

# Evaluation of duration of corneal anesthesia induced with ophthalmic 0.5% proparacaine hydrochloride by use of a Cochet-Bonnet aesthesiometer in clinically normal horses

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**Objective**—To measure duration of corneal anesthesia and time and degree of maximal anesthetic effect of 0.5% proparacaine hydrochloride by use of a Cochet-Bonnet aesthesiometer in horses.

**Animals**—10 clinically normal adult horses.

**Procedures**—Baseline corneal touch threshold (CTT) was measured in millimeters for 1 randomly selected eye of each horse by use of the aesthesiometer by applying the filament to the cornea at maximum length (60 mm) and decreasing in 5-mm increments until a consistent blink response was elicited. Following baseline CTT measurement, 0.2 mL of 0.5% proparacaine hydrochloride was instilled in the selected eye. The CTT was measured within 1 minute following proparacaine administration and every 5 minutes thereafter for 60 minutes. A mixed-model ANOVA with tested eye varying between subjects and measurement time varying within subject was used to test for main effects and any interaction between these factors. A contrast between means of baseline and each subsequent CTT identified the duration of corneal anesthesia as the time at which there was no difference from baseline. Maximal anesthetic effect occurred at the time with the lowest mean CTT.

**Results**—Duration of corneal anesthesia achieved by use of proparacaine was 25 minutes, and maximal anesthetic effect occurred within 5 minutes, although CTT never went to 0 in any horse at any time.

**Conclusions and Clinical Relevance**—Duration of corneal anesthesia in horses was shorter than in dogs, and degree of maximal effect was less than in cats and dogs, most likely because of increased sensitivity of the equine cornea, compared with corneal sensitivity in those species. (*Am J Vet Res* 2008;69:1655–1658)

The equine cornea is provided with sensory innervation by the long ciliary nerves, which are branches of the ophthalmic division of the trigeminal nerve.<sup>1,2</sup> The superficial portion of the cornea receives more sensory innervation with pain receptors than the middle and deeper portions.<sup>2</sup> Corneal sensitivity has been evaluated in a number of species by use of a CTT. Corneal sensitivity varies with a number of factors, including species, area of the cornea, and skull type. It has been reported that the cornea of humans is considered the most sensitive of those species studied, followed by the cornea of cats, rabbits, and dogs.<sup>3–8</sup> Corneal sensitivity has been measured in horses and guinea pigs as well, with horses having relatively high corneal sensitivity<sup>3,9</sup> (although direct comparison is difficult because results are variably reported in different measurement units [grams per square millimeter or centimeter] and by use

ABBREVIATION	
CTT	Corneal touch threshold

of different aesthesiometer filament strengths) and guinea pigs having relatively low corneal sensitivity, comparable to that of brachycephalic cats.<sup>10</sup> The central portion of the cornea is more sensitive than the peripheral portion in dogs,<sup>8</sup> cats,<sup>4</sup> horses,<sup>3,9</sup> and guinea pigs,<sup>10</sup> although differences are not always significant. For cats<sup>4</sup> and dogs,<sup>7</sup> having a brachycephalic skull type is associated with having lower corneal sensitivity.

Corneal sensitivity was measured by use of the CTT in previous equine studies with the Cochet-Bonnet aesthesiometer. Brooks et al<sup>9</sup> found that the mean CTT for adult horses, sick foals, and healthy foals was  $4.82 \pm 0.87$  cm,  $3.21 \pm 0.24$  cm, and  $5.01 \pm 0.61$  cm, respectively, suggesting that healthy foals had the most sensitive corneas, whereas sick foals had the most insensitive corneas and highest CTT.

Topical ophthalmic anesthetics are routinely used to facilitate measurement of intraocular pressure, collection of corneal and conjunctival scrapings for cytologic examination, and removal of ocular foreign bodies in many species. In horses, a topical anesthetic is used

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in conjunction with a local anesthetic to place a subpalpebral lavage catheter. The most widely used topical ophthalmic anesthetic agent is 0.5% proparacaine hydrochloride. Tetracaine, another topical ophthalmic anesthetic, is more likely to cause pain upon administration, conjunctival irritation, and chemosis.<sup>11</sup> Recent studies by Herring et al<sup>12</sup> and Binder and Herring<sup>13</sup> have determined the duration of effect of proparacaine in dogs and cats; however, the duration of effect in horses is unknown. In dogs, a significantly greater anesthetic effect resulted after instillation of 2 drops of proparacaine, compared with 1 drop. Also, the maximal anesthetic effect lasted for 15 minutes with 1 drop and for 25 minutes with 2 drops.<sup>12</sup> In cats, the maximal anesthetic effect lasted only 5 minutes after instillation of 1 drop of proparacaine, as measured by use of the Cochet-Bonnet aesthesiometer.<sup>13</sup> The latter duration is considerably shorter than that of dogs.

The Cochet-Bonnet aesthesiometer, a commercially available aesthesiometer, has been used routinely to determine corneal sensitivity in many species and to identify the duration of effect of proparacaine in cats and dogs by measuring the CTT.<sup>3,4,6-10</sup> The CTT corresponds to the length of nylon filament that induces a blink reflex upon contact with the cornea. The Cochet-Bonnet aesthesiometer contains an adjustable-length nylon filament, which is applied to the cornea. The length of the nylon filament directly corresponds to the amount of pressure being applied to the corneal surface at a particular time. When the CTT for a particular horse is reached, the corneal reflexive response is elicited via blinking, retraction of the globe, and prolapse of the nictitating membrane (ie, the third eyelid). Therefore, a higher CTT will correspond with a shorter filament length because of increased pressure and decreased corneal sensitivity, whereas a lower CTT will correspond with a longer filament length from decreased applied pressure and therefore increased corneal sensitivity.<sup>3</sup> This instrument has also been safely and effectively used to measure corneal sensitivity in foals and adult horses.<sup>9</sup> The purpose of the study reported here was to use the Cochet-Bonnet aesthesiometer to measure the onset and duration of effect of 0.5% proparacaine hydrochloride in the eyes of healthy adult horses. We hypothesized that the duration of corneal anesthesia induced with 0.5% proparacaine hydrochloride in horses would be shorter than that of dogs and cats because of the increased sensitivity of the equine cornea, compared with corneal sensitivity in cats and dogs.

## Materials and Methods

**Animals**—This study used 10 clinically normal, adult Thoroughbreds from the University of Pennsylvania New Bolton Center research teaching herd. The study group consisted of 8 geldings and 2 mares ranging in age from 4 to 9 years, with a mean age of 6.1 years. Only clinically normal horses with no evidence of corneal or adnexal disease detected by use of slit lamp biomicroscopic examination that did not have corneal fluorescein retention and had a Schirmer tear test value of > 10 mm/min were included in the study.<sup>14</sup> The experiment was conducted without the use of sedation. After measurement of baseline corneal sensitiv-

ity, administration of proparacaine, and measurement of sensitivity over a period of 60 minutes, the corneas were stained with fluorescein to ensure that no corneal ulceration was sustained during data collection. The protocol and all procedures used for this study were approved by the Animal Care and Use Committee of the University of Pennsylvania.

**Measurement of corneal sensitivity**—Corneal touch threshold was measured for 1 randomly selected eye of each horse (5 right eyes, 5 left eyes) with the Cochet-Bonnet aesthesiometer. The aesthesiometer had a nylon filament adjustable from 5 to 60 mm in length, with a defined diameter of 0.12 mm, which was directly applied to the central portion of the cornea to determine sensitivity. The aesthesiometer readings in millimeters can be converted to applied force measurements as either grams per square millimeters or milligrams per S, where S equals 0.0113 mm<sup>2</sup> of sectional area of the filament.

At first, the filament was applied at maximum length (60 mm), and the length was then decreased by 5-mm increments once it was determined that the CTT had not been met at that particular filament length (ie, no blink response). To ensure that the response was consistent with the CTT, a positive response was considered to be 3 consecutive blinks.

**Treatment**—Following initial CTT measurement, 0.2 mL of 0.5% proparacaine hydrochloride was applied to the treated eye by drawing 0.2 mL of proparacaine into a syringe, breaking a 25-gauge needle off at the hub, and instilling the proparacaine into the horse's eye. Although this volume, which is approximately equal to 4 drops of anesthetic, was greater than the volume used in studies<sup>12,13</sup> evaluating the onset and duration of proparacaine in cats and dogs, which used only 1 to 2 drops, this volume is the amount typically instilled in clinical application in horses. In addition, volume may not be directly comparable among dogs, cats, and horses because the latter have larger corneas and conjunctival fornices. This anesthetic instillation technique ensured that the correct amount of anesthetic was applied to the equine cornea, which poses a challenge relative to small animal patients for which one can control the animal's head position and drop the medication onto the cornea. This is not feasible in horses. The same bottle of proparacaine, which remained refrigerated, was used throughout the study period. The time of initial CTT measurement was designated as time 0. The CTT was measured 1 minute following proparacaine administration and again every 5 minutes thereafter in each eye for 60 minutes or until the cornea was determined to no longer be desensitized. The aesthesiometer obtained measurements when the operator touched the central aspect of the cornea. Following completion of CTT measurements in millimeters and time recordings at each 5-mm increment change, each tested eye was stained with fluorescein and examined with a slit lamp biomicroscope with a cobalt blue filter to ensure that no epithelial damage had occurred.

**Statistical analysis**—Corneal touch threshold, defined as the mean filament length in millimeters at which a consistent blink response was elicited, was

measured at each time point, starting with a baseline measurement prior to administration of proparacaine, then continuing with a measurement just after administration of proparacaine and every 5 minutes thereafter for 60 minutes. Corneal touch threshold data were analyzed by use of a mixed-model ANOVA, testing for main effects of the tested eye, which varied between subjects, and measurement time, which varied within subject, and a contrast between baseline CTT and CTT measured at each subsequent time. Standard software was used for all analyses.<sup>a</sup> Values of  $P < 0.05$  were considered significant.

## Results

Mean baseline Cochet-Bonnet aesthesiometer filament length was 48 mm. The maximum effect of 0.5% proparacaine hydrochloride on corneal sensitivity was a 12.5-mm filament length 5 minutes after initial proparacaine instillation. There was a significant ( $P < 0.001$ ) effect of measurement time (Figure 1). The contrast between baseline and each subsequent measurement time revealed that readings up to 25 minutes after proparacaine administration were significantly lower than baseline, but after 25 minutes, CTT was not significantly different from baseline. Horses returned to baseline corneal sensitivity 25 minutes after initial proparacaine instillation. No significant difference in CTT was noted at any time point between left and right eyes.

## Discussion

Baseline corneal sensitivity was higher in this study of horses than in previous studies<sup>12,13</sup> of cats and dogs, but return to baseline corneal sensitivity in horses was similar to that in cats.<sup>13</sup> All 3 of these studies, however, did not specifically evaluate corneal sensitivity but rather simply evaluated the onset and duration of effect of proparacaine because only central CTT was measured, not sensitivity of other corneal regions; thus, only the onset and duration of effect of proparacaine can be compared across the 3 species. Baseline corneal sensitivity in the present study of horses was higher

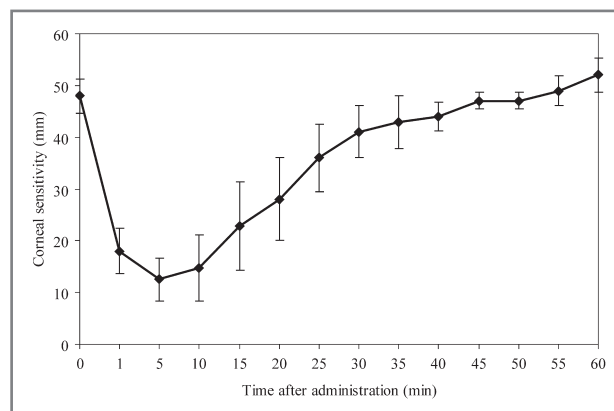


Figure 1—Mean  $\pm$  95% confidence limits for aesthesiometer filament length used to determine corneal sensitivity in 10 horses before and after topical administration of 0.2 mL of 0.5% proparacaine administration. Baseline filament length is recorded at time 0. Times after 0 correspond to minutes after proparacaine administration.

than corneal sensitivity previously reported by Kaps et al<sup>3</sup> but identical to that reported by Brooks et al<sup>9</sup> in adult Thoroughbreds.

The maximum effect of 0.5% proparacaine hydrochloride on equine corneal sensitivity reported in the present study was a 12.5-mm filament length 5 minutes after initial proparacaine instillation. This was in contrast to results obtained with cats and dogs, which both sustained a period of corneal anesthesia in which corneal contact even with a 0.5-mm Cochet-Bonnet filament failed to induce a blink.<sup>12,13</sup> In horses in the present study, such a period never occurred; rather, the mean filament length above which a blink did not occur was 12.5 mm. That is, horses in this study never failed to blink when the Cochet-Bonnet filament reached some minimum length. Horses returned to baseline corneal sensitivity 25 minutes after initial proparacaine instillation, which was similar to that for cats and shorter than that reported for dogs. Therefore, manipulations to the equine cornea would likely need to be performed within the first 10 minutes after proparacaine administration to ensure the highest degree of corneal anesthesia, which even so may not be complete. However, examination and treatment of equine patients typically are performed over a time period of greater than the 5-minute duration reported for maximum effect in cats and at times over a period even greater than the 25 minutes reported for any significant decrease in sensitivity in cats.<sup>13</sup> For example, it may be necessary to keep the cornea anesthetized from the time of the initial examination of the eye, through collection of a sample for cytologic examination, to placement of a subpalpebral catheter.

Kaps et al<sup>3</sup> evaluated sensitivity of different regions of the equine cornea. Of 100 equine eyes, they found variation in corneal sensitivity, with the central aspect being the most sensitive region and the dorsal aspect being the least sensitive area. This variation may be attributable to an increased number of nerve trunks in the central region, compared with other regions. It is reported that the cornea in humans has more nerve trunks and is more sensitive than the cornea in cats, rabbits, and dogs.<sup>3-10</sup> Kaps et al<sup>3</sup> did not find a significant difference in CTT among different age groups or sexes in horses. Anecdotal data from 4 aged horses in a research herd (2 mares with pituitary pars intermedia dysfunction and 2 draft-breed geldings) suggested a decreased baseline corneal sensitivity and prolonged duration of effect of proparacaine relative to horses in the present study, but it is unclear whether this anecdotal result, if indeed representing a real difference, was attributable to age, endocrine status, or breed, all of which may predispose to reduced corneal sensitivity.

A potential limitation of this study included difficulty in obtaining aesthesiometry readings on the cornea because of the numerous and lengthy cilia of the horses. It may have been beneficial and allowed for more accurate aesthesiometry readings if the cilia were trimmed before readings were obtained. Also, the study was performed with horses kept in stalls in a barn in which ambient light and wind varied across reading times, and each of these factors may have contributed to blink threshold. In addition, evaluation of the blink response in horses can be subjective. We attempted to

minimize this by having the same 2 investigators perform all readings, with the same restraint and in a similar stall environment for each subject.

Results suggested that topical corneal anesthesia with 0.5% proparacaine hydrochloride may not provide adequate anesthesia in horses. Because of the length of time required to perform diagnostic and therapeutic procedures on the cornea in the awake, standing horse, one may need to readminister anesthetic frequently because maximal effect occurred at 5 minutes and the anesthetic effect of proparacaine waned by 25 minutes.

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a. SAS, version 9.1.3, SAS Institute Inc, Cary, NC.

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