Effects of oxygen insufflation rate, respiratory rate, and tidal volume on fraction of inspired oxygen in cadaveric canine heads attached to a lung model

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Objective—To assess the effects of oxygen insufflation rate, respiratory rate, and tidal volume on fraction of inspired oxygen (FIO_2) in cadaveric canine heads attached to a lung model.

Sample—16 heads of canine cadavers.

Procedures—Each cadaver head was instrumented with a nasal insufflation catheter through which oxygen was delivered. The trachea was attached to a sample collection port connected by means of corrugated tubing to a lung model. Eight treatment combinations that varied in respiratory rate (10 or 20 breaths/min), tidal volume (10 or 15 mL/kg), and oxygen insufflation rate (50 or 100 mL/kg/min) were applied to each head in a replicated Latin square design. Gas samples were manually collected, and inspired oxygen concentrations were analyzed. The FIO_2 and end-tidal CO_2 concentration were determined and compared among sample groups.

Results—Estimated least squares mean FIO_2 for various treatment combinations ranged from 32.2% to 60.6%. The FIO_2 was significantly increased at the higher insufflation rate (estimated marginal least squares mean, 48.7% vs 38.6% for 100 and 50 mL/kg/min, respectively), lower respiratory rate (48.9% vs 38.3% for 10 and 20 breaths/min, respectively), and smaller tidal volume (46.8% vs 40.0% for 10 and 15 mL/kg, respectively).

Conclusions and Clinical Relevance—FIO_2 in the model was affected by oxygen insufflation rate, respiratory rate, and tidal volume. This information may potentially help clinicians interpret results of blood gas analysis and manage canine patients receiving oxygen insufflation via a nasal catheter. (*Am J Vet Res* 2013;74:1247–1251)

Supplemental oxygen is commonly administered to patients to prevent or resolve hypoxemia in clinical veterinary practice. There are various methods to provide supplemental oxygen, including delivery via a nasal insufflation catheter, flow-by, face mask, use of an oxygen chamber, and transtracheal administration.[1–9]

Delivery of oxygen with flow-by and face mask techniques can be simple, but these are not always well tolerated and usually require technical support to hold the oxygen line or face mask close to the nose of the patient and create an increased oxygen concentration in that area.[5] Commercially available oxygen chambers are sealed compartments with mechanisms to provide oxygen supplementation, eliminate exhaled CO_2, and regulate humidity and ambient temperature.[8] These chambers are helpful for long-term oxygen supplementation but are not always available and can make patient evaluation more difficult, especially when continuous oxygen administration is required. Transtracheal or nasotracheal oxygen supplementation requires invasive measures under sedation or general anesthesia for catheter placement. However, supplemental oxygen administration via catheters extending to the mid trachea may be beneficial when considerable oropharyngeal swelling is present (eg, following surgical manipulation or trauma).[6]

Insufflation via nasal catheter is an effective, economical, and minimally invasive method of providing supplemental oxygen to dogs.[5] Nasal catheter placement is a simple procedure that can be easily implemented in most patients without sedation. The catheter, once secured in place, allows for easy transportation, examination, and treatment of dogs during supplemental oxygen delivery. These catheters are well tolerated at flow rates between 50 and 150 mL/kg/min in most patients.[1–4]

Abbreviations

$ETCO_2$	End-tidal carbon dioxide
FIO_2	Fraction of inspired oxygen
LSM	Least squares mean

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Monitoring of patients receiving supplemental oxygen includes the use of pulse oximetry and blood gas analysis. In particular, arterial blood gas analysis is sometimes necessary to accurately evaluate and monitor a patient's response to oxygen treatment.[5] Knowing the F_{IO_2} is necessary to critically evaluate arterial blood gas data, particularly when managing hypoxemic patients. The alveolar-to-arterial oxygen difference is commonly calculated to help evaluate gas exchange. This calculation also requires knowledge of the F_{IO_2}. During oxygen insufflation with a nasal catheter, accurate measurements of F_{IO_2} require gas collection from the mid trachea. The inspired oxygen concentration changes continuously during nasal oxygen delivery; therefore, gas samples must be taken throughout the entire inspiratory phase to accurately determine mean F_{IO_2}. This makes the measurement of the F_{IO_2} difficult in awake clinical patients receiving oxygen via this route.

Several factors may affect the F_{IO_2} during oxygen insufflation via a nasal catheter, including tidal volume, respiratory rate, and oxygen flow rate.[1–4] Increasing the flow rate during nasal oxygen delivery has been shown to increase the F_{IO_2} in various species, including dogs.[1–4,9] Because control of tidal volume and respiratory rate is not possible in awake clinical patients, previous studies have not determined how these factors may affect F_{IO_2}. Additionally, air-containing space in a dog's head may act as a reservoir for insufflated oxygen during the expiratory pause between breaths. These spaces include the nasal cavity, pharyngeal region, and oral cavity.

The objective of the study reported here was to measure the effects of tidal volume, respiratory rate, and oxygen insufflation rate on the F_{IO_2} in cadaveric canine heads attached to a lung model consisting of corrugated tubing, a sample port, and a variable-volume piston ventilator. We hypothesized that higher insufflation rates, lower respiratory rates, and smaller tidal volumes would result in increased F_{IO_2}, compared with values achieved with lower insufflation rates, higher respiratory rates, and larger tidal volumes. Because, to our knowledge, no techniques to measure the air-containing spaces in the heads of canine patients have been previously published, a secondary aim was to estimate the volume of air-containing spaces in canine cadaver heads by use of a water displacement method.

Materials and Methods

Sample—Heads were obtained from 16 cadaver dogs received from the Kansas State University Veterinary Health Center necropsy service and local animal shelters. Cadavers were weighed prior to severing the heads at the level of C4. Body weight ranged from 11.8 to 42.8 kg (mean weight, 24.9 kg).

Length of the trachea was measured from the carina to the point of transection. The diameter of the trachea at the transected end was determined with a digital micrometer.[a] A probe was placed in the portion of the trachea remaining with the cadaver until it rested on the carina. The probe was marked at the level of tracheal transection and removed, and the distance was measured with a metric tape measure. Volume of the distal portion of the trachea was calculated as follows:

$$V = \pi(d/2)^2 \times L$$

where V is the volume, d represents the measured diameter, and L represents the measured length.

Model—Each cadaver head was placed with the right side ventral and the severed tracheal stump was attached to a sample port connected to plastic corrugated tubing (**Figure 1**). The adaptor with a sample port and tubing was constructed to attain the same volume as the measured portion of the trachea that remained in each cadaver. The distal end of the corrugated tubing was attached to the lung model, with the adaptor placed between the severed tracheal end and the cor-

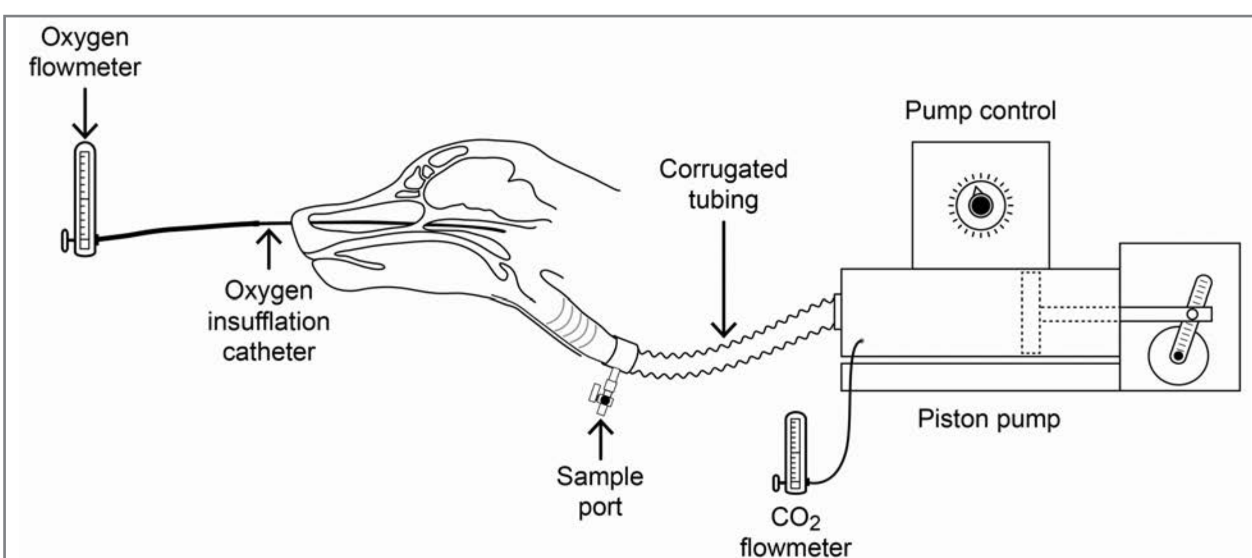

Figure 1—Diagram of an experimental model for evaluation of the effects of tidal volume, respiratory rate, and oxygen insufflation rate on F_{IO_2} in 16 heads of canine cadavers. Eight treatment combinations, including 2 respiratory rates (10 or 20 breaths/min), 2 tidal volumes (10 or 15 mL/kg), and 2 oxygen insufflation rates (50 or 100 mL/kg/min), were applied to each head, and inspired oxygen concentrations were measured. © Mal Hoover.

rugated tubing to allow for gas samples to be collected manually and to ensure a gas-tight seal. Connections were either 22-mm taper fit connections or chlorinated polyvinyl chloride fittings. Nylon cerclage material was used to secure a leakproof seal between tracheal tissue and chlorinated polyvinyl chloride fittings. The adaptor with the sample port was constructed of polycarbonate plastic with a luer sample port threaded into the side of the adaptor. The lung model was a modified variable volume piston ventilator controlled with a variable electric control pump.[b] Tidal breaths of 10 or 15 mL/kg were delivered in a to-and-fro manner through the cadaver head to simulate a normal breathing pattern.

The tip of an 8-F feeding tube catheter[c] was positioned at the nasal fold and extended to the lateral canthus of the ipsilateral eye. The catheter was marked at the level of the nasal fold, inserted into the ventral nasal meatus, and passed caudally until the mark on the catheter reached the nasal fold. The catheter was secured with 3-0 nylon suture at the nasal fold to prevent movement during experiments. The nasal insufflation catheter was then attached to a set of precision oxygen flowmeters,[d,e] which were adjusted to deliver 50 or 100 mL of oxygen/kg/min. Each dog's basal minute oxygen consumption was calculated according to the following equation[10]:

$$\text{Minute oxygen consumption} = \text{body weight (kg)}^{0.75} \times 10$$

This amount of oxygen was subtracted from the insufflated flow to account for expected oxygen consumption. Concurrently, CO_2 was flowed into the lung model with a precision CO_2 flowmeter[f] to account for CO_2 production. The amount of CO_2 delivered was calculated by multiplying the minute oxygen consumption by 0.8.[10] When the lung model was cycling, the inspired and expired air contained mixtures of insufflated oxygen, added CO_2, and room air in various proportions depending on the oxygen insufflation rate, tidal volume, and respiratory rate (ie, number of simulated breaths/min).

Gas sample collection and analysis—Aliquots of gas manually collected from the sample port during the entire inspiratory phase of ventilation were used to determine mean inspired oxygen concentrations. The ET_{CO_2} concentration was measured from gas samples obtained at the end of expiration with each treatment combination. Gas samples were collected in 5-mL aliquots into a 20-mL polypropylene syringe during 3 consecutive breaths for a total of 15 mL. These gas samples were analyzed by use of appropriately calibrated gas analyzers to determine the F_{IO_2} and ET_{CO_2} concentration.[g,h] Three samples were analyzed, and the mean of the 3 measurements was used for statistical comparisons. Prior to each set of experiments, the electrochemical oxygen analyzer was calibrated with room air and 100% oxygen as specified by the manufacturer. Before any experiment was performed, the linearity of the oxygen analyzer was tested against a calibrated gas monitor[i] over a full range of oxygen concentrations from 21% to 100%.[i] The oxygen analyzer was calibrated with manufacturer-supplied calibration gas. The infrared CO_2 analyzer was calibrated prior to the beginning of the experiments as recommended by the manufacturer with a manufacturer-supplied calibration gas mixture.

Experimental treatments—Eight treatment combinations that varied the respiratory rate (10 or 20 breaths/min), tidal volume (10 or 15 mL/kg), and oxygen insufflation rate (50 or 100 mL/kg/min) were applied to each cadaver head in a replicated Latin square design. All 3 variables were appropriately adjusted for each treatment. Tidal volume, oxygen insufflation flow, and CO_2 flow were adjusted to the body weight of each dog.

Before each set of experiments, the settings for the 2 treatment tidal volumes of 10 and 15 mL/kg were determined by connecting a ventilometer at the end of the corrugated tubing on the lung model and adjusting the piston pump stroke until the appropriate tidal volume was attained, after which the ventilometer was removed.[j] The ventilometer was serviced and calibrated ≤ 6 months prior to the start of the study at a manufacturer-approved repair station. Prior to the study, ventilometer accuracy was verified at 3 volumes delivered from a calibration syringe.[k] The tidal volumes were set and measured to be accurate within 5% of the set volume for 10 consecutive respiratory cycles.

After completing the treatment sequence for each cadaver head, the volume of the air-containing spaces of the head, including the nares, pharyngeal region, and oral cavity, was estimated with a water displacement method. The trachea was disconnected from the lung model, and a cuffed endotracheal tube was passed retrograde through the tracheal stump until the tip of the tube was at the laryngeal opening. The cuff was then inflated to create a watertight seal. This cuff inflation also created pressure on the esophagus and eliminated any observable leakage during water infusion. Petroleum jelly was applied around the commissure of the mouth to assure a seal against leaks, and the length of the muzzle, including the mouth, was wrapped with clear plastic wrap to the tip of the nose. The head was positioned with the nose up, and water was infused into the endotracheal tube with a 450-mL syringe until water was observed at the level of the external nares. The water was then drained from the cadaver head and measured in a graduated cylinder to estimate the volume of the air-containing spaces.

Statistical analysis—The experimental design consisted of a replicated Latin square with 8 treatment combinations and 8 periods for the 16 dogs. A general linear mixed model was fitted to each of the response variables F_{IO_2} and ET_{CO_2}, expressed in the natural log scale. In each case, the linear predictor of the statistical model included the fixed effect of treatment in factor level forms, consisting of the main effects of tidal volume (10 or 15 mL/kg), respiratory rate (10 or 20 breaths/min), and oxygen insufflation rate (50 or 100 mL/kg/min) as well as all 2- and 3-way interactions. Linear and quadratic effects of body weight, minute ventilation, and volume of air-containing spaces were evaluated as potential explanatory covariates in the model. For F_{IO_2}, volume of air-containing spaces showed the greatest improvement

Table 1—Estimated LSM and 95% confidence intervals of F_{IO_2} for various combinations of oxygen insufflation rate, respiratory rate, and tidal volume in 16 heads of canine cadavers attached to a lung model.

Treatment combination			
Oxygen insufflation rate	Respiratory rate (breaths/min)	Tidal volume (mL/kg/min)	F_{IO_2} (95 CI [%])
50	10	10	46.6 (43.5–49.9)
50	10	15	39.6 (37.0–42.4)
50	20	10	36.8 (34.4–39.4)
50	20	15	32.2 (30.1–34.5)
100	10	10	60.6 (56.6–64.9)
100	10	15	51.2 (47.9–54.8)
100	20	10	46.1 (43.1–49.4)
100	20	15	39.2 (36.7–42.0)

CI = Confidence interval.

Table 2—Estimated marginal LSM F_{IO_2} and ET_{CO_2} concentration with corresponding 95% confidence intervals for the main effects of respiratory variables evaluated in the same 16 experimental samples as in Table 1.

Variable	F_{IO_2} (95% CI [%])	ET_{CO_2} (95% CI [mm Hg])
Oxygen insufflation rate (mL/kg/min)		
50	38.6 (36.2–40.9)	50.3 (46.6–54.3)
100	48.7 (45.8–51.8)	46.2 (42.8–49.9)
Respiratory rate (breaths/min)		
10	48.9 (46.0–52.0)	62.4 (57.8–67.3)
20	38.3 (36.0–40.7)	37.2 (34.5–40.2)
Tidal volume (mL/kg)		
10	46.8 (44.0–49.8)	56.0 (51.9–60.5)
15	40.0 (37.6–42.6)	41.5 (38.4–44.8)

See Table 1 for key.

in model fit to the data and was incorporated into the final model. For ET_{CO_2}, none of the evaluated covariates improved model fit and none were retained.

Random effects for dog and period were also fitted. The random effect of treatment by period was evaluated but dropped from the model on the basis of a variance component that converged to zero. Variance components were estimated by use of the restricted maximum likelihood with removed boundary constraints. The Kenward-Roger method was used to estimate degrees of freedom and make corresponding adjustments in estimation of SEs. Model assumptions were evaluated with externally studentized residuals and were considered to be reasonably met. The model was fitted by use of commercially available statistical software[l] implemented via the Newton-Raphson method, with ridging as the optimization technique. Estimated LSMs and corresponding 95% confidence intervals for each treatment were reported in the original scale following backtransformation. Relevant pairwise comparisons were conducted with the Tukey-Kramer method to avoid inflation of the type 1 error rate due to multiple comparisons.

Results

Estimates of LSM F_{IO_2} were summarized for various combinations of insufflation rate, respiratory rate, and tidal volume in canine cadaver heads attached to a lung model (**Table 1**). Values for this variable ranged from 32.2% to 60.6% across all combinations of these factors.

There was no evidence for any 2- or 3-way interactions among insufflation rate, respiratory rate, and tidal volume effects on F_{IO_2}. However, main effects for each of these 3 treatment factors on F_{IO_2} were significant ($P < 0.001$ for each factor). The estimated marginal LSMs, corresponding to the main effects of each treatment factor on F_{IO_2} were summarized (**Table 2**). In particular, F_{IO_2} was increased by approximately 26% with an oxygen insufflation rate of 100 mL/kg/min, compared with a rate of 50 mL/kg/min (estimated marginal LSM F_{IO_2}, 48.7% and 38.6%, respectively). Further, a respiratory rate of 10 versus 20 breaths/min and tidal volume of 10 versus 15 mL/kg also increased F_{IO_2} by approximately 28% and 17%, respectively.

The volume of air-containing spaces was positively associated with F_{IO_2} ($P = 0.025$). After accounting for treatment factors, each 1 mL in volume of air-containing spaces was associated with an estimated multiplicative increase of approximately 0.15% in F_{IO_2}.

The main effects of oxygen insufflation rate, respiratory rate, and tidal volume on ET_{CO_2} concentration were also significant ($P < 0.001$ for each factor), with no evidence for interactions among these variables. Specifically, an insufflation rate of 50 versus 100 mL/kg/min, respiratory rate of 10 versus 20 breaths/min, and tidal volume of 10 versus 15 mL/kg were each independently associated ($P < 0.001$) with increased ET_{CO_2} concentration (Table 2).

Discussion

Administration of oxygen through a nasal catheter is an effective, economical, minimally invasive method of providing supplemental oxygen to clinical patients that often requires little or no sedation. This treatment is easy to implement and allows for uninterrupted supplemental oxygen delivery during routine care. The catheters are very well tolerated in most dogs.[1–4]

Arterial blood gas analysis is beneficial in monitoring a clinical patient's response to oxygen therapy. Fitzpatrick and Crowe[1] first reported the use of nasal insufflation catheters for delivery of oxygen to dogs in 1986. This group analyzed gas samples to determine F_{IO_2} in healthy awake dogs instrumented with nasal catheters and tracheal catheters for oxygen administration. By evaluation of arterial blood samples, they found that there was an increase in the Pa_{O_2} with increasing insufflation rates and that insufflation rates of 50 to 100 mL/kg/min were associated with an F_{IO_2} of 30% to 60%. Other studies[2–4] in live dogs found similar values for F_{IO_2} and found increases in oxygen insufflation rate to be correlated with increases in Pa_{O_2}. In the present study, we found that an oxygen insufflation rate of 100 mL/kg/min resulted in an increase of approximately 26% in F_{IO_2}, compared with a rate of 50 mL/kg/min (estimated marginal LSM F_{IO_2}, 48.7% and 38.6%, respectively).

The results of our study indicated that the F_{IO_2} during oxygen insufflation via a nasal catheter was influenced by not only insufflation rate but also tidal volume and respiratory rate and supported our hypothesis that higher insufflation rates, lower respiratory rates, and smaller tidal volumes would result in increased FIO_2, compared with the values obtained with lower insufflation rates, higher respiratory rates, and higher tidal volumes. Because respiratory rate and tidal volume cannot be controlled in awake patients, we used cadaver heads attached to a lung model to help elucidate these effects. At a lower respiratory rate (10 vs 20 breaths/min), FIO_2 of the model was significantly (P < 0.001) increased (estimated marginal LSM, 48.9% vs 38.3%). This may be explained by a longer expiratory pause that provides more time for insufflated oxygen to accumulate in air-containing spaces, displacing expired gases and increasing the oxygen concentration. A smaller tidal volume (10 vs 15 mL/kg) also resulted in a significantly increased FIO_2 (estimated marginal LSM, 46.8% vs 40.0%). Smaller tidal volume results in less room air being inspired, which makes the proportion of supplemental oxygen delivered greater relative to the volume of room air and increases the FIO_2.

The information obtained in the present study may be helpful during clinical evaluation of canine patients receiving supplemental oxygen via a nasal catheter. The results showed no evidence for interactions among the 3 treatment factors, so the main effects of insufflation rate, respiratory rate, and tidal volume on FIO_2 were interpreted as mutually independent and additive. Therefore, our results indicated that respiratory rate and tidal volume are independent of each other, and thus dogs taking rapid or deep breaths may require higher insufflation rates to achieve an FIO_2 sufficient to prevent or resolve hypoxemia. Together with arterial blood gas analysis, knowledge of the effects of respiratory rate and tidal volume may be used to more accurately adjust oxygen supplementation in canine patients.

Carbon dioxide was insufflated into the lung model, and resulting changes in the $ETCO_2$ concentration were used as an indication of changes in minute ventilation. In particular, we observed that a lower respiratory rate (10 vs 20 breaths/min) and smaller tidal volume (10 vs 15 mL/kg) each resulted in increased $ETCO_2$ concentrations (62.4 vs 37.2 mm Hg and 56.0 vs 41.5 mm Hg, respectively; P < 0.001 for both comparisons), as expected to occur because of decreased minute ventilation. Another factor affecting $ETCO_2$ concentration was the oxygen insufflation rate. With an increased insufflation rate, there is greater displacement and washout of CO_2 from the spaces containing expired gases, which causes a decrease in $ETCO_2$ concentration.

The present study included the use of a water displacement technique to estimate the volume of air-containing spaces in the cadaver heads, which to our knowledge has not been previously reported. Volume of the air-containing spaces had a significant (P = 0.025) positive association with FIO_2 and helped explain part of the variability in FIO_2 in the model. Because insufflation via a nasal catheter provides a continuous supply of oxygen during inspiration and expiration, it may be possible that a larger anatomic dead space allows for accumulation of more insufflated oxygen and results in a greater proportion of insufflated oxygen relative to room air, increasing the FIO_2.

Results of the present study may help clinicians more accurately estimate FIO_2 and interpret arterial blood gas measurements in clinical patients. This information may aid in management of canine patients receiving oxygen insufflation via nasal catheters.

a. Digital micrometer Absolute Digmatic, Mitutoyo Co, Kawasake, Kanagawa, Japan.
b. Modified air pump, Respiration pump model No. 607, Harvard Apparatus, Holliston, Mass.
c. Kendall feeding tube, Tyco Healthcare, Mansfield, Mass.
d. Oxygen flowmeter B250-2-B3123, Parker Hannifin Co, Hartfield, Penn.
e. Flowmeter F150-AHR-4/B125-40B1557, Parker Hannifin Co, Hartfield, Penn.
f. Carbon dioxide flowmeter F65-AHR-1/A 125-B3670, Parker Hannifin Co, Hartfield, Penn.
g. Teledyne AX 300 oxygen analyzer, Teledyne Technologies Inc, City of Industry, Calif.
h. Nelcor N-85 microstream capnograph, Tyco Healthcare, Pleasanton, Calif.
i. Datex Ohmeda Cardiocap/5 Anesthesia Monitor, Datex-Ohmeda Inc, Madison, Wis.
j. Ohmeda ventilometer, Datex-Ohmeda Inc, Madison, Wis.
k. Hans Rudolf calibration syringe Model 5530, Hans Rudolph Inc, Shawnee, Kan.
l. GLIMMIX, SAS, version 9.2, SAS Institute Inc, Cary, NC.

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10. Lowe HJ, Ernst EA. *The quantitative practice of anesthesia: use of closed circuit*. Baltimore: Williams & Wilkins, 1981;16–19.