Evaluation of nasolacrimal fluorescein transit time in ophthalmically normal dogs and nonbrachycephalic cats

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Objective—To evaluate fluorescein nasolacrimal transit (NLT) times in ophthalmically normal dogs and nonbrachycephalic cats by use of 2 methods of the Jones test.

Animals—73 dogs and 36 cats.

Procedures—Fluorescein dye was applied to the ocular surface of both eyes by means of a wetted fluorescein strip and, in a subsequent test, by administration of a drop of 0.2% fluorescein solution. During each test, the nares were monitored for the appearance of fluorescein for up to 30 minutes after application. Time of fluorescein appearance at the nares was recorded as NLT time. Recorded variables for all study animals included age, reproductive status, body weight, and Schirmer tear test values. For dogs, skull index, snout length, and cephalic conformation were also recorded. Data were grouped for statistical comparisons according to test results.

Results—in both dogs and cats, NLT was faster when the fluorescein solution versus fluorescein strip was used. In cats, none of the recorded variables had a significant effect on NLT, irrespective of the testing method used. In dogs, several variables had a significant effect on NLT, including cephalic conformation, snout length, age, and reproductive status, but these findings varied with testing method and testing group.

Conclusions and Clinical Relevance—NLT was highly variable in dogs and cats, regardless of testing method used. Assessment of nasolacrimal patency in brachycephalic dogs by use of either method evaluated here is not likely to be clinically useful. In cats, assessment of nasolacrimal patency with the fluorescein drop method was faster and more conclusive than with the fluorescein strip method. (Am J Vet Res 2010;71:570–574)

In dogs and cats, the nasolacrimal drainage system is composed of paired nasolacrimal punctae, which are located at the medial aspect of the superior and inferior eyelids and open into the nasolacrimal duct. The duct passes rostrally through the lacrimal and maxillary bones to empty via an ostium on the ventrolateral floor of the nasal vestibule. Approximately 40% of dogs have an additional communication of the duct with the ventral nasal meatus at the level of the canine tooth root. In usual anatomic and physiologic circumstances, tears are drained continuously from the ocular surface via the nasolacrimal system. Obstruction or inadequacy of the nasolacrimal system leads to epiphora and, in some circumstances, dacryocystitis.

Evaluation of nasolacrimal patency is an important step in the diagnosis of the various conditions causing epiphora, including tear overproduction and nasolacrimal obstruction caused by anatomic malformations or acquired conditions such as foreign bodies, neoplasia, dental disease, and inflammatory disease. In veterinary species, assessment of nasolacrimal system patency is generally limited to visual inspection of nasolacrimal punctae, performance of a nasolacrimal fluorescein passage test (ie, the Jones test), anterograde and retrograde irrigation of the nasolacrimal duct, passage of a catheter through the nasolacrimal duct, computed tomography, and dacryocystorhinography. Of these methods, only visual inspection of the nasolacrimal punctae, the fluorescein passage test, and anterograde irrigation of the duct can be performed in the examination room without the need for anesthesia and specialized equipment. Failure of fluorescein to pass to the nares does not confirm nasolacrimal obstruction because in many such situations, the nasolacrimal system can be successfully irrigated. Rather, failure of passage may be an indication of physiologic or functional inadequacy of the nasolacrimal duct. Similarly, whereas appearance of fluorescein at the nares confirms patency of the nasolacrimal system, it does not confirm that the system is anatomically...
normal. Although anterograde irrigation can be used to assess absolute anatomic patency of the nasolacrimal drainage apparatus, only the Jones test can be used to assess physiologic patency without altering the current state of the nasolacrimal system.

Passage of fluorescein through the nasolacrimal system is a quick and simple diagnostic procedure and therefore perhaps the most commonly used test of nasolacrimal patency. Typical nasolacrimal fluorescein passage times in companion animal species have been variably reported as 30 to 60 seconds, 30 seconds to 5 minutes in dogs and 15 seconds to 1 minute in cats, within 5 minutes in dogs and cats, and up to 5 to 10 minutes in clinically normal dogs. Although these stated ranges mirror our own clinical impressions, we are unaware of any studies performed to evaluate NLT times in healthy animals or standardized methods for assessment of NLT in dogs or cats. Similarly, variables affecting fluorescein NLT times have not been evaluated in these species. The purpose of the study reported here was to establish a range of NLT times by use of 2 distinct modifications of the Jones test in ophthalmically normal dogs and cats and to evaluate the effects of age, body weight, reproductive status, tear production, and skull conformation on NLT time.

Materials and Methods

Animals—Over a 6-month period, client-owned animals, including 73 dogs and 36 cats, were enrolled in the study with consent from their owners. Animals were recruited for the study if they were likely to be maintained in the veterinary teaching hospital for the period required to complete nasolacrimal testing. All animals had unremarkable results of external ophthalmic examination in both eyes based on slit-lamp biomicroscopy, including detectable nasolacrimal puncta and no evidence of corneal or adnexal disease. Results of STTs were > 15 mm/min for all study dogs. Although STT results were recorded for cats, those with STT values < 15 mm/min were not excluded because we commonly encounter cats at the teaching hospital that have low STT values yet no ophthalmologic manifestations of keratoconjunctivitis sicca. Dogs and cats with overt clinical evidence of epiphora were excluded from the study. The protocol for all procedures in this study was approved by the Institutional Animal Care and Use Committee of Virginia Tech.

Data collection—For each animal, data were collected including age, reproductive status, body weight, and STT values. In dogs, skull index, defined as skull width divided by skull length, was recorded, as were snout length, as measured from the tip of the nose to the most caudal aspect of the skull (occipital bone), and cephalic conformation. For the latter classification, dogs were judged to be brachycephalic, mesaticephalic, or dolichocephalic on the basis of their breed and cranial appearance.

Assessment of NLT—During the fluorescein passage tests, study animals were kept on the floor and were allowed to orient their heads freely (ie, they were not restrained). Fifteen or more minutes after performing the STT, a wetted fluorescein-impregnated strip was lightly touched to the dorsal bulbar conjunctiva of both eyes of each animal to transfer stain. Immediately afterward, continuous monitoring of the nares with a cobalt-blue light source was performed for up to 30 minutes. The interval to appearance of fluorescein stain at the nares was recorded as the NLT time. This test was referred to as the FST.

After completion of the FST, both eyes were rinsed with ophthalmic wash to remove remaining fluorescein stain from the ocular surface and animals were checked periodically with a cobalt-blue light source for evidence of residual fluorescein staining at the eyes and nares. Once absence of stain was confirmed, 1 drop of 0.2% fluorescein solution was applied to the dorsal bulbar conjunctiva of both eyes by use of a 1-mL tuberculin syringe. Immediately afterward, continuous monitoring of the nares with a cobalt-blue light source was performed for up to 30 minutes. The interval to appearance of fluorescein stain at the nares was recorded as the NLT time. This test was referred to as the FDT.

Statistical analysis—For dogs, data from the study were compiled into 4 groups. The FDT group 1 included FDT results of all dogs. In that group, the results for dogs that failed to have nasolacrimal fluorescein passage by 1,800 seconds after dye application were recorded as 1,800 seconds. The FST group 2 represented FST results for all dogs, excluding those that lacked fluorescein passage within the 30-minute observation period. The FDT group 1 represented FDT results for all dogs. In that group, the result for dogs that failed to have nasolacrimal fluorescein passage by 1,800 seconds after dye application was recorded as 1,800 seconds. The FDT group 2 represented FDT results for all dogs, excluding those lacking fluorescein passage within the 30-minute observation period. An identical scheme was used to group the data from study cats.

Results for variables with normally distributed values (age, body weight, and STT) are reported as mean ± SD. Interval (in seconds) to nasal passage of fluorescein after a strip or drops were applied to the eyes was logarithmically transformed to obtain an approximate Gaussian distribution. Accordingly, NLT values are summarized as medians (range). After verifying that the right and left eyes did not differ with respect to STT or NLT time for the strip test or drop test, a simple mean (for each dog or cat) of their (STT and NLT) values was used for the Spearman correlation analysis between NLT time and each of age, body weight, skull index, STT, and snout length.

To assess the predictive effects of dog or cat characteristics (separately for each species) on the interval to fluorescein passage, results of the strip and drop tests were separately analyzed by means of univariable and multivariable statistical methods (linear mixed models with dog or cat as a random effect). Univariable analysis included linear regression (for age, skull index, snout length, and body weight) and an ANOVA (for STT rate, conformation, and reproductive status). Because the multivariable model included both categorical and continuous variables, an ANCOVA was used. Only variables with significant associations detected during univariable analysis were included in multivariable models, in which all interactions between pairs of variables were considered.
of variables were evaluated one at a time. When a significant interaction was detected, both variables were included in the final model. Residual plots from each of the final models were examined to ensure model adequacy. All analyses were performed by use of commercial software. A value of \( P < 0.05 \) was considered significant for all analyses.

**Results**

**Animals**—The 73 dogs in the study included 34 neutered males, 7 sexually intact males, 28 spayed females, and 4 sexually intact females. Fifty-one dogs were mesaticephalic, 10 were dolichocephalic, and 12 were brachycephalic. Mean ± SD age was 61 ± 39.5 months, and mean body weight was 19.5 ± 11.4 kg. Mean STT rate was 21.4 ± 3.3 mm/min. Because 3 study dogs left the hospital between NLT tests, only 70 were included in the FDT portion of the study.

The 36 cats in the study included 20 neutered males, 1 sexually intact male, and 15 spayed females. All cats were domestic shorthair; none were brachycephalic. Mean age was 63.9 ± 53.7 months, and mean body weight was 5.2 ± 1.8 kg. Mean STT rate was 17.6 ± 5.7 mm/min.

**FST time in dogs**—Median NLT time for all 73 dogs in the FST group 1 was 248 seconds (range, 35 to 1,800 seconds). Snout length was significantly \( (P < 0.001) \) associated with NLT time, such that dogs with a long snout had a lower NLT time than those with a short snout. Cephalic conformation also had a significant \( (P = 0.033) \) effect on NLT. Specifically, brachycephalic dogs had a significantly \( (P = 0.025) \) longer NLT time than did mesaticephalic dogs. Differences between brachycephalic and dolichocephalic conformations and between mesaticephalic and dolichocephalic conformations were not significant. A significant effect of reproductive status was also detected within this group, with sexually intact males having a significantly \( (P = 0.018) \) longer NLT time, compared with that of spayed females \( (P = 0.018) \). No other comparisons involving reproductive status were significant. Age, body weight, skull index, and STT rate were not significantly associated with NLT time.

In FST group 2 (same dogs as in group 1, but excluding those that lacked fluorescein passage within the 30-minute observation period), 61 dogs were included (48 mesaticephalic, 10 dolichocephalic, and 3 brachycephalic; 27 neutered males, 4 sexually intact males, 27 spayed females, and 3 sexually intact females). Mean age was 66.2 ± 38.6 months, and mean body weight was 21.7 ± 11 kg. Mean STT rate in this group was 21.5 ± 3.3 mm/min, and median NLT time was 160 seconds (range, 35 to 802 seconds). None of the recorded variables were significantly associated with NLT time when this grouping scheme was used.

**FST time in cats**—Median NLT time for all 36 cats in FST group 1 was 46 seconds (range, 4 to 1,800 seconds). There was no significant association of age, reproductive status, body weight, or STT rate with NLT time in this group.

In FST group 2 (same cats as in group 1, but excluding those that lacked fluorescein passage within the 30-minute observation period), 34 cats were included (20 neutered males, 1 sexually intact male, and 13 spayed females). Mean age was 63.9 ± 53.3 months, and mean body weight was 3.3 ± 1.8 kg. Mean STT rate in this group was 17.9 ± 5.4 mm/min. Median NLT time was 30 seconds (range, 4 to 722 seconds). There was no significant association of age, reproductive status, body weight, or STT rate with NLT time in this group. The FST time did not differ significantly between left and right eyes in either group.

**FDT time in dogs**—Seventy dogs were included in FDT group 1 (49 mesaticephalic, 10 dolichocephalic, and 11 brachycephalic; 33 neutered males, 7 sexually intact males, 26 spayed females, and 4 sexually intact females). Mean age was 58.4 ± 37.6 months, and mean body weight was 19.5 ± 11.4 kg. Mean STT rate in this group was 21.6 ± 3.3 mm/min.

In FDT group 1, median NLT time was 48 seconds (range, 2 to 1,800 seconds). Snout length was significantly \( (P < 0.001) \) associated with NLT time, such that dogs with a long snout had a lower NLT time than did those with a short snout. Cephalic conformation was also significantly \( (P = 0.022) \) associated with NLT time. Specifically, brachycephalic dogs had a significantly higher NLT time than did mesaticephalic \( (P = 0.049) \) and dolichocephalic \( (P = 0.016) \) dogs. However, there was no significant difference in NLT time between mesaticephalic and dolichocephalic dogs in this study group. Age, reproductive status, body weight, skull index, and STT rate did not significantly affect NLT time.

The FDT group 2 consisted of 60 dogs (46 mesaticephalic, 10 dolichocephalic, and 4 brachycephalic; 28 neutered males, 4 sexually intact males, 25 spayed females, and 3 sexually intact females). Mean age was 61.8 ± 37 months, and mean body weight was 21.3 ± 11.7 kg. Mean STT rate in this group was 21.6 ± 3.3 mm/min.

Median NLT time was 41 seconds (range, 2 to 840 seconds). Age was significantly \( (P = 0.027) \) associated with NLT time, such that older dogs had a higher NLT time than did younger dogs. Increased snout length was significantly \( (P = 0.008) \) associated with decreased NLT time. Cephalic conformation was also significantly \( (P = 0.012) \) associated with NLT time. Specifically, brachycephalic dogs had a significantly higher NLT time than did mesaticephalic \( (P = 0.030) \) and dolichocephalic \( (P = 0.008) \) dogs. However, there was no significant difference in NLT time between mesaticephalic and dolichocephalic dogs. There was also no significant association of reproductive status, body weight, skull index, or STT rate with NLT time in this study group.

The FDT time did not differ significantly between left and right eyes in either group. For all dogs in both FDT groups, the FDT time was significantly \( (P < 0.05) \) shorter than the FST time.

**FDT time in cats**—All 36 cats were included in FDT group 1. Median NLT time for these cats was 7 seconds (range, 2 to 496 seconds). All cats had evidence of fluorescein passage within 30 minutes when the FDT was administered. Age, reproductive status, body weight, and STT rate were not significantly associated with NLT time.
Because all cats had evidence of fluorescein passage within 30 minutes with the FDT, there was no need to establish an FDT time for group 2. The FDT time did not differ significantly between left and right eyes in either group. For all cats studied, the FDT time was significantly shorter than the FST time.

Discussion

Results of the present study suggested that establishment of reference limits for NLT time for all dogs regardless of cephalic conformation may be problematic. However, of the dogs that had fluorescein passage within 30 minutes after FST or FDT administration, all had detectable fluorescein at the nares within approximately 14 minutes. The range of fluorescein transit times was wide with both tests in dogs. However, in dogs that had fluorescein passage within 30 minutes, the median interval to fluorescein detection at the nares was significantly shorter with the FDT (41 seconds), compared with that of the FST (160 seconds).

Although some cats (2/36) in the study did not have fluorescein passage within the 30-minute observation period when the FST was used, all cats had passage within 9 minutes after dye application when the FDT was used (median FDT time, 7 seconds; range, 2 to 496 seconds). These results suggested that nonbrachycephalic cats with an FDT result >10 minutes may have a dysfunctional nasolacrimal drainage system, warranting additional diagnostic testing. Because of described anatomic differences in the nasolacrimal system between brachycephalic and nonbrachycephalic cats, our findings likely do not apply to brachycephalic cats.

A substantial proportion of our canine sample (16% of dogs when the FST was used and 14% when the FDT was used) did not have visible fluorescein at the nares (ie, a positive test result) after 30 minutes of observation. Most dogs with a negative FST or FDT test result after 30 minutes were brachycephalic. Of the dogs with a negative FST result, 9 were brachycephalic and 3 were mesaticephalic. This represented 9 of all 12 brachycephalic dogs and 3 of all 51 mesaticephalic dogs in the study. Of the dogs with a negative FDT result, 7 were brachycephalic and 3 were mesaticephalic, representing 7 of 11 brachycephalic dogs and 3 of 49 mesaticephalic dogs in the study. The same 3 mesaticephalic dogs that had a negative FST result also had a negative FDT result, whereas all other mesaticephalic dogs had positive results for both tests. All of the dolichocephalic dogs had a positive FST and FDT result within the 30-minute observation period. These findings suggested that both tests of nasolacrimal fluorescein passage may have more clinical relevance when used in mesaticephalic and dolichocephalic breeds and may be clinically irrelevant in brachycephalic breeds.

Several authors suggest that anomalous drainage of the nasolacrimal system into the caudal aspect of the nasal cavity or nasopharynx occurs in brachycephalic dogs. The same situation is believed to be true in brachycephalic cats. As such, it has been recommended that fluorescein dye can sometimes be detected in these animals by visual inspection of the pharynx after topical ophthalmic application. Although pharyngeal examination is likely effective in select situations, we have not found this to be rewarding in clinical practice. Although it was not an established aspect of the experimental protocol applied to all dogs in the present study, detection of fluorescein in the pharynx was attempted for all dogs in which fluorescein had not exited the nares by 30 minutes after application; such attempts were unsuccessful. Alternative explanations for poor fluorescein passage in brachycephalic dogs include punctal occlusion caused by medial entropion common among these breeds or altered anatomy and course of the nasolacrimal duct associated with this cranial conformation, resulting in physiologic inadequacy of the duct. Substantially altered duct anatomy associated with brachycephalic conformation was detected in an anatomic study of cats and was suggested to account for physiologic duct inadequacy in the presence of anatomic normal duct diameter. In that study, the nasolacrimal duct opened onto the ventrolateral floor of the nasal vestibule below the alar fold in all cats, with no anomalous openings into the caudal aspect of the nasal cavity. An anatomic study of the canine nasolacrimal duct involving 30 dogs also revealed no connections of the duct with the nasopharynx or caudal aspect of the nasal cavity; however, breed and cranial conformation were not reported, so brachycephalic dogs may not have been represented in that study.

Since the Jones test was introduced in humans, the predictive value of a negative test result has been debated. In ophthalmologically normal human subjects, the proportion of positive test results can vary, ranging from 48% to 91%. This would appear to be the situation in ophthalmologically normal dogs as well. One study in which the Jones test was used not only revealed a consistent correlation between fluorescein detection at the nares and patent nasolacrimal ducts in humans with epiphora, but also a lack of correlation between absence of fluorescein passage and nasolacrimal obstruction in the same sample. Similarly, in a study of 68 humans with epiphora who were patent with lacrimal irrigation, 81% had negative Jones-test results. We did not attempt to irrigate the nasolacrimal system in any of the dogs in the present study, although doing so would have helped determine the absolute patency of the nasolacrimal duct in those dogs that did not pass fluorescein with either test.

In humans, several variables affect the results of the Jones-test assessment of NLT. The volume of fluorescein dye applied to the conjunctival sac is inversely correlated with NLT time. A similar volume effect likely explains the finding of faster FDT than FST time in dogs and cats in the present study. When the Jones test was used to assess NLT time in humans of various ages, it was determined that NLT time increases with increasing age. In the dogs in our study, increasing age was significantly associated with NLT time when the FDT but not the FST was used. The effect was similar to that described in humans. Interestingly, the study in humans involved a similar testing modality as the FDT (ie, a single drop of fluorescein was used). Although it has been stated that NLT time is influenced by rate of tear production in animals, our results suggested that this does not appear to be true for dogs or cats with clinically normal tear production. No statement can be made regarding NLT times in animals with subnor-
nal tear production because such animals were excluded from our study. Whereas a significant association of reproductivity status with NLT time was detected in one of our canine data groups, with sexually intact males having a longer NLT time than did spayed females as assessed by FST, this finding lacks a plausible biological explanation and we do not believe it has any clinical relevance.

Most dogs with a negative FDT result (n = 12) also had a negative FDT result (10). Neither duct cannulation and irrigation nor dacryocystorhinography was performed on any of the study subjects, so the definitive status of absolute nasolacrimal patency was not determined. It is possible that this phenomenon represented a group of dogs with subclinical nasolacrimal duct obstruction, either partial or complete. Although no overt clinical signs of external ophthalmic disease or tear overflow were detected during initial ophthalmic examination, 3 brachycephalic dogs with negative FST and FDT results had overflow of fluorescein-stained tears during testing. It would be worthwhile to compare our results with findings in dogs with epiphora or a confirmed diagnosis of nasolacrimal duct abnormality.

Limitations of the study reported here include unequal numbers of dogs of the various cephalic conformations and the consistent evaluation of FST time prior to FDT time. Although the fixed order of testing was a potential confounding factor, the order was chosen for a specific reason. The FST minimally alters physiologic tear volume and flow because no fluid is added to the tear film, whereas the FDT likely alters these variables because a drop of fluid is added to the tear film. Therefore, we believed the potential effects of the FST on the results of a subsequently performed FDT would be less important than the effects of the FDT on the results of a subsequently performed FST. By careful observation of the conjunctival fornices and nares for a lack of any evidence of residual fluorescein prior to performing the FDT, we ensured to the best of our ability that observation of fluorescein during the FDT would be specific to that test. Although it is possible that a small amount of residual fluorescein from the FST may have persisted within the nasolacrimal duct to be eluted during the FDT, we believed this is unlikely because of the observed clearance from the ocular and nasal surfaces following irrigation. Additionally, we observed that the FDT resulted in large volumes of fluorescein at the nares, which is inconsistent with a small amount of residual fluorescein within the duct. Ideally, the order of testing would have been randomized, with a sufficient period between tests to allow for any potential influences of a test on a subsequent one to diminish; however, our dependence on outpatients at the veterinary teaching hospital precluded a prolonged testing period.

It is important to establish a universal method for testing nasolacrimal duct patency that would allow for comparison of all patients’ values to standard reference limits that ideally would not be influenced by the individual performing the test. For all dogs and cats in the present study, FDT was significantly faster than FST. This, combined with the fact that all cats had a positive FDT result, suggested that the FDT is perhaps a more clinically useful and efficient method of performing the Jones test to evaluate nasolacrimal fluorescein passage. However, because of the volume of fluorescein used in the FDT, the FST may more accurately reflect physiologic tear flow than the FDT. In our study, the FDT involved application of 1 drop of fluorescein from a standard 1-mL tuberculin syringe. Additional volume administered to the eye may yield different results than those reported here, as occurs when fluorescein solution is used in humans.19

References


a. Ful-Glo 1.0-mg Fluorescein Sodium Ophthalmic Strips, Akorn Inc, Buffalo Grove, Ill.
b. Eye Irrigating Solution, Rugby Laboratories Inc, Duluth, Ga.