

# Evaluation of the repeatability of rhinomanometry and its use in assessing transnasal resistance and pressure in dogs

Thomas S. Wiestner, BS; Daniel A. Koch, DVM; Natascha Nad, DVM; Aaron Balli, DVM; Malgorzata Roos, PhD; Richard Weilenmann, DVM; Erika Michel, DVM; Susanna Arnold, PhD

**Objective**—To evaluate a modified posterior rhinomanometric method for clinical application in dogs.

**Animals**—15 healthy Beagles and 8 Bulldogs (4 healthy and 4 with respiratory problems).

**Procedures**—Rhinomanometry was performed 3 times within a 15-minute period in anesthetized dogs. Transnasal pressure ( $P_{NA}$ ) and nasal resistance ( $R_{NA}$ ) were determined by use of artificial airflow (adjusted for body weight) for inspiration ( $P_{NAin}$  and  $R_{NAin}$ , respectively) and expiration ( $P_{NAout}$  and  $R_{NAout}$ ). Procedures were repeated for the Beagles 7 days later.

**Results**—For the Beagles, mean  $\pm$  SD of  $P_{NAin}$  for both days ( $0.162 \pm 0.042$  kPa) was significantly lower than  $P_{NAout}$  ( $0.183 \pm 0.053$  kPa). Similarly,  $R_{NAin}$  ( $1.47 \pm 0.41$  kPa/(L/s)) was significantly lower than  $R_{NAout}$  ( $1.64 \pm 0.46$  kPa/(L/s)). Pairwise comparison of values for  $P_{NA}$  and  $R_{NA}$  for the 2 days revealed no significant difference. Repeatability of the method (estimated as within-day variation) for  $R_{NA}$  was  $\pm 0.19$  kPa/(L/s), whereas variation between the days was  $\pm 0.36$  kPa/(L/s) for  $R_{NAin}$  and  $\pm 0.44$  kPa/(L/s) for  $R_{NAout}$ . The 4 clinically normal Bulldogs had  $R_{NA}$  values ranging from 1.69 to 3.48 kPa/(L/s), whereas in the 4 Bulldogs with respiratory problems,  $R_{NA}$  ranged from 9.83 to 20.27 kPa/(L/s).

**Conclusions and Clinical Relevance**— $R_{NA}$  is inversely dependent on body size and nonlinearly associated with airflow. We propose that  $R_{NA}$  in dogs should be determined for airflows standardized on the basis of body size. The  $P_{NA}$  and  $R_{NA}$  in Beagles can be measured with sufficient repeatability for clinical use and nasal obstructions are detectable. (*Am J Vet Res* 2007;68:178–184)

The cause of brachycephalic syndrome in dogs is usually unknown. It is speculated that an increase in  $R_{NA}$  is the underlying cause,<sup>1,2</sup> although the final proof of this hypothesis has not been provided. It is assumed that increased  $R_{NA}$  causes various soft tissues to be drawn into the lumen by the air stream, which leads to airway obstruction. Typical clinical findings of dogs with brachycephalic syndrome are stenotic nostrils, an elongated soft palate, enlarged tonsils, everted lateral sacculles of the larynx, narrowed rima glottidis, and laryngeal collapse.<sup>3,4</sup> Each of these findings may be detected alone or in combination and, depending on the degree of severity, may be manifested as light snoring, inspiratory stridor, or even as fatal asphyxiation.

Received March 14, 2006.

Accepted September 8, 2006.

From the Equine Hospital (Wiestner), Clinic for Small Animal Surgery (Koch, Nad), and Clinic for Small Animal Reproduction (Balli, Michel, Arnold), Vetsuisse Faculty, University of Zurich, Zurich CH-8057, Switzerland; the Institute of Social and Preventive Medicine, Faculty of Medicine, University of Zurich, Zurich CH-8001, Switzerland (Roos); and F Hoffmann La Roche Ltd, Grenzacherstrasse 124, Basel, Switzerland (Weilenmann). Dr. Koch's present address is Koch & Bass Small Animal Referral Clinic, Basadingerstrasse 26, 8253 Diessenhofen, Switzerland.

Supported in part by the Swiss Federal Veterinary Office, Bern, Switzerland.

The authors thank Adrian Fairburn and Dr. Pete Ossent for technical assistance.

Address correspondence to Dr. Koch.

## ABBREVIATIONS

$P_{NA}$	Transnasal pressure difference
$R_{NA}$	Nasal resistance
$Q_v$	Airflow of ventilation
BW	Body weight
$P_{NAin}$	$P_{NA}$ during inspiration
$P_{NAout}$	$P_{NA}$ during expiration
$R_{NAin}$	$R_{NA}$ during inspiration
$R_{NAout}$	$R_{NA}$ during expiration
$SD_{day}$	Partial SD value for repeated measurements obtained on 2 days
$SD_{error}$	Partial SD value for repeated measurements obtained for repeated measurements on the same day
$SD_w$	SD for within-day measurements
$SD_b$	SD for between-day measurements
RC	Repeatability coefficient
$RC_w$	RC for within-day measurements
$RC_b$	RC for between-day measurements
CV	Coefficient of variation

Brachycephalic syndrome is nearly exclusively limited to brachycephalic dogs. However, the development of clinical signs varies considerably among breeds and among dogs of the same breed. There are also reports<sup>5–8</sup> of brachycephalic syndrome in nonbrachycephalic breeds.

Rhinomanometry is the method commonly used to determine  $R_{NA}$ , calculated from simultaneous measurement of  $Q_v$  and  $P_{NA}$ . The pressure immediately in front of the nostrils and the pressure in the nasopharynx are

measured to determine  $P_{NA}$ . Airflow is measured by use of a flow meter attached to a breathing mask that has been placed tightly over the nose. Two methods can be used (posterior and anterior rhinomanometry). When  $Q_v$  is generated by the respiratory cycle, the method is referred to as active rhinomanometry, whereas when  $Q_v$  is driven by an extrinsic source, the method is referred to as passive rhinomanometry.

For posterior rhinomanometry, nasopharyngeal pressure is measured by a pressure-sensing tube placed into the nasopharynx (transorally or through one of the nasal airways). Alternatively, in experimental settings, the tube may be placed directly into the nasopharynx by use of a piercing canula. With posterior rhinomanometry, both airways are investigated simultaneously and combined  $R_{NA}$  assessed directly.<sup>9</sup> In dogs, the mouth may remain open, which allows transoral intubation and surveillance of the tip of the pressure sensor to ensure it does not come in contact with the soft tissues of the nasopharynx.

In anterior rhinomanometry, the nasal passages are investigated unilaterally. Air is fed into 1 nostril (ie, the airway being investigated) while a pressure probe placed in the contralateral nostril tightly closes that nasal passage. In this manner, pressure measured at the seal of the closed passage equals the pressure at the unification of the 2 nasal passages in the nasopharynx. Thus, the pressure difference measured between the entrance of the active passage and the closed nostril is the decisive pressure difference of the passage being investigated. Both nasal passages are measured successively, and combined  $R_{NA}$  is calculated by use of a standard equation for parallel resistors.<sup>9,10</sup> Determination of nasal resistance by use of anterior rhinomanometry results in a value for total resistance, which does not include resistance of the nasopharynx.<sup>11</sup>

Active anterior rhinomanometry is widely used in humans and relies on cooperation of the patient.<sup>9,10,12</sup> The primary uses are to objectively evaluate impairment of the airflow attributable to pathologic changes in the nasal ducts, monitor the success of surgical or conservative treatments,<sup>13,14</sup> quantify allergic reactions,<sup>15</sup> document reactive mucosal swelling during challenge-exposure tests,<sup>16</sup> or assess apnea during sleep.<sup>17</sup>

Nasal resistance is the sum of at least 3 components (ie, nostril orifice, nasal passages, and nasopharynx).<sup>11</sup> Short-headed dogs of the brachycephalic type often have extremely narrow nostrils that dominantly contribute to total resistance. A method to quantify total  $R_{NA}$  should measure these 3 components as undistortedly as possible. Inserting a pressure probe into the passive nostril for active anterior rhinomanometry in dogs is not possible without distorting the geometry of the closely adjacent nostril. Another study<sup>18</sup> in which investigators used passive anterior rhinomanometry to evaluate allergic rhinitis in dogs by the use of nasal catheters inserted bilaterally into both nostrils ignored this important influence of the nasal entrance.

For all the aforementioned reasons, passive posterior rhinomanometry performed in anesthetized animals appears to be the best method for nasal investigations, even for dogs with brachycephalic syndrome. We assume that this investigation technique can be applied to dogs because this species has often been used in the de-

velopment<sup>19,20</sup> and research for possible applications in humans.<sup>12,13,16</sup> Repeatability of this method in humans has been proven.<sup>21</sup>

The objective of the study reported here was to examine the short- and long-term repeatability of posterior rhinomanometry in dogs. Examinations were performed in Beagles, a breed in which brachycephalic syndrome has not been observed and that belongs to the group of mesaticephalic dogs.<sup>22</sup> To determine the level at which pathologic changes are detected, a small group of brachycephalic dogs (ie, Bulldogs), with and without evidence of brachycephalic syndrome, were also examined.

## Materials and Methods

**Animals**—Fifteen Beagles (7 spayed females and 8 castrated males) were used in the repeatability study. Body weight of dogs ranged from 8.2 to 16.5 kg (mean, 11.4 kg), and dogs were 0.8 to 10.2 years old (mean, 6.0 years). Dogs had been used in kinetic studies at a pharmaceutical company.

Three weeks before the study, the dogs were transported to kennels with outside runs. Dogs were fed dry food, and water was available at all times. Dogs were considered healthy on the basis of results of a clinical examination, hematologic evaluation, and blood biochemical analysis.

Eight Bulldogs, which are classified as brachycephalic dogs,<sup>22,23</sup> were also examined. The dogs were owned by 1 breeder, who explicitly agreed to the use of the dogs in the study. Four dogs had no clinical signs of brachycephalic syndrome, whereas the other 4 dogs snored during inspiration and had exercise intolerance at temperatures > 25°C. Body weight of the Bulldogs ranged from 22 to 30 kg, and dogs ranged from 1 to 9 years of age.

**Procedures**—The study was conducted in accordance with Swiss laws for animal welfare. Rhinomanometric examinations were performed twice (day 1 and day 2) on all Beagles. There was a 7-day interval between day 1 and day 2. Rhinomanometric examinations of the 8 Bulldogs were conducted once; all examinations were performed on the same day.

The spirometer<sup>a</sup> was calibrated once on the morning of the rhinomanometric examinations. Twenty cycles were manually performed by use of a calibration pump.<sup>b</sup> Flow values were recorded, and the spirometer was adjusted accordingly.

**Rhinomanometry**—Dogs were sedated by IM administration of a combination of buprenorphine<sup>c</sup> (0.007 mg/kg) and acepromazine maleate<sup>d</sup> (0.03 mg/kg). Anesthesia was then induced by IV administration of propofol<sup>e</sup> (4 mg/kg). After endotracheal intubation, anesthesia was maintained by administration of a mixture of nitrous oxide:oxygen (3:2) and 1% to 2% halothane.<sup>f</sup>

Each dog was positioned in dorsal recumbency in a foam rubber support. The breathing mask was placed over the maxilla with the dorsal portion of the sealing ring positioned over the os nasale and the ventral portion positioned caudal to the upper canine teeth. The gap between the sealing ring of the mask and concave

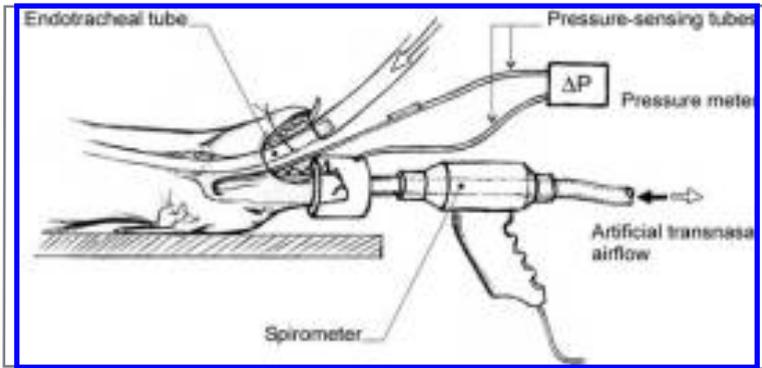


Figure 1—Illustration depicting the experimental configuration for posterior rhinomanometry in a dog. (Copyright by University of Zurich, Zurich, Switzerland, 2004. Reprinted with permission.)

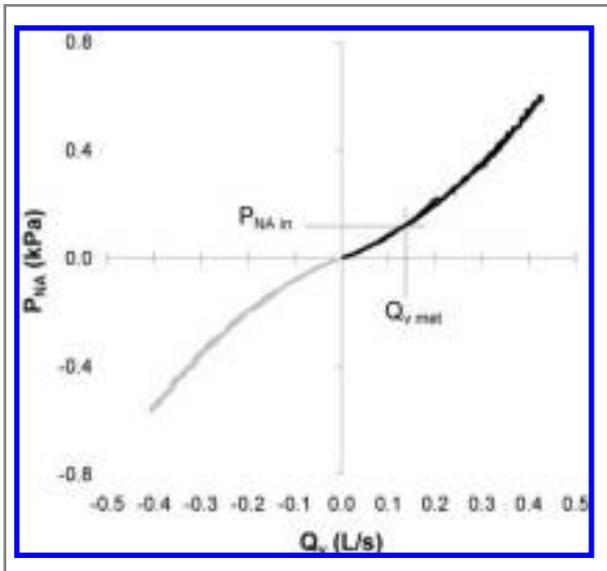


Figure 2—Relationship between pressure and airflow during inspiration (black lines) and expiration (gray lines) for a representative Beagle that weighed 14.5 kg and therefore had a metabolic  $Q_v$  of 0.134 L/s. The mathematic approximation was  $P_{NAin} = 1.61 \times Q_v^{1.25}$  kPa and  $P_{NAout} = 1.73 \times Q_v^{1.31}$  kPa.  $Q_{vmet} = Q_v$  on the basis of metabolic BW.

hard palate was sealed with a doughy mixture of flour and water. The spirometer was connected to the mask, and an artificially generated flow of filtered air was then directed into the mask (Figure 1). A metal spatula was used to pull the soft palate slightly rostrally so as not to impede escaping air. Airflow was slowly increased by use of a manually controlled valve. The airflow was passed through the nasal cavity at a rate of  $\leq 0.5$  L/s or a maximum pressure difference of 1.2 kPa, whichever condition was achieved first. Subsequently, the valve was slowly closed.

The  $P_{NA}$  that was generated by  $Q_v$  was recorded by use of a pressure meter<sup>g</sup> with a differential pressure sensor.<sup>h</sup> One pressure-sensing tube recorded the inner pressure of the mask, and the second pressure-sensing tube (which was affixed to the metal spatula) measured pressure within the nasopharynx. Measurements were then repeated with the  $Q_v$  reversed (ie, air was sucked out of the breathing mask and thus out of the nasal passages). Data for both directions

comprised 1 measurement cycle, with the first flow representing inhalation and the second flow representing exhalation. Before each measurement, output of the pressure sensor was assessed to ensure it was  $< 0.01$  kPa while the air intake of the breathing mask was closed.

A rhinomanometric examination consisted of 3 measurements for each dog and required approximately 15 minutes to complete. Between subsequent measurements on each dog, the mask was removed and then repositioned. Administration of the inhalation anesthetic was stopped after the third measurement was obtained. Dogs were extubated as soon as the gag reflex was evident.

**Calculation of standardized rhinomanometric variables**—Values for  $Q_v$  and  $P_{NA}$  were recorded at a sampling rate of 200 Hz and graphically depicted by use of a multipurpose recording unit.<sup>i</sup> For each measurement, the relationship between  $P_{NA}$  and  $Q_v$  was plotted (Figure 2). Data for inhalation and exhalation were then transformed into a mathematic description by means of a potential approximation by use of the following equation:

$$P_{NA} = r \times (Q_v)^n$$

where  $r$  was the resistance cofactor, and  $n$  was the power by which  $P_{NA}$  increased with  $Q_v$ . The value for  $n$  is 1 for laminar flow and approaches 2 for an increasingly turbulent flow. Numeric values of  $r$  and  $n$  were obtained from the approximation calculated on a spreadsheet program.<sup>j</sup>

To compare spirometric data for dogs of various body weights, first a maximum  $Q_v$  at rest was calculated for each dog, which is adapted to the metabolic BW ( $BW^{0.75}$ ) for that dog. Mean oxygen requirement of dogs is  $0.014 \times (BW^{0.75})$  L/min.<sup>24</sup> Assuming a mean difference of 4% in oxygen concentration between inspired and expired air, the oxygen requirement is  $0.35 \times BW^{0.75}$  L/min. Thus, for inhalation (50% of a breathing cycle) and assuming a sinusoidal breathing curve, the theoretic metabolic peak  $Q_v$  needed for a particular dog was calculated as follows:

$$\text{metabolic peak } Q_v = \pi \times 0.0058 \times BW^{0.75} = 0.018 \times BW^{0.75}$$

Next,  $P_{NA}$  associated with the metabolic peak  $Q_v$  was calculated from the measured  $P_{NA}$ -versus- $Q_v$  relationship by use of the following equation:

$$P_{NA} = r \times (\text{metabolic peak } Q_v)^n$$

which leads to a single, defined value on the  $P_{NA}$ -versus- $Q_v$  curve (Figure 2).

The corresponding  $R_{NA}$ , ejective while metabolic peak  $Q_v$  flows, was calculated as follows:

$$R_{NA} = P_{NA} / \text{metabolic peak } Q_v$$

In this manner, a single standardized value for  $P_{NA}$  and  $R_{NA}$ , respectively, was calculated for that particular dog, representing its nasal state at metabolic peak  $Q_v^f$ .

**Data analysis**—For the inspiratory and expiratory cycles, values of  $P_{NAin}$ ,  $P_{NAout}$ ,  $R_{NAin}$ , and  $R_{NAout}$  were calculated. To analyze possible differences among the Beagles as well as between the 2 measurement days (ie, days 1 and 2), the following hierarchic ANOVA model was used<sup>25</sup>:

$$y_{ijr} = \mu + \text{dog}_i + \text{day}_{ij} + e_{ijk}$$

where  $\mu$  denotes the grand mean value and  $e_{ijk}$  represents the residual error. For this model, the influencing random factors of dog ( $i = 1$  to 15) and day ( $j = 1$  and 2) were examined, and repeated measurements on the same day ( $k = 1$  to 3) were summarized in the residual error. Normality of data distribution was confirmed by use of residual analysis. Partial SD values ( $SD_{\text{day}}$  and  $SD_{\text{error}}$ ) were derived from the ANOVA model and used to describe variability of the method. The within-day (intraday) variability  $SD_w$  equals  $SD_{\text{error}}$ , whereas between-day (interday) variability  $SD_b$  was calculated as  $SD_b = (SD_{\text{day}}^2 + SD_{\text{error}}^2)^{0.5}$ .

Repeatability was quantified by the RC calculated as  $RC_w = 1.96 \times 2^{0.5} \times SD_{\text{error}}$  or  $RC_b = 1.96 \times 2^{0.5} \times (SD_{\text{day}}^2 + SD_{\text{error}}^2)^{0.5}$ , respectively. The RC values indicate the range within which (with a 95% probability) the differences between 2 arbitrary repeated measures for the same animal are located.<sup>26,27</sup>

To obtain a perspective of the rhinomanometric variables for the entire group of Beagles, the 3 repeated measures obtained from the same dog on each day were clustered to form a value representative of the respective variable for that day. On the other hand, clustered values for all dogs were averaged to determine a group mean  $\pm$  SD for the Beagles. Clustered data from inspiratory and expiratory measurements as well as data from days 1 and 2 were compared by use of paired  $t$  tests. The latter was conducted to reveal a possible deterministic structure for the influence of day. For all tests, significance was set at values of  $P \leq 0.05$ .

## Results

The ANOVA revealed differences in  $P_{NA}$  and  $R_{NA}$  among the Beagles. Values differed significantly for the inspiratory ( $P = 0.018$ ) and expiratory ( $P = 0.037$ ) portions of the measurement cycle. It was also found that

there was a significant ( $P < 0.001$ ) effect attributable to day of measurement.

Partial variability values were obtained for  $P_{NAin}$ ,  $P_{NAout}$ ,  $R_{NAin}$ , and  $R_{NAout}$  by use of the hierarchic ANOVA model (Table 1). There was approximately as much variability among the dogs as between the days on which rhinomanometry was performed, whereas the repeated measurements within a single day had considerably less variability.

Repeatability of the method can be estimated on the basis of these partial variability values. Analysis of within-day variability revealed that repeated measurements from a single dog on the same day were within  $\pm 0.02$  kPa for  $P_{NA}$  and within  $\pm 0.19$  kPa/(L/s) for  $R_{NA}$  for both inspiration and expiration of the measurement cycle (Table 1). The between-day variability for repeated measurements from a single dog was up to twice as high as the value for the within-day variability and was higher for expiration than for inspiration.

Mean data of all repeated measurements of the Beagles (days 1 and 2) as well as day-specific group means for  $P_{NA}$  and  $R_{NA}$  were summarized (Table 2). There were no significant differences detected between the clustered values of the 2 measurement days for  $P_{NA}$  or  $R_{NA}$ . For both measurement days,  $P_{NAout}$  and  $R_{NAout}$  were significantly ( $P = 0.01$ ) higher than values for  $P_{NAin}$  and  $R_{NAin}$ , respectively. Differences between  $P_{NAout} - P_{NAin}$  and  $R_{NAout} - R_{NAin}$  on day 2 were significantly higher (twice as high) than the corresponding differences for day 1.

Rhinomanometric data for the Bulldogs were reported as single values. Values for  $P_{NAin}$  and  $P_{NAout}$  and for  $R_{NAin}$  and  $R_{NAout}$  were used to calculate mean  $P_{NA}$  and  $R_{NA}$  values for the Bulldogs. The 4 Bulldogs with-

Table 1—Partial variability values and RCs obtained by use of a hierarchic ANOVA for  $P_{NAin}$ ,  $P_{NAout}$ ,  $R_{NAin}$ , and  $R_{NAout}$  for 15 Beagles.

ANOVA variable	$P_{NAin}$ (kPa)	$P_{NAout}$ (kPa)	$R_{NAin}$ (kPa/[L/s])	$R_{NAout}$ (kPa/[L/s])
$SD_{\text{dog}}$	0.035	0.042	0.338	0.365
$SD_{\text{day}}$	0.031	0.043	0.307	0.390
$SD_{\text{error}}$	0.020	0.021	0.192	0.191
Within day				
$SD_w$	0.020	0.021	0.192	0.191
$RC_w$	0.056	0.057	0.532	0.531
Between days				
$SD_b$	0.037	0.048	0.362	0.435
$RC_b$	0.103	0.136	1.008	1.242
SD <sub>dog</sub> = Partial SD value for 15 Beagles.				

Table 2—Group mean  $\pm$  SD  $P_{NA}$  and  $R_{NA}$  measured on days 1 and 2 (interval of 7 days between days 1 and 2) for 15 Beagles by use of an extrinsically driven  $Q_v$  to simulate inspiration and expiration.

Variable	Day 1	Day 2	Days 1 and 2	Day 1 – day 2
Metabolic $Q_v$ (L/s)	0.11 $\pm$ 0.02	0.11 $\pm$ 0.02	0.11 $\pm$ 0.02	ND
$P_{NAin}$ (kPa)	0.167 $\pm$ 0.044	0.157 $\pm$ 0.053	0.162 $\pm$ 0.042	0.010 $\pm$ 0.047
$P_{NAout}$ (kPa)	0.179 $\pm$ 0.050	0.187 $\pm$ 0.072	0.183 $\pm$ 0.053	-0.007 $\pm$ 0.065
$R_{NAin}$ (kPa/[L/s])	1.522 $\pm$ 0.475	1.410 $\pm$ 0.466	1.466 $\pm$ 0.409	0.112 $\pm$ 0.464
$R_{NAout}$ (kPa/[L/s])	1.635 $\pm$ 0.539	1.650 $\pm$ 0.563	1.643 $\pm$ 0.464	-0.015 $\pm$ 0.594
$P_{NAout} - P_{NAin}$ (kPa)	0.012 $\pm$ 0.012*	0.029 $\pm$ 0.027*	0.021 $\pm$ 0.016*	ND
$R_{NAout} - R_{NAin}$ (kPa/[L/s])	0.113 $\pm$ 0.115*	0.241 $\pm$ 0.212*	0.177 $\pm$ 0.129*	ND
*Value represents a significant ( $P = 0.01$ ) difference between values for inspiration and expiration. Metabolic $Q_v$ = Value for $Q_v$ standardized on the basis of each dog's metabolic BW. ND = Not determined.				

out brachycephalic syndrome had  $P_{NA}$  values of 0.68, 0.49, 0.55, and 0.37 kPa, respectively, and  $R_{NA}$  values of 3.27, 3.48, 2.89, and 1.69 kPa/(L/s), respectively. The 4 Bulldogs with brachycephalic syndrome had  $P_{NA}$  values of 4.20, 3.24, 1.82, and 4.10 kPa, respectively, and  $R_{NA}$  values of 20.25, 20.27, 9.83, and 18.46 kPa/(L/s), respectively.

## Discussion

The choice of posterior rhinomanometry must be considered in view of its intended use in brachycephalic dogs. Regarding the postulated pathogenesis of the brachycephalic syndrome<sup>23-25</sup> and the success of surgically widening the nostrils,<sup>3</sup> it can be concluded that the entrance to the nasal cavity contributes dominantly to gradients in  $P_{NA}$  and  $R_{NA}$ . Additional support is provided from anatomic results in humans<sup>28</sup> as well as functional tests with nasal dilator strips in humans.<sup>14</sup> It was not considered appropriate to use anterior rhinomanometry in our study because placing a probe into the contralateral passive nostril would probably have altered the geometry and physical condition of the nostril being investigated. In addition, anterior rhinomanometry implies that the mouth is closed and that small nasal masks are used, which additionally would deform the nasal entrances. Anterior and posterior rhinomanometry were compared in humans,<sup>29,30</sup> and it was revealed that posterior rhinomanometry had values up to 20% higher. It was concluded that this difference was attributable to the nasopharyngeal area, which is not measured during anterior rhinomanometry. However, it could also be partially attributed to the nasal entrance, which is deformed by the pressure-sensing tube in the adjacent nostril.

One purpose of the method developed here was to compare nasal variables among dogs and to assess whether the dogs had respiratory problems because of their nasal geometry. The method had to be adjusted for the large range of body sizes among dogs and the large range for nose geometry. We proposed to standardize rhinomanometric measurements by determining  $P_{NA}$  and  $R_{NA}$  by use of airflows adjusted on the basis of body size. We termed this the metabolic  $Q_v$ , which was calculated from the oxygen requirement of each dog at rest on the basis of its own metabolic BW. It was not convenient to measure  $P_{NA}$  solely at this metabolic  $Q_v$  because it was difficult to adjust the desired air stream and maintain a constant flow for the entire recording period. Instead, we recorded 2 entire curves for  $Q_v$  versus  $P_{NA}$  for inspiration and expiration airflows, respectively, for each dog, and then obtained a mathematic description for both curves. Values for  $P_{NA}$  and  $R_{NA}$  could then easily be calculated at any desired airflow, especially at metabolic  $Q_v$ .

Determining  $R_{NA}$  at metabolic  $Q_v$  only describes the lower end of the relationship between workload and  $Q_v$ . However, with regard to brachycephalic dogs, and especially for dogs with brachycephalic syndrome, it appears adequate to compare the  $R_{NA}$  values for that point. Most dogs with a severe form of brachycephalic syndrome have little or no activity because they are fully occupied just with breathing. Standardization of metabolic  $Q_v$  meant that the rhinomanometric data for

dogs of various sizes could be compared. To compare rhinomanometric data for higher workloads (eg, during performance tests), the  $R_{NA}$  values at 5 times the metabolic  $Q_v$  can be used. However, it would be most difficult to generate a curve of  $Q_v$  versus  $P_{NA}$  at such high airflows because the high amount of pressure would lift the face mask off the nose. Therefore, performance tests should be conducted as pure respiration measurements on animals on a treadmill, without determining  $R_{NA}$ .

In the study reported here, measurements were obtained during inhalation anesthesia and by use of artificial airflow conditions. Blowing and aspirating the air through the breathing mask was only a simulation of inspiration and expiration. The pressure conditions were reversed, compared with those for spontaneous respiration. As reported in another study<sup>31</sup> in dogs, this reversal did not cause a change in airflow. The values we recorded for  $P_{NA}$  of 0.16 to 0.19 kPa were similar to results for 2 comparable studies<sup>19,32</sup> in dogs in which the airflow and pressure conditions corresponded to the physiologic respiratory cycle. However, the application of a slowly increasing or decreasing airflow may not reflect the real airflow velocity in exercising dogs. Therefore, dynamic stenosis was not fully measured. Dynamic alterations are only possible at the nostrils and alar fold, which are not supported by bone, whereas in the nasal cavity, the mucosa is intimately attached to the conchae and not moveable.<sup>23</sup> The soft palate and mucosa of the nasopharynx were not included in our measurements.

Environmental and pharmacologic factors may influence mucosal vascular conditions and may also change  $R_{NA}$ .<sup>9,33,34</sup> The anesthetic protocol described here is commonly used in our clinic, and to our knowledge, it should not have had an effect on the nasal airways.

The temperature and humidity of the inhaled air were not monitored. Water vapor saturation does not appear to influence nasal patency.<sup>35</sup>

The repeatability of the method was estimated by use of a hierarchic ANOVA model (Table 1). The  $SD_w$ , which represents the pure measurement SD for the method, revealed that repeated measurements from a single dog on the same day will scatter within  $\pm 0.020$  kPa for  $P_{NA}$  and within  $\pm 0.191$  kPa/(L/s) for  $R_{NA}$ . These method variations were equal for the inspiration and expiration cycles. The method CV for the group mean values of the Beagles was approximately  $\pm 12\%$  for  $P_{NA}$  and for  $R_{NA}$ . Two repeated measurements on the same day and the same dog differed maximally for  $RC_w$ , which was  $\pm 0.057$  kPa for  $P_{NA}$  and  $\pm 0.532$  kPa/(L/s) for  $R_{NA}$ .

The Beagles were reexamined 7 days later. The  $SD_b$  for repeated measures from a single dog between the 2 days yielded  $\pm 0.037$  kPa for  $P_{NA}$  and  $\pm 0.362$  kPa/(L/s) for  $R_{NA}$ . Furthermore,  $SD_b$  was more pronounced for the expiration cycle, and  $SD_b$  was up to 2 times as much as the respective  $SD_w$  (Table 1). Thus, the ANOVA revealed that the day of measurement had a significant ( $P < 0.001$ ) influence for all investigated variables. The  $RC_b$  indicating the maximum difference between 2 arbitrary measurements on different days from the same dog was  $\pm 0.103$  kPa for  $P_{NA}$  and  $\pm 1.008$  kPa/(L/s) for  $R_{NA}$ .

The  $P_{NA}$  and  $R_{NA}$  values differed significantly ( $P < 0.037$ ) among the various Beagles. Even dogs with ex-

tremely similar nasal shape had differing results, which was also an observation reported<sup>36</sup> for the total airway resistance from the trachea to the nostrils in 10 Collies. Hence, it can be suspected that the values for various breeds will vary considerably, which may necessitate breed-specific reference values or limiting an investigation to a treatment-versus-reference comparison in the same animal.

The 3 repeated measurements on the same day were used to determine cluster means for the respective dogs, which then were used to calculate a group mean for all 15 Beagles. Group mean  $\pm$  SD for all measurements (days 1 and 2) of  $P_{NA}$  was  $0.162 \pm 0.042$  kPa for  $P_{NAin}$ , which was significantly ( $P = 0.01$ ) less than the value for  $P_{NAout}$  ( $0.183 \pm 0.053$  kPa). This pattern was similar for the respective mean values for  $R_{NAin}$  ( $1.47 \pm 0.41$  kPa/[L/s]) and  $R_{NAout}$  ( $1.64 \pm 0.46$  kPa/[L/s]) and for the separate group mean values for each day. This result was surprising because the nose with its bony base and almost immobile mucosa would seem to be a rigid, hollow organ. It could therefore be assumed that the flow direction would be unimportant with regard to  $P_{NA}$  and  $R_{NA}$ . However, there is no conclusive evidence that can explain this observed difference in higher  $P_{NA}$  and  $R_{NA}$  values during expiration.

The CV value of 28% for Beagles determined in the study reported here is smaller than CV values reported in other studies.<sup>14,18,36</sup> In 1 study,<sup>18</sup> investigators determined a CV of  $> 80\%$  for  $R_{NA}$  in 5 Beagles, whereas in another study,<sup>36</sup> investigators determined a CV of 38% for airway resistance of 10 Collies. In a study<sup>14</sup> in 15 humans, a CV  $> 90\%$  was determined for  $R_{NA}$ . We attributed the smaller CV value in our study to the standardization procedure that used metabolic  $Q_v$  to determine  $R_{NA}$ .

Results of the ANOVA revealed that there was a significantly greater dispersion between the measurements obtained on different days than between those obtained on the same day. The origin of this influence is unknown, and we are not aware of a way to identify it. It could be speculated that temperature, environmental air pressure, humidity, or a combination of these factors influenced  $Q_v$  values; however, the flow meter was calibrated each day and should have excluded such factors. There was no plausible additional reason for the increase in variability because methods and investigators were the same on both days.

It is possible that biological factors could explain discrepancies in the rhinomanometric measurements. The applied technique measured the bilateral airflow through both of the nostrils. Therefore,  $P_{NA}$  and  $R_{NA}$  were the combined values of the 2 nasal airways in parallel. It is known that both airways are not always equal with regard to airflow because periodic reciprocal swelling of the mucosa results in temporary changes in unilateral  $R_{NA}$ . The origin of this phenomenon, termed the nasal cycle, is not yet fully understood, but it has been observed in humans and other animals.<sup>37</sup> If changes in unilateral resistance were attributable to the nasal cycle, the combined  $R_{NA}$  would also change, even if changes in unilateral resistance are reciprocal. This could be an influential part of variability among dogs of the same breed (ie, same nasal configuration) and may

also explain the increase in variability between repeated measurements obtained from the same dog when there is a long interval between those measurements.

Pairwise comparison of the pooled values for  $P_{NA}$  and  $R_{NA}$  revealed there was no significant difference between the 2 measurement days. This finding seems to contradict the significant influence of day in the ANOVA results. However, it merely confirms that there was no measurement bias between the days. This again supports the conclusion that there was no method error in our investigative procedures. Nevertheless, there was a day-specific influence in the dispersion, which we assigned to the fluctuating nasal changes explained previously.

Our mean results for  $P_{NA}$  (0.17 kPa) and  $R_{NA}$  (1.5 kPa/[L/s]) were within a range comparable to that reported for other studies<sup>18,20,33,36</sup> in dogs. In one of the first studies that measured airway  $R_{NA}$ ,<sup>20</sup> investigators determined in dogs in a controlled setting that nasal pressure was approximately 0.164 kPa and  $R_{NA}$  was between 2.0 and 8.3 kPa/[L/s]. Total upper airway resistance (including the larynx) measured in another study<sup>36</sup> was between 0.4 and 1.2 kPa/[L/s] in mesocephalic and dolichocephalic dogs. The  $R_{NA}$  was between 1.86 and 2.34 kPa/[L/s] by use of posterior rhinomanometry,<sup>33</sup> and resistance was approximately 0.78 kPa/[L/s] for a group of Beagles in another study<sup>18</sup> in which investigators used passive anterior rhinomanometry and delivered the air stream via nasal catheters. Results of the study reported here compare favorably considering that the drag resistance of the nostril was omitted for their method and that anterior rhinomanometry always yields lower values than posterior rhinomanometry.<sup>11,29,30</sup> It is interesting that  $R_{NA}$  in dogs is 2 to 6 times as high as it is in humans.<sup>38</sup>

Regarding the designated clinical use of the proposed method, it is of primary interest to determine whether rhinomanometric data can be used to identify dogs with brachycephalic syndrome and to quantify the degree of severity. An experiment that involved nasal obstruction mimicking the brachycephalic syndrome was conducted.<sup>32</sup> Varying degrees of obstruction were achieved by scarifying the nasal mucosa and resecting parts of the nasal wall, which led to a 6- to 10-fold increase in  $R_{NA}$ . In the study reported here, in which we compared results for Beagles with results for a limited number of Bulldogs, we clearly determined that Bulldogs without brachycephalic syndrome had an  $R_{NA}$  that was approximately twice as high as the  $R_{NA}$  for the Beagles. However, for Bulldogs with brachycephalic syndrome,  $R_{NA}$  was at least 6 times as high as the mean values for the Beagles and  $> 5$  times as high as the value for the Bulldogs that did not have brachycephalic syndrome.

We conclude that our method has the potential to detect obstructions in the nasal cavity, such as in brachycephalic dogs with brachycephalic syndrome. The suspected relationship between rhinomanometric data and the severity of brachycephalic syndrome will need to be evaluated in additional studies.

The proposed rhinomanometric procedure we evaluated here can be rapidly and easily performed in dogs. Because of the dependence of  $R_{NA}$  on body size

and the nonlinear relationship between  $R_{NA}$  and airflow, we propose that determination of  $R_{NA}$  should be related to an airflow standardized on the basis of body size. The pure repeatability of the method for determining  $P_{NA}$  and  $R_{NA}$ , estimated by the within-day variation, was  $\pm 0.02$  kPa and  $\pm 0.19$  kPa/(L/s), respectively. This corresponded to a CV of  $\pm 12\%$  for the respective value in the Beagles. Variability was approximately twice as high between 2 measurements obtained 7 days apart. The reproducibility is sufficient to detect pathologic changes because nasal obstructions heavily increase  $R_{NA}$ . We observed differences in rhinomanometric variables among the Beagles, which imply that values may differ even more among breeds and there may be a need to establish breed-specific reference values.

- a. Spiroson, Eco Medics AG, Duernten, Switzerland.
- b. Model S-500, Hamilton Co, Reno, Nev.
- c. Temgesic, Essex Chemie AG, Luzern, Switzerland.
- d. Prequillan, FATRO S.p.A., Ozzano Emilia, Italy.
- e. Propofol-Lipuro 1%, Braun Medical AG, Emmenbruecke, Switzerland.
- f. Halotano, Rhodia Ltd, Avonmouth, Bristol, UK.
- g. DP-04, Equine Clinic, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland.
- h. Type 163PC01D36, FS, Honeywell, Morristown, NJ.
- i. Exhalizer-D with Spiroware software, Eco Medics AG, Duernten, Switzerland.
- j. Excel 2003, Microsoft Corp, Redmond, Wash.

## References

1. Orsher RJ. Brachycephalic airway disease. In: Bojrab J, ed. *Disease mechanisms in small animal surgery*. 2nd ed. Philadelphia: Lea & Febiger, 1993;369–370.
2. Wykes PM. Brachycephalic airway obstructive syndrome. *Probl Vet Med* 1991;3:188–197.
3. Harvey CE. Upper airway obstruction surgery I: stenotic nares surgery in brachycephalic dogs. *J Am Anim Hosp Assoc* 1982;18:535–537.
4. Leonard HC. Eversion of the lateral ventricles of the larynx in dogs—five cases. *J Am Vet Med Assoc* 1957;131:83–84.
5. Aron DN, Crowe DT. Upper airway obstruction. General principles and selected conditions in the dog and cat. *Vet Clin North Am Small Anim Pract* 1985;15:891–917.
6. Knecht CD. Upper airway obstruction in brachycephalic dogs. *Compend Contin Educ Pract Vet* 1979;1:25–31.
7. Wilson FD, Rajendran EI, David G. Staphylectomy in a dachshound. *Indian Vet J* 1960;37:639–642.
8. Koch DA, Arnold S, Hubler M, et al. Brachycephalic syndrome in dogs. *Compend Contin Educ Pract Vet* 2003;25:48–55.
9. Pallanch JF, McCaffrey TV, Kern EB. Evaluation of nasal breathing function. In: Cummings CW, ed. *Otolaryngology—head and neck surgery*. 2nd ed. St Louis: Mosby Year Book Inc, 1993;665–686.
10. Lund V. Allergic rhinitis—making the correct diagnosis. *Clin Exp Allergy* 1998;28(suppl 6):25–28.
11. Jones AS, Lancer JM, Stevens JC, et al. Rhinomanometry: do the anterior and posterior methods give equivalent results? *Clin Otolaryngol Allied Sci* 1987;12:109–114.
12. Hagemann H, Bauer PC, Costabel U. Comparability of various measurement methods in nasal provocation with allergens. *Pneumologie* 2002;56:363–368.
13. Cuddihy PJ, Eccles R. The use of nasal spirometry as an objective measure of nasal septal deviation and the effectiveness of septal surgery. *Clin Otolaryngol Allied Sci* 2003;28:325–330.
14. Gehring JM, Garlick SR, Wheatly JR, et al. Nasal resistance and flow resistive work of nasal breathing during exercise: effects of a nasal dilator strip. *J Appl Physiol* 2000;89:1114–1122.
15. Haavisto L, Sipila J, Suonpaa J. Nonspecific nasal mucosal reactivity, expressed as changes in nasal airway resistance after bilateral saline provocation. *Am J Rhinol* 1998;12:275–278.
16. Grutzenmacher S, Mlynski G, Mlynski B, et al. Objectivation of nasal swelling—a comparison of four methods. *Laryngorhinootologie* 2003;82:645–649.
17. Virkkula P, Maasilta P, Hytonen M, et al. Nasal obstruction and sleep-disordered breathing: the effect of supine body position on nasal measurements in snorers. *Acta Otolaryngol* 2003;123:648–654.
18. Tiniakov RL, Tiniakova OF, McLeod RL, et al. Canine model of nasal congestion and allergic rhinitis. *J Appl Physiol* 2003;94:1821–1828.
19. Amis TC, O'Neill N, Van der Touw T, et al. Supraglottic airway pressure-flow relationships during oronasal airflow partitioning in dogs. *J Appl Physiol* 1996;81:1958–1964.
20. Ohnishi T, Ogura JH. Partitioning of pulmonary resistance in the dog. *Laryngoscope* 1969;79:1847–1878.
21. Silkoff PE, Chakravorty S, Chapnik J, et al. Reproducibility of acoustic rhinometry and rhinomanometry in normal subjects. *Am J Rhinol* 1999;13:131–135.
22. Brehm H, Loeffler K, Komeyli H. Schädelformen beim Hund. *Zentralbl Veterinarmed [C]* 1985;14:324–331.
23. Evans HE. The skeleton. In: Evans HE, ed. *Millers' anatomy of the dog*. 3rd ed. Philadelphia: WB Saunders Co, 1993;122–218.
24. Gros G. Atmung. In: Engelhardt W, Breves G, eds. *Physiologie der Haustiere*. Stuttgart: Enke Verlag, 2000;217–253.
25. Neter J, Kutner M, Nachtsheim C, et al. Study designs: repeated measures. In: Neter J, Kutner M, Nachtsheim C, et al, eds. *Applied linear statistical models*. 4th ed. New York: McGraw-Hill Book Co, 1996;1164–1194.
26. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–310.
27. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res* 1999;8:135–160.
28. Bachmann W, Legler U. Studies on the structure and function of the anterior section of the nose by means of luminal impressions. *Acta Otolaryngol* 1972;73:433–442.
29. Cole P, Ayiomamitis A, Ohki M. Anterior and posterior rhinomanometry. *Rhinology* 1989;27:257–262.
30. Ghaem A, Martineaud JP. Determination of nasal resistance in healthy subjects using 2 techniques of rhinomanometry. *Bull Eur Physiopathol Respir* 1985;21:11–16.
31. Dawes JDR. The course of the nasal airstreams. *J Laryngol Otol* 1952;66:583–593.
32. Ohnishi T, Ogura JH, Nelson JR. Effects of nasal obstruction upon the mechanics of the lung in the dog. *Laryngoscope* 1972;82:712–736.
33. Lung MA, Phipps RJ, Wang JC, et al. Control of nasal vasculature and airflow resistance in the dog. *J Physiol* 1984;349:535–551.
34. McCaffrey TV, Kern EB. Response of nasal airway resistance to hypercapnia and hypoxia in the dog. *Acta Otolaryngol* 1979;87:545–553.
35. Lindemann J, Leiacker R, Rettinger G, et al. The relationship between water vapour saturation of inhaled air and nasal patency. *Eur Respir J* 2003;21:313–316.
36. Rozanski EA, Greenfield CL, Alsup JC, et al. Measurement of upper airway resistance in awake untrained dolichocephalic and mesocephalic dogs. *Am J Vet Res* 1994;55:1055–1059.
37. Flanagan P, Eccles R. Spontaneous changes of unilateral nasal airflow in man. A re-examination of the 'nasal cycle.' *Acta Otolaryngol* 1997;117:590–595.
38. Davies AM, Eccles R. Reciprocal changes in nasal resistance to airflow caused by pressure applied to the axilla. *Acta Otolaryngol* 1985;99:154–159.