

# Effect of lacrimal punctal occlusion on tear production and tear fluorescein dilution in normal dogs

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## Abstract

**Objective** To evaluate effects of lacrimal punctal plugs positioned in either the upper, lower, or combination of upper and lower lacrimal canaliculi on plug retention and tolerance; tear production, as measured by the Schirmer tear test; and the dilution of fluorescein within the tear film in normal dogs.

**Material and methods** Lacrimal punctal plugs were positioned in the lower, upper, or combination of lower and upper plugs in six laboratory-quality Beagles under topical anesthesia. Retention of plugs was evaluated daily from 8 to 23 days by visual inspection and slit-lamp biomicroscopy. Schirmer tear tests (STT 1 without topical anesthesia) were performed at 48-h intervals. Dilution of fluorescein was determined at 5- and 45-min post-fluorescein instillations once weekly.

**Results** Lacrimal punctal plugs of 0.4 and 0.6 mm in diameter were retained for 14 (lower plugs: 100%) and 23 days (75%), and for the upper plugs at 8 days less often (75%), and were infrequently locally nonirritating. Combination of lower and upper plugs seemed to adversely affect retention of either plug. When loss of the plugs occurred, a next larger size plug was necessary suggesting some stretching of the lacrimal canaliculi occurred. Pre- and postplug placement STT results indicated no change with lower and combination lacrimal punctal plugs, but decreased levels following upper lacrimal punctal plugs. Tear fluorescein levels at 5 and 45 min in control eye (no punctum plugs) were 3.39% and 0.14%, respectively. With lower, upper, and the combination of lower and upper lacrimal puncta plugs, tear fluorescein levels at 45 min were higher than the controls (lower: 0.76%; upper: 0.45%, and combination 0.56%).

**Conclusion** Lacrimal punctal silicone plugs are retained for 8–23 days in the lower, upper, and combined lower and upper canaliculi at high rates. Effects on STT levels appear limited. Fluorescein within the tear film persists longer with all different positioned lacrimal punctum plugs than in the control eyes.

**Key Words:** dogs, fluorescein tear clearance, lacrimal punctal plugs, Schirmer tear test

## INTRODUCTION

Lacrimal punctal plugs were introduced for the therapy of chronic keratoconjunctivitis sicca in man in the late 1970 s.<sup>1–5</sup> The primary effect of these devices is to block tear drainage and possibly increase the volume of tears within the conjunctival fornix and corneoconjunctival tear film. Hence, some marginal tear production as well as tear replacement are necessary for the success of these silicone lacrimal canaliculi and punctal plugs. Complications appear limited and include premature plug loss, plug migration within the canaliculi

and nasolacrimal sac, local irritation and swelling, epiphora, and focal infections.<sup>6–8</sup>

The efficacy of silicone lacrimal punctal plugs have been reported in canine keratoconjunctivitis sicca, and demonstrated either increased Schirmer tear test (STT) levels, improved clinical improvement, or a combination in the majority of the patients.<sup>9</sup> The STT levels before placement of lower lacrimal canaliculi plugs were  $2.3 \pm 1.7$  mm wetting/min; after placement of the plugs the STT levels were  $6.1 \pm 4.1$  mm wetting/min. Concurrent therapy consisted of topical cyclosporine and tear replacements.

In recent studies, tear production, tear clearance, and ocular surface sensation were evaluated in normal human eyes before and after lacrimal punctal plug placement following either lower or combination of lower and upper punctal occlusion.<sup>10</sup> With lower punctal plugs, conjunctival sensation was reduced, but corneal sensation was unchanged. Tear fluorescein clearance was unchanged, but the STT levels were reduced with near-significant levels ( $P = 0.056$ ). With both puncta occluded, there were decreases in conjunctival and corneal sensation, STT levels, and by linear regression, no significant change in fluorescein clearance. However, fluorescein clearance changed from the first few days (decrease in clearance rates) to improvement by day 14–17. In normal human eyes there may be an autoregulatory mechanism during and after lacrimal punctal placement that may affect tear production, fluorescein tear clearance, and ocular sensation.<sup>10</sup>

Studies of the punctal plug in normal dog eyes have not been reported. This study reports the retention rates, local irritation, effects on the STT, and fluorescein dilution or clearance in the tear film of silicone lacrimal punctal plugs in normal laboratory quality beagles.

## MATERIALS AND METHODS

Six laboratory-quality beagles were purchased and conditioned for 60–90 days during which time they were acclimated to handling and 1-day trials of lacrimal punctal plug placement in both the upper and lower lacrimal puncta. The silicone (dimethyl siloxane) lacrimal punctum plugs were custom molded based on the design of an existing human product (Veterinary Medical Solutions, Pembroke Pines, FL USA). Normal eyes were determined by detailed eye examinations using slit-lamp biomicroscopy, applanation tonometry, indirect ophthalmoscopy, and STTs.

Plugs were inserted initially with the dog sedated with acepromazine (0.05 mg/kg PO; Ft Dodge, FT Dodge, IA USA) and local anesthesia (0.5% tetracaine Bausch and Lomb, Tampa, FL USA); after limited practice, only topical anesthesia was required. The nasolacrimal system was flushed with sterile saline to determine patency of the system, and function of each lacrimal punctum. Slit-lamp biomicroscopy was used to confirm proper position of the lacrimal plugs within either the upper or lower lacrimal punctum each day after insertion. Eventually, only topical anesthesia was necessary for the lacrimal punctum and canaliculus dilation and immediate placement of the punctum plug(s).

Each lacrimal punctum was dilated with the lacrimal device (Ciba Vision, Duluth GA USA), and the appropriate size lacrimal plug inserted immediately. Proper insertion positioned the top or external end of the plug just superficial to the mucosa of the surrounding lacrimal punctum orifice. Occasionally, a punctal plug was placed more deeply during insertion so that the device could not be observed. Within a day or two, the end of the device reappeared within the lacrimal punctal orifice. Plugs 0.4 and 0.6 mm in diameter were the most useful size for the laboratory quality beagle (9–12 kg).

The lacrimal punctal plug study was a 6-week study with the plugs inserted for 2 weeks each into lower, lower and upper, and upper lacrimal puncta. This avoided manual removal of the lacrimal plugs by forceps and any possible damage to the lacrimal puncta and canaliculi. Lacrimal puncta seemed to enlarge and require larger plugs throughout the 6-week study. If a plug was lost, another same or usually larger size plug was inserted the same day.

The STT has been performed in dogs for the measurement of tear formation rates and diagnosis of keratoconjunctivitis sicca since 1965.<sup>11–17</sup> The test is divided into: STT1 (for one minute without topical anesthesia), and STT2 (with topical anesthesia and lower conjunctival fornix dried by cotton swab). The STT1 tests measures both basal and reflex levels of tear formation as well as the tears already within the conjunctival cul de sac; the STT2 measures only the basal tear formation levels. Reports of STT1 tests (mean  $\pm$  SD) in normal dogs are:  $21.0 \pm 4.2$  mm;  $21.9 \pm 4.4$ ;  $23.9 \pm 5.1$ ;  $18.9 \pm 5.3$ ;  $18.6 \pm 5.3$ ;  $18.6 \pm 4.5$ ;  $22.6 \pm 3.8$ ; and  $21.3 \pm 3.8$  mm/wetting/min.<sup>11–17</sup> The STT2 levels are approximately 50–60% of the STT1 levels.<sup>14</sup> The STT1 test was performed in control eyes and those eyes with the lacrimal punctal plugs visible three times weekly at the same time of each day.

In the fluorescein tear clearance test, the rate of the loss of a selected volume and concentration of fluorescein instilled into the tear film was measured. In this study, predetermined amounts of sodium fluorescein (6  $\mu$ L-1% fluorescein) were instilled onto the eye. At later times (5 and 45 min for control eyes; 45 min for all punctal plugs studies), tear samples, obtained by capillary tubes inserted at the eyelid margin, were collected. The dilution of fluorescein within the tears was measured by fluorophotometry and was determined to provide an estimate of tear dynamics and loss to the opposite lacrimal punctum (with either upper or lower lacrimal plugs), or over the eyelid margin (with both lacrimal puncta occluded with plugs). Samples were obtained twice weekly and on those days when the STTs were not performed.

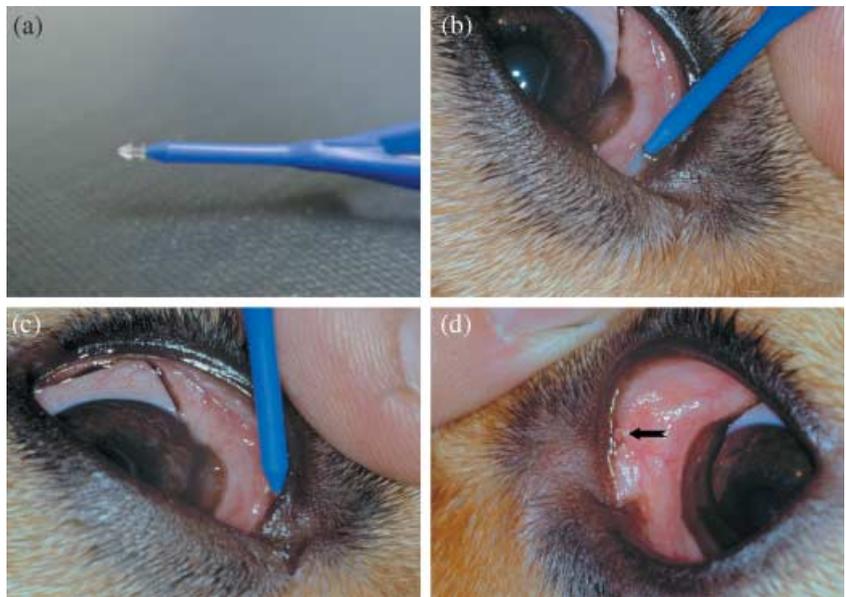
## RESULTS

### *Lacrimal punctal plug size*

Initially the 0.4 or 0.6 mm lacrimal plugs were utilized, and appeared to fit snugly in either the upper or lower lacrimal punctum (Fig. 1a,b,c,d). As the study progressed, the largest (0.8 mm) lacrimal punctal plugs were necessary. Based on the ease of later plug insertions, it appeared the lacrimal puncta and canaliculi were dilating in response to the lacrimal punctal plugs.

### *Local irritation associated with lacrimal punctal plugs*

The lacrimal punctal plugs were well tolerated based on absence of local irritation, i.e., conjunctival hyperemia and chemosis, blepharospasm, and conjunctival exudation. In two dogs with upper lacrimal punctal plugs, some local



**Figure 1.** (a) The lacrimal punctal plug held by the tip of the inserter. (b) Dilation of the lacrimal punctum with the lacrimal punctal device. (c) Insertion of the lacrimal punctal plug into the punctum. (d) Top of the lacrimal punctal plug protruding from the upper lacrimal punctum (arrow).

**Table 1.** Retention of the lower, upper and combination of lower and upper lacrimal punctal plugs in normal dog eyes

Plug position and size	Days	Number of plugs in position per day				
		0	3	7	9	14
Lower 0.6 mm	12	12	12	12	12	12
Combination						
Upper 0.6 mm	12	12	9	9	9	9
Lower 0.6 mm	12	12	12	12	12	12
Upper 0.6 mm			12	6	10	10

conjunctival hyperemia and chemosis developed, but disappeared without therapy after 2 days postinsertion.

#### *Punctal plug retention*

The lacrimal punctal plug study was for 6 weeks with the lacrimal punctal plugs were inserted for 2 weeks each into lower, lower and upper, and upper lacrimal puncta. This avoided manual removal of the lacrimal plugs by forceps and any possible damage to the lacrimal puncta and canaliculi. As the lacrimal puncta seemed to enlarge and require larger plugs during the second study, the first 6-week study is the most accurate indicator for retention of these plugs and is shown in succeeding discussions. If a plug was lost, another similar or usually larger size plug was inserted the same day. For the 6-week study, the retention rates for the lower, upper and lower combination, and lower punctal plugs are summarized in Table 1.

The lower punctal plugs were retained at much higher rates than the upper plugs. The lower retention rates by the upper plugs seemed associated with occasional local irritation, greater upper eyelid movements, and perhaps gravity. For initial plug insertions, 2–3 weeks of retention was the standard. Once a punctal plug was lost, the replacement should be 0.2 mm larger. Replacement with same size lacrimal plug adversely affected retention rates.

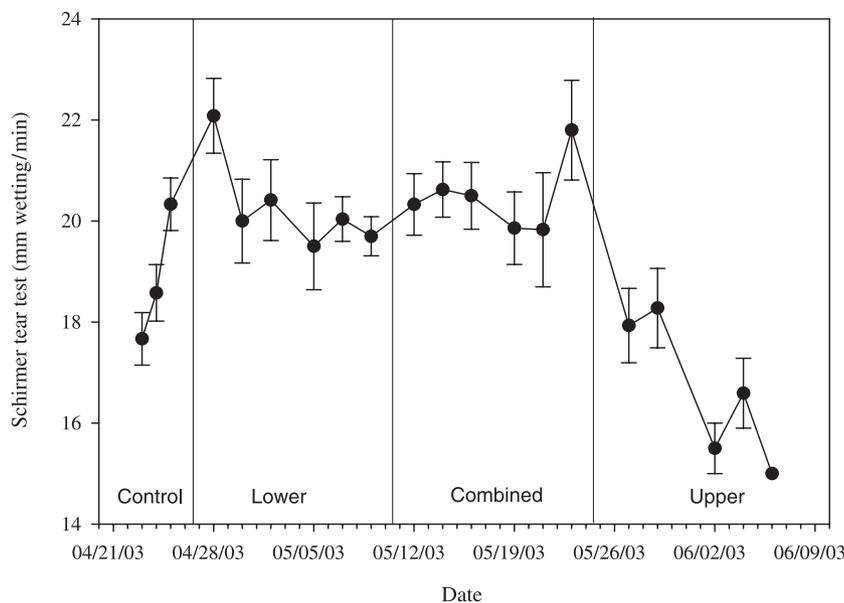
#### *Effect of lacrimal punctal plug on STT levels*

The STT1 levels for the control (no lacrimal plug); upper plug; lower plug, and both upper and lower plugs are summarized in Fig. 2. Tear formations rates, as measured by the STT1, appear not affected by lower and combined (lower and upper lacrimal plugs), but are decreased by placement of only the upper lacrimal plugs compared to the lower plugs or the combination of lower and upper plugs.

#### *Effect of lacrimal punctal plugs on tear fluorescein clearance*

The dilution of fluorescein within the tears was determined to provide an estimate of tear dynamics and loss to the opposite lacrimal puncta (with either upper or lower lacrimal plugs), or over the eyelid margin (with both lacrimal puncta occluded with plugs). Samples were obtained on those days when the STTs were not performed (Table 2).

Hence, based on percent of fluorescein in the tear film at 5 and 45 min: (1) At 5 min in control eyes, 3.39% of the 'drug' remains. At 45 min in the normal or control eye, the fluorescein remaining is 0.14%. With all lacrimal punctal plugs, fluorescein clearance is delayed. Remaining fluorescein in the tears is highest with the lower punctal plugs (0.757%), second with the combination of upper and lower punctal plugs (0.563%), and lowest with the upper punctal plugs (0.454%).



**Figure 2.** Effects of lower, upper, and combination of lower and upper lacrimal punctal plugs on the Schirmer tear test (STT; mm wetting/min; mean  $\pm$  SEM).

**Table 2.** Percent fluorescein remaining after instillation of 6  $\mu$ L of 1% fluorescein in control, and eyes with lower, upper and combination of lower and upper lacrimal punctal plugs.

Location of plug(s)	% of fluorescein in tears
Control (at 5 min)	3.396%
Control (at 45 min)	0.139%
Lower plugs (at 45 min)	0.757%
Upper plugs (at 45 min)	0.454%
Combined (at 45 min)	0.563%

## DISCUSSION

Punctal plugs are well tolerated in the dog as in man. The optimal size of lacrimal punctal plug is usually inserted with little difficulty. In the 14–21 day studies in normal dog eyes retention of lacrimal plugs was quite acceptable, and could provide a means for the slow delivery or release of topical drugs to the external eye over several days to a few weeks. Punctal plugs have studied for their effects on topical glaucoma medications.<sup>18</sup> Compared to clinical studies with dogs with spontaneous keratoconjunctivitis sicca, lacrimal plug retention in healthy eyes in dogs may be of less duration. Replacement lacrimal plugs should be 0.2 mm larger in diameter for continued lacrimal plug presence. In man variations in size of the puncta has also affected punctum plug results.<sup>19</sup>

It is believed that the lower lacrimal punctum drains the majority of the tears in dogs. Lower and combination of lower and upper lacrimal punctal plugs did not affect the STT1 levels. However, the upper lacrimal plugs, by some mechanism, lowered STT1 levels. With these STT results and the punctal plugs, there appears to be little to no irritation secondary to the plugs.

Fluorescein-labeled aqueous tears provide an estimate of the drug loss over time by measurement of the tears levels. Functional lower lacrimal puncta as well as excessive tear formation rates should cause more rapid loss or lower fluorescein tear levels. The lower punctal plugs as well as the combined upper and lower punctal plugs delay the dilution of fluorescein (or preserve tear levels of fluorescein for longer time) within the tear film the most. However, the upper punctal plugs also delay tear fluorescein clearance, perhaps because of reduced tear formation rates (as suggested by the STT study). In the control eye after 5 and 45 min instillation of fluorescein only, 3.4% and 0.14% of the dye remained, respectively. With lacrimal punctal plugs in the lower, upper, and combination of both puncta, fluorescein concentrations at 45 min remained considerably higher, with dye levels of 0.77%, 0.45% and 0.56%, respectively.

There are currently several different lacrimal punctal plugs available, constructed of either silicone or collagen. The silicone plugs are designed for long-term punctal occlusion and the collagen dissolves over time, usually up to 2 weeks. Some plugs offer only partial punctum occlusion, whereas others offer plugs with rounded tops or angled top to reduce local irritation. Critical for the treatment of 'dry eyes' in humans and dogs, some amount of tear formation is necessary for these plugs to be effective.<sup>2,4,9</sup>

## REFERENCES

- Dohlman CH. Punctal occlusion in keratoconjunctivitis sicca. *Ophthalmology* 1978; **85**: 1277–1281.
- Murube J, Murube E. Treatment of dry eye by blocking the lacrimal canaliculi. *Survey of Ophthalmology* 1996; **40**: 463–480.
- Gordonson LC. Efficacy and tolerability outcomes after punctal occlusion with silicone plugs in dry eye syndrome. *American Journal of Ophthalmology* 2001; **132**: 600–601.

4. Tai MC, Cosar CB, Cohen EJ *et al*. The clinical efficacy of silicone punctal plug therapy. *Cornea* 2002; **21**: 135–139.
5. Nava-Castaneda A, Tovilla-Canales JL, Rodriguez L *et al*. Effects of lacrimal occlusion with collagen and silicone plugs on patients with conjunctivitis associated with dry eye. *Cornea* 2003; **22**: 10–14.
6. Nelson CC. Complications of Freeman plugs. *Archives of Ophthalmology* 1991; **109**: 923–924.
7. White WL, Bartley GB, Hawes MJ *et al*. Iatrogenic complications related to the use of Herrick lacrimal plugs. *Ophthalmology* 2001; **108**: 1835–1837.
8. Lee J, Flanagan JC. Complications associated with silicone intracanalicular plugs. *Ophthalmic Plastic and Reconstructive Surgery* 2001; **17**: 465–469.
9. Williams DL. Use of punctal occlusion in the treatment of canine keratoconjunctivitis sicca. *Journal of Small Animal Practice* 2002; **43**: 478–481.
10. Yen MT, Pflugfelder SC, Feuer WJ. The effect of punctal occlusion on tear production, tear clearance, and ocular surface sensation in normal subjects. *American Journal of Ophthalmology* 2001; **131**: 314–323.
11. Roberts SR, Erickson OF. Dog tear secretion and tear proteins. *Journal of Small Animal Practice* 1962; **3**: 1–5.
12. Rubin LF, Lynch RK, Stockman WS. Clinical estimation of lacrimal function in dogs. *Journal of the American Veterinary Medical Association* 1965; **147**: 946–947.
13. Harker DB. A modified Schirmer tear test technique. *Veterinary Record* 1970; **86**: 196–199.
14. Gelatt KN, Peiffer RL, Erickson JL *et al*. Evaluation of tear formation in the dog, using a modification of the Schirmer tear test. *Journal of the American Veterinary Medical Association* 1975; **166**: 368–370.
15. Hawkins EC, Murphy CJ. Inconsistencies in the absorptive capacities of Schirmer tear test strips. *Journal of the American Veterinary Medical Association* 1986; **188**: 511–513.
16. Hirsh SG, Kaswan RL. Comparative study of Schirmer tear test strips in dogs. *Veterinary and Comparative Ophthalmology* 1995; **5**: 215–217.
17. Wyman M, Gilger B, Mueller P *et al*. Clinical evaluation of a new Schirmer tear test in the dog. *Veterinary and Comparative Ophthalmology* 1995; **5**: 211–214.
18. Ariturk N, Oge I, Erkan D *et al*. The effects of nasolacrimal canal blockage on topical medications for glaucoma. *Acta Ophthalmologica Scandinavica*; **996** (74): 411–413.
19. Carter KD, Nelson CC, Martonyi CL. Size variation of the lacrimal punctum in adults. *Ophthalmic Plastic and Reconstructive Surgery* 1988; **4**: 231–233.