasis.<sup>18</sup>

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<sup>10</sup> Williams DL. A comparative approach to topical cyclosporine therapy. *Eye*. 1997;11:453-464.

<sup>11</sup> Sansom J, Barnett KC, Neumann W, Schulte-Neumann A, Clerc B, Jegou JP, De Haas V, and Weingarten A. Treatment of keratoconjunctivitis sicca in dogs with cyclosporine ointment: a European clinical field trial. *Vet Rec*. 1995;137:504-507.

<sup>12</sup> Gilger BC, Andrews J, Wilkie DA, Wyman M, and Lairmore MD. Cellular immunity in dogs with keratoconjunctivitis sicca before and after treatment with topical 2% cyclosporine. *Veterinary Immunology and Immunopathology*. 1995;49:199-208.

<sup>13</sup> Kaswan RL and Salisbury MA. A new perspective on canine keratoconjunctivitis sicca. Treatment with ophthalmic cyclosporine. *Vet Clin North Am (Small Anim Pract)*. 1990;20:583-613.

<sup>14</sup> Gilger BC et al, 1999. Op. cit.

<sup>15</sup> Smith EM, Buyukmihci NC, and Farver TB. Effect of topical pilocarpine treatment on tear production in dogs. *JAVMA*. 1994;205(9):1286-1289.

<sup>16</sup> Barabino S, Rolando M, Camicione P, Ravera G, Zanardi S, Giuffrida S, and Calabria G. Systemic linoleic and gamma-linolenic acid therapy in dry eye syndrome with an inflammatory component. *Cornea*. 2003;22(2):97-101.

<sup>17</sup> Williams DL. Use of punctal occlusion in the treatment of canine keratoconjunctivitis sicca. *J Small Animal Practice*. 2002;43:478-481.

<sup>18</sup> Termote S. Parotid salivary duct mucocoele and sialolithiasis following parotid duct transposition. *J Small Animal Practice*. 2003;44:21-23.

Research is currently underway at Colorado State University to explore the value of comparative neuroanatomical acupuncture for the treatment of dogs who are resistant to the therapeutic effects of cyclosporine (which is roughly 5% of those affected<sup>19</sup>). Acupuncture in humans provides significant improvement of xerophthalmia and xerostomia secondary to Sjögren's syndrome and other pathological circumstances.<sup>20 21</sup> For human KCS, research has shown that acupuncture produces a statistically significant difference in STT, BUT, and the frequency in which patients required eyedrops.<sup>22</sup> In a preliminary study, 91% of patients reported an improvement in ocular symptoms and 59% became symptom-free after acupuncture.<sup>23</sup> Both acupuncture needling and laser treatment (4mW, 780 nm, gallium-aluminum-arsenide) showed statistically significant differences over control approaches.<sup>24</sup>

Acupuncture improves eye health by stimulating sensory and autonomic nerve fibers from the trigeminal and facial nerves. Lacrimal secretion depends in part on reflexes involving the sensory afferent fibers of the trigeminal nerve, along with the secretory potential of the lacrimal glands, controlled by parasympathetic fibers arising from the facial nerve.<sup>25</sup> The trigeminal nerve provides sensation to the lacrimal gland (specifically, via the lacrimal nerve), periocular structures, and the globe. Stimulation of nerve endings from these branches of the trigeminal nerve results in reflex tear formation. Postganglionic sympathetic fibers arrive at the lacrimal gland after traveling with the lacrimal nerve. Postganglionic parasympathetic fibers from the facial nerve reach the lacrimal gland via the lacrimal nerve, subsequent to synapsing in the pterygopalatine ganglion. In addition, acupuncture helps lower the temperature of the ocular surface, likely as a result of improved balance between sympathetic and parasympathetic input.<sup>26</sup>

Acupuncture points around the eye, as shown in Figure 1, occur at specific locations involving the trigeminal and facial nerves and their autonomic

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<sup>19</sup> Williams DL. Reported as personal observations in: Williams DL. Use of punctal occlusion in the treatment of canine keratoconjunctivitis sicca. *J Small Animal Practice*. 2002;43:478-481.

<sup>20</sup> Niemtow RC, Kempf KJ, Johnstone PAS. Acupuncture for xerophthalmia – case report. *Medical Acupuncture*. 2002; 13:21-22.

<sup>21</sup> List T, Lundeberg T, Lundström I, and Ravalid N. The effect of acupuncture in the treatment of patients with primary Sjögren's syndrome – a controlled study. *Acta Odontol Scan*. 1998;56:95-99.

<sup>22</sup> Nepp J, Wedrich A, Akramian J, Derbolav A, Mudrich C, Ries E, and Schauersberger J. Dry eye treatment with acupuncture. A prospective, randomized, double-masked study. In Sullivan et al. (eds.): *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2*. New York: Plenum Press, 1998. pp. 1011-1016.

<sup>23</sup> Nepp J, Wedrich A, Akramian J, Strenn K, and Velikaj M. Keratoconjunctivitis sicca. *Deutsch Z Akup*. 1993;2:26-37.

<sup>24</sup> Nepp J et al, 1998. Op. cit.

<sup>25</sup> Hamor RE, Roberts SM, Severin GA, and Chavkin MJ. Evaluation of results for Schirmer tear tests conducted with and without application of a topical anesthetic in clinically normal dogs of 5 breeds. *AJVR*. 2000;61(11):1422-1425.

<sup>26</sup> Nepp J, Tsubota K, Goto E, Schauersberger J, Schild G, Jandrasits K, Abela C, and Wedrich A. The effect of acupuncture on the temperature of the ocular surface in conjunctivitis sicca measured by non-contact thermography: preliminary results.

components. The point **Triple Heater 23**, or **TH 23**, lies lateral to the zygomatic process of the frontal bone in dogs, above the lateral canthus of the eye. Needling this point stimulates the maxillary divisions of the trigeminal nerve via the zygomaticofacial and zygomaticotemporal nerves that provide sensation to the skin of the temporal region and the lateral wall of the orbit, along with the temporal and zygomatic branches of the facial nerve, innervating the local muscles of facial expression. The lacrimal gland lies deep to this point. **Bladder 2 (BL 2)** is found just dorsal to the orbital rim, above the medial canthus of the eye. The frontal branch of the ophthalmic nerve innervates the skin at this point. The facial nerve innervates the underlying muscles. **Gallbladder 1 (GB1)** lies dorsal to the frontal process of the zygomatic bone in dogs, lateral to the lateral canthus of the eye. Needling this point stimulates the temporal and zygomatic branches of the facial nerve that innervate the orbicularis oculi muscle, as well as the aforementioned branches of the maxillary nerve. GB 1 serves as the site of entry for lacrimal nerve block in humans.<sup>27</sup> Additional point options include those on the ear, in regions innervated by the auricular branch of the vagus nerve, providing parasympathetic stimulation<sup>28</sup> and points on the distal extremities, presumably affecting sympathetic fibers carried along peripheral nerves in those sites. For animals in which needling is not acceptable, laser acupuncture could be considered.<sup>29</sup>

Creating comparative acupuncture treatment designs to compare the effects of needling between species requires anatomical precision and careful forethought. Neuroanatomical acupuncture treatment designs provide the means to develop sensible, effective, and efficient needling protocols. Based on anatomic and physiologic principles, the neuroscientific rationale behind these approaches can be communicated in a straightforward and easily understood manner to colleagues and fellow researchers, leading to more opportunities to improve both human and animal health.

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<sup>27</sup> Cousins MJ and Bridenbaugh PO (eds.). *Neural Blockade in Clinical Anesthesia and Management of Pain*, 3<sup>rd</sup> edition. Philadelphia: Lippincott-Raven Publishers, 1998, p. 553.

<sup>28</sup> Niemtow RC, Kempf KJ, Johnstone PAS. Acupuncture for xerophthalmia – case report. *Medical Acupuncture*. 2002; 13:21-22.

<sup>29</sup> Nepp J, Wedrich A, Akramian J, Derbolav A, Mudrich C, Ries E, and Schauersberger J. Dry eye treatment with acupuncture. A prospective, randomized, double-masked study. In Sullivan et al. (eds.): *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2*. New York: Plenum Press, 1998. pp. 1011-1016.

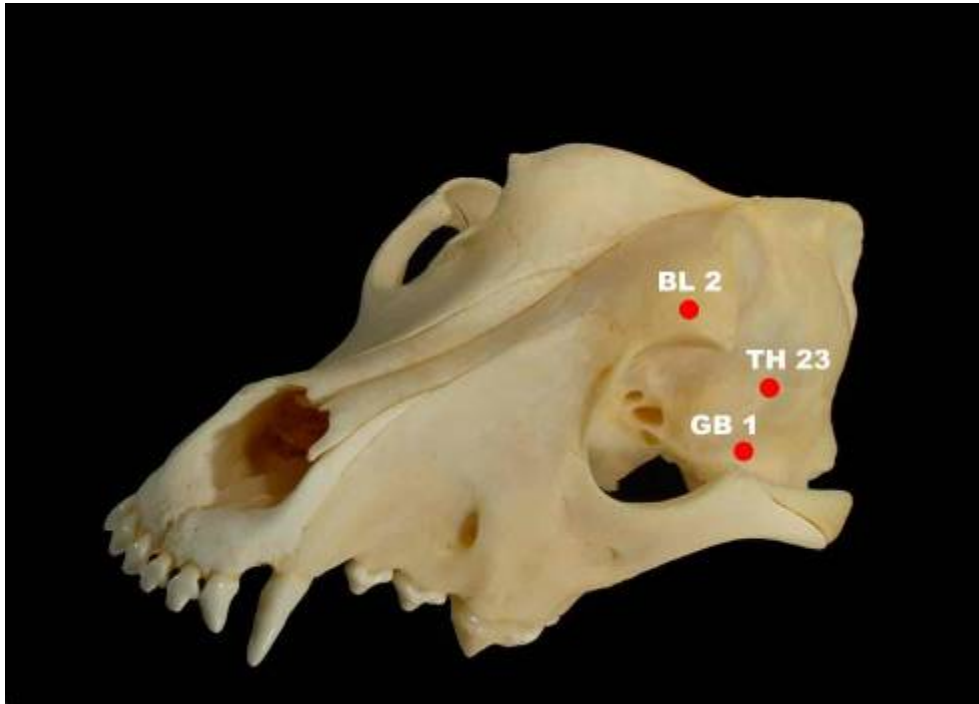


Figure 1. Three of the main acupuncture points for KCS.