Updates on Pulmonary Function Testing in Small Animals

Anusha Balakrishnan, BVSc[a], Lesley G. King, MVB[b],*

KEYWORDS

- Pulmonary function testing • Spirometry • Tidal breathing flow-volume loops
- Plethysmography • Arterial blood gas • Capnography • Pulse oximetry

KEY POINTS

- Lung function tests can be divided broadly into those that measure lung mechanics and those that measure gas exchange capabilities.
- Pulmonary function tests do not identify specific diagnoses but instead are used to quantify the severity of respiratory system dysfunction.
- In some cases, these tests are used to determine the anatomic location of disease in the respiratory tract; for example, upper versus lower airway disease.
- The most widely available tool for assessment of pulmonary function is pulse oximetry; however, it provides only a crude assessment of oxygenation.

PULMONARY FUNCTION TESTING

Tests of pulmonary function are widely used in humans in respiratory medicine, sports medicine, and in occupational health. In human and veterinary medicine, pulmonary function testing is used to evaluate patients with known or suspected respiratory disease and is an invaluable tool for assessing the efficacy of therapeutic interventions and determining prognosis. It is also helpful during preanesthetic evaluation of patients and can help identify patients at greater risk for complications.

It is important to remember that pulmonary function tests (PFTs) do not identify specific diagnoses. Instead they are used to quantify the severity of respiratory system dysfunction, and in some cases to determine the anatomic location of the disease in the respiratory tract (eg, upper vs lower airway disease). Widespread use of PFTs is limited by the need for some expertise and specialized equipment to accurately perform and interpret these tests. The application of some PFTs used in humans to veterinary medicine is further hampered because many of these tests require patient

[a] Emergency and Critical Care, Department of Clinical Studies-PHL, School of Veterinary Medicine, University of Pennsylvania, 3900 Delancey Street, Philadelphia, PA 19104, USA;
[b] Section of Critical Care, Department of Clinical Studies-PHL, School of Veterinary Medicine, University of Pennsylvania, 3900 Delancey Street, Philadelphia, PA 19104, USA
* Corresponding author.
E-mail address: kingl@vet.upenn.edu

cooperation and depend heavily on voluntary maneuvers. However, instruments such as blood gas analyzers and pulse oximeters are now readily available in most practices, and this type of PFT can easily be applied to small animal patients.

Tests of pulmonary function can be broadly divided into 2 major categories:

1. Tests of lung mechanics
2. Tests of pulmonary gas exchange

Tests of Lung Mechanics

Lung mechanics reflect the physical properties of the lung and evaluate the relationship between airway pressure, air flow, and lung volumes.

Spirometry

Spirometry is among the oldest and most well-known tests of pulmonary function. The spirometer measures the volume of air or rate of airflow in and out of the respiratory system (ie, volume is measured as a function of time). This method is the accepted standard for diagnosis of obstructive respiratory disease in human medicine,[1–3] and can be used to diagnose airway obstructions in veterinary patients with conditions such as laryngeal paralysis, tracheal collapse, or brachycephalic airway disease. Spirometry can also be used to evaluate ventilatory function in animals with neuromuscular disease, or after anesthesia. Table 1 lists normal values for dogs and cats.

Spirometry can be performed using a handheld spirometer or a pneumotachograph, which is connected to an endotracheal tube in an anesthetized patient, or attached to a tight face mask fitted over the snout of an awake patient. The pneumotachograph is used to measure flow rates and duration of the various segments of a given breath, including inspiratory time, expiratory time, tidal volume, and peak inspiratory flow (PIF) and peak expiratory flow (PEF) rates.[2] Human patients undergoing spirometry are instructed to take a full inspiration and then exhale forcefully for as long as possible, thereby measuring the forced vital capacity (FVC). Achieving this in veterinary patients is challenging. Therefore, use of spirometry in veterinary medicine is largely confined to tests of spontaneous tidal volumes in anesthetized patients as a measure of neuromuscular function and respiratory drive.

Table 1 Normal reported values for respiratory parameters in dogs and cats		
Parameter (Unit)	**Dog**	**Cat**
Tidal volume (mL/kg)	10–20	10–20
Minute ventilation (mL/min)	150–250	150–250
Respiratory rate (bpm)	32 ± 10	43 ± 7
Inspiratory time (ms)	920 ± 350	716.6 ± 139.5
Expiratory time (ms)	1170 ± 480	703.7 ± 133.0
Peak inspiratory flow (mL/s)	740 ± 240	110.0 ± 26.6
Peak expiratory flow (mL/s)	780 ± 230	113.7 ± 29.1
Dynamic compliance (mL/cm H_2O)	117 ± 46	19.8
Static compliance (mL/cm H_2O)	42.25 ± 32	NA
Lung resistance (cm H_2O/L/s)	0.8–4.2	28.9

Abbreviations: bpm, beats per minute; NA, not available.
Data from Rozanski EL, Hoffman AM. Pulmonary function testing in small animals. Clin Tech Small Anim Pract 1999;14(4):237–41.

Tidal breathing flow-volume loops

Flow-volume loops are graphical representations of the relationship between dynamic parameters of airflow and volume during various stages of inspiration and expiration. These loops have wide application and can identify airway obstruction. In humans, flow-volume loops are measured during forced inspiration and expiration. Forced respiratory maneuvers cannot be performed reliably in veterinary patients; therefore, tidal breathing flow-volume loops (as used in human pediatric or neonatal patients) are used instead.[4,5] Airway function in awake animals can be evaluated during tidal breathing by analyzing airflow patterns and waveforms using a face mask. This method is potentially more clinically useful than testing an intubated patient in which the upper airway is bypassed by the endotracheal tube. Causing temporary hyperventilation either by administration of a respiratory stimulant such as doxapram (2.2 mg/kg intravenously) or by temporarily exposing the patient to higher than normal inspired CO_2 levels can help amplify evidence of abnormalities by increasing the changes in air flow and airway resistance during tidal breathing.[6] Induced hyperpnea augments transmural pressure, and therefore exacerbates flow limitation, whether it is intrathoracic or extrathoracic.

To record these loops, patients are typically fitted with a face mask. A pneumotachograph, along with an X-Y recorder to plot a graph, is used to document the relationship between air flow, volume, and time. In awake patients, the inspiratory arm of the loop is negative and the expiratory arm is positive during spontaneous breathing. This pattern is reversed for loops measured during positive-pressure ventilation, when the inspiratory arm becomes positive. Loops are analyzed to evaluate qualitative and quantitative parameters (Fig. 1). Qualitative parameters include the overall shape of the loop. Quantitative parameters include:
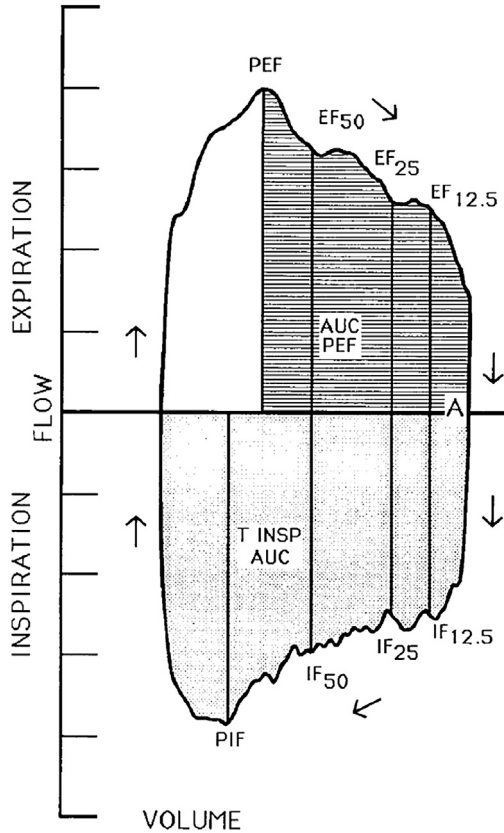
- Tidal volume (VT)
- Respiratory rate (RR)
- Peak inspiratory and expiratory flow rates (PIF and PEF)
- Midtidal inspiratory and expiratory flow rates (IF_{50}, EF_{50})
- Inspiratory and expiratory flow at end-expiratory volume plus 25% of VT
- Inspiratory and expiratory times

Tidal breathing flow volume loops are useful for detecting changes in airflow in animals with fixed and dynamic upper airway obstructions.[7,8] Fixed upper airway obstructions (extrathoracic and intrathoracic) such as masses cause limitations in airflow (flattening) in both the inspiratory and expiratory portions of the loops. Dynamic airflow obstructions cause more marked changes in one phase of the loop than the other, depending on the location of the obstruction. Dynamic upper airway obstruction such as laryngeal paralysis causes flattening of the inspiratory phase, whereas dynamic lower airway obstruction such as chronic bronchitis causes concavity or flattening of the late expiratory phase of the loop (Fig. 2).[7,8]

The usefulness of these loops has been evaluated in healthy cats as well as cats with chronic bronchial disease.[9] Cats with bronchial disease have an increased ratio of expiratory time to inspiratory time, lower expiratory flow rates, decreased area under total and PEF curves, and decreased tidal breathing expiratory volumes (Fig. 3).[9–11] This finding has also been shown experimentally in cats that are challenged with aerosolized methacholine, a nonselective muscarinic receptor agonist that causes marked bronchoconstriction.[12]

Lung compliance

Compliance is a measure of the distensibility of elastic lung tissue, and is described as the change in lung volume for a given change in airway pressure. It is typically

Fig. 1. Tidal breathing flow-volume loop from a healthy cat. Peak expiratory flow (PEF), peak inspiratory flow (PIF), and area under the curve (AUC) are shown. IF_{50}, inspiratory mid-tidal flow rate; EF_{50}, expiratory mid-tidal flow rate. (*From* McKiernan BC, Dye JA, Rozanski EL. Tidal breathing flow-volume loops in healthy and bronchitic cats. J Vet Intern Med 1993;7:390; with permission.)
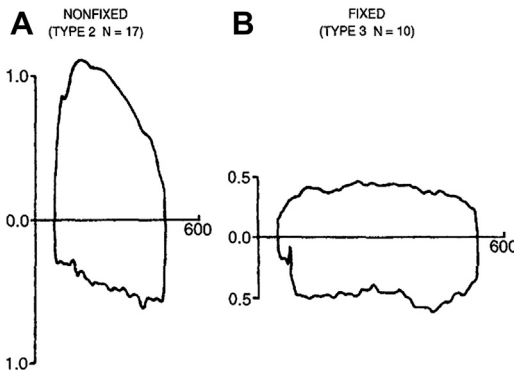
Fig. 2. Tidal breathing flow-volume loops from dogs with laryngeal obstruction. (*A*) A dog with a dynamic laryngeal obstruction. Note the early decrease in peak inspiratory flow. (*B*) A dog with a fixed laryngeal obstruction in which both the inspiratory and expiratory portions of the loops are blunted. (*Data from* Amis TC, Kupershoek C. Tidal breathing flow-volume loop analysis for clinical assessment of airway obstruction in dogs. Am J Vet Res 1986;47:1002–6.)
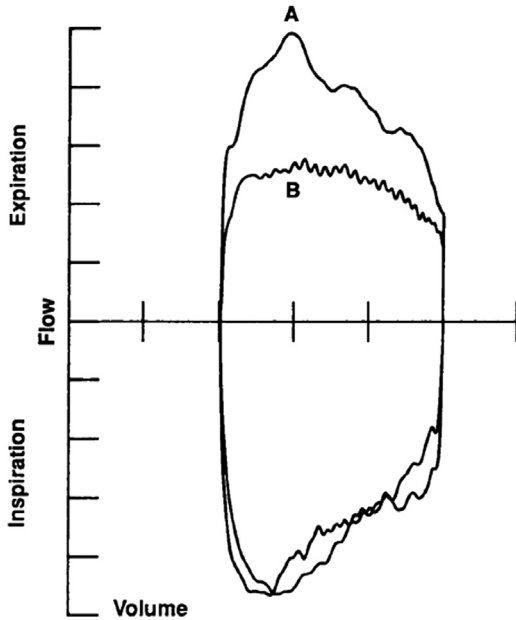
Fig. 3. Tidal breathing flow-volume loops of healthy and bronchitic cats. Note the similar inspiratory flow but marked difference in expiratory flow between normal (A) and bronchitic (B) cats. (*From* McKiernan BC, Dye JA, Rozanski EL. Tidal breathing flow-volume loops in healthy and bronchitic cats. J Vet Intern Med 1993;7:392; with permission.)

expressed as liters per centimeter of H_2O.[13,14] Compliance is routinely monitored during positive-pressure ventilation in veterinary patients. Reported values reflect compliance of both the lungs and the thoracic wall. In order to measure compliance of the lungs independent of the chest wall, esophageal pressure is used as an approximation of intrapleural pressure to calculate transpulmonary pressures. Thus, lung compliance is typically measured in intubated patients. Respiratory volumes are measured by a pneumotachometer that is attached to the endotracheal tube. At points of zero gas flow (ie, at the end of inspiration or exhalation during active breathing, or during a plateau pressure created by an inspiratory hold), pressures measured at the airway are equal to alveolar pressures. Compliance depends strongly on the size of the patient; the lung volume developed by a given airway pressure is much larger in the lungs of a Great Dane compared with a Chihuahua.

Compliance can be either static or dynamic. Static compliance is defined as the change in volume for a given change in transpulmonary pressure, measured when there is zero gas flow.[15] In order to calculate static compliance, airway pressures and volumes are measured during a brief inspiratory hold (plateau). The inspiratory plateau allows redistribution of air throughout small airways that have variable time constants and are slower to open at the end of inspiration.

Static compliance = ΔV/(plateau pressure − PEEP)

where ΔV is change in volume and PEEP is positive end-expiratory pressure.

Dynamic compliance is defined as the change in volume for a given change in transpulmonary pressure during active gas flow, such as during inspiration and expiration in animals on positive-pressure ventilation. Dynamic compliance is therefore the slope of
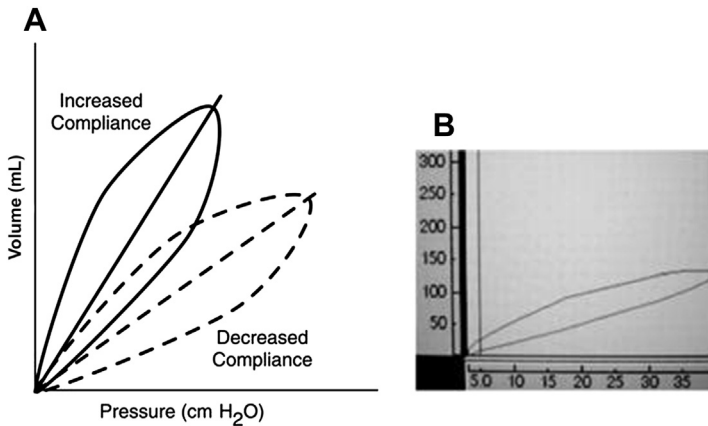
Fig. 4. (*A, B*) Pressure volume loops and dynamic compliance. Note the markedly decreased dynamic compliance (*B*) in a patient on a ventilator. (*From* Corona TM, Aumann M. Ventilator waveform interpretation in mechanically ventilated small animals. J Vet Emerg Crit Care 2011;21(5):508; with permission.)

the line between the two points of zero airflow at the end of exhalation and at the end of inspiration (Fig. 4).[15]

Dynamic compliance = $\Delta V / (PIP - PEEP)$

where PIP is peak inspiratory pressure.

In disease conditions in which lung compliance is reduced, higher airway pressures are required to deliver a normal tidal volume. Such diseases include[14]:

- Acute respiratory distress syndrome (ARDS)
- Pneumonia
- Pulmonary fibrosis
- Pulmonary edema (cardiogenic and noncardiogenic)

Lung resistance

Resistance is a measure of the amount of pressure required to deliver a given gas flow, and is expressed as centimeters of H_2O per liter per second.[13] Lung resistance is a function of the nondistensible components of the respiratory system (ie, the airways rather than the lung parenchyma). It is a test of the patency of small bronchi that are deep within the lung. Lung resistance is measured using the same equipment as compliance, namely a pneumotachometer and pressure transducer attached to the end of the endotracheal tube in an intubated patient.

In the normal lung, airway resistance is low, allowing easy flow of air during either spontaneous or positive-pressure breaths. Like compliance, resistance depends on body weight, with higher flow rates expected in bigger animals for a given change in airway pressure. Pathologic conditions that increase airway resistance include those that impede airflow in the small bronchi, such as canine chronic bronchitis and feline lower airway disease (bronchitis or feline asthma).

Whole-body plethysmography

Plethysmography measures total lung volume, functional residual capacity, and residual volume of the lung. In human medicine, it is largely accepted as the gold standard test for determining lung volumes, particularly in cases of airway obstruction.[16–18]

Plethysmography can occasionally overestimate lung volumes in patients that are panting or hyperventilating, with some human studies finding differences of as much as 1 L when lung volumes are measured via plethysmography compared with helium dilution techniques.

Traditional whole-body plethysmography in human medicine involves placing the patient inside a sealed chamber with a single mouthpiece. At the end of normal expiration, the mouthpiece is closed and the patient is then asked to make an inspiratory effort. As the patient inhales against the closed mouthpiece, the chest cavity and lungs expand, decreasing pressure within the lungs. The increase in thoracic volume increases pressure within the closed system of the box, and the volume of the box decreases to accommodate the new volume of the patient's body. The volume within the lungs is then calculated using Boyle's law, which is a useful way of evaluating a patient for objective evidence of lung disease. For example, a large residual volume/total lung capacity ratio with a large total lung capacity indicates hyperinflation, whereas a large ratio with a normal total lung capacity indicates air trapping.[18]

Plethysmography in small animals is challenging because the increase in resistance to flow imposed on the animal during inspiration is usually not tolerated well. Several modifications to this technique have been developed to facilitate its use in small animals.

Barometric whole-body plethysmography In this technique, signals are recorded as a net result of both thoracic and nasal airflow. Exhaled air, which is humidified and warmed, creates a larger pressure change than inspired air even though the flow rates are identical. A pneumotachograph of known resistance is mounted on the wall of the chamber in which the animal is placed, and a pressure transducer is connected to the recording device. The animal moves around the chamber freely and signals produced by inhaled and exhaled air are recorded. The relationship between effort and flow with respect to amplitude and timing can then be evaluated. This technique is useful for evaluating bronchoconstriction in laboratory animals and is well tolerated in small animals, even in cats with asthma that are in respiratory distress.[19–21]

Head-out whole-body plethysmography This modified technique was developed for use in dogs to overcome the tendency of canine patients to pant when in an enclosed box, thereby rendering plethysmographic measurements inaccurate. In this technique, dogs are placed in an airtight glass box that has a fixed volume, with their heads protruding out of the box. A pneumotachograph and face mask are then fitted over the nose and mouth and flow measurements are obtained.[22–24]

TESTS OF PULMONARY GAS EXCHANGE
Arterial Blood Gas Analysis

Arterial blood gas analysis is considered the gold standard test for evaluating oxygenation and ventilation.[25] Samples in small animal patients can be drawn from various locations including the dorsal metatarsal, coccygeal, sublingual, femoral, or aural arteries. In animals requiring repeated sampling, arterial catheters can be placed for easy access. Samples are ideally collected into preheparinized arterial blood gas syringes. All air bubbles should be removed to render the sample anaerobic, and the syringe is capped and processed immediately. Samples can also be collected in regular 1-mL to 2-mL syringes that have been preheparinized by drawing up heparin and then squirting it out immediately. Samples not run within 5 to 10 minutes should be capped to avoid gas diffusion and equilibration with atmospheric oxygen and carbon dioxide (CO_2), and are refrigerated or placed in ice water to prevent cell metabolism, which would distort the results.

A typical arterial blood gas analysis measures the following values (reference ranges for dogs and cats are listed in **Table 2**):

- Pa_{O_2}
- Pa_{CO_2}
- pH
- Other acid-base parameters are calculated rather than directly measured, including bicarbonate (HCO_3^-) and base excess (BE)

For proper interpretation of an arterial blood gas analysis, an understanding of the major physiologic causes of hypoxemia is necessary.

Decreased inspired oxygen

Decreased fraction of inspired oxygen (Fi_{O_2}) is usually not a clinically relevant cause of hypoxemia unless animals are under general anesthesia and the oxygen valve is accidentally turned off. Decreased barometric pressure at high altitudes leads to lower Pa_{O_2} values in animals with normal lungs because there is less oxygen in inspired air, even though the Fi_{O_2} is normal.

Ventilation-perfusion (VQ) mismatch

This is the most common cause of hypoxemia in animals with respiratory disease. For optimal oxygenation, ventilation and perfusion should be closely matched throughout the lungs. Perfusion of areas of the lung without ventilation, or vice versa, results in inefficient gas exchange, typically hypoxemia. Hypercarbia is less common as a result of VQ mismatch because CO_2 is more diffusible than oxygen. Pulmonary parenchymal disease such as pneumonia or ARDS results in VQ mismatch because alveolar flooding and collapse impair ventilation but perfusion is normal, resulting in decreased ventilation/perfusion ratio in the affected lung regions. In contrast, pulmonary thromboembolism impairs perfusion, whereas ventilation remains normal.

True right-to-left shunting

Anatomic shunts result in mixing of unoxygenated venous blood with oxygenated blood returning to the left side of the heart. Examples include animals with ventricular septal defects or a patent ductus arteriosus that have concurrent increase of pulmonary vascular pressure creating reverse shunting of blood. Intrapulmonary shunting can occur if pulmonary arterial blood is flowing to an area of lung tissue where oxygenation is impossible; for example, a lung mass.

Diffusion impairment

This is caused by abnormalities in the alveolar-capillary barrier resulting in impaired gas diffusion. Diffusion abnormalities are a less common cause of hypoxia, but can be seen in interstitial lung diseases such as pulmonary fibrosis that result in thickening of the alveolar-capillary barrier.

Table 2
Normal arterial blood gas values in dogs and cats

Value	Dog	Cat
pH	7.31–7.46	7.21–7.41
Pa_{O_2} (mm Hg)	92 (80–105)	105 (95–115)
Pa_{CO_2} (mm Hg)	37 (32–43)	31 (26–36)
Sa_{O_2} (%)	>95	>95

Abbreviation: Sa_{O_2}, hemoglobin oxygen saturation.

Hypoventilation

Reduced alveolar ventilation causes hypoxemia, and is seen clinically in animals with upper airway obstruction, respiratory center depression, neuromuscular disease, or severe chest wall or pleural space disease.

Ventilation is a function of the physical ability of the animal to move air into and out of the lungs. CO_2 that is produced in the tissues as a normal by-product of metabolism is eliminated through the airways. Elimination of CO_2 depends on minute ventilation, the volume of air moving through the airways in a given period of time, VT $\times$ RR, usually expressed as liters per minute. Because CO_2 is about 20 times more soluble than oxygen, there is a linear relationship between Pa_{CO_2} and minute ventilation. Disease processes that result in abnormal ventilation and can be detected by changes in the Pa_{CO_2} are listed in Table 3:

An arterial blood gas sample is the gold standard for assessing ventilation, however if arterial blood cannot be obtained, a venous blood gas can be used. Central venous samples obtained from a large central vein such as the jugular vein or vena cava, or mixed venous samples obtained from a pulmonary arterial catheter, provide the most accurate results. If these are not available, peripheral venous samples can be used to evaluate the pressure of venous CO_2 (Pv_{CO_2}). However, caution is advised in regard to interpretation of these results, because peripheral venous samples reflect CO_2 production in the extremity sampled, rather than the whole body.

Venous samples are not useful for evaluation of the ability of the lungs to oxygenate the blood. Instead, serial measurement of venous oxygen concentrations can be used to assess the ability of tissues to extract oxygen. Poor tissue perfusion can lead to high values for venous oxygen (because it is not being extracted), which then decrease as the tissues become better perfused with treatment. In normal animals, the venous partial pressure of CO_2 is usually about 5 mm Hg higher than the arterial partial pressure of CO_2. This normal arteriovenous gradient occurs because CO_2 is removed from tissues and transported in venous blood back to the lungs as dissolved CO_2 in plasma (about 10%), and buffered within red blood cells as bicarbonate (about 90%). An increased arterial–mixed venous P_{CO_2} gradient can occur in states of compromised perfusion or poor cardiac output.

The approach to assessment of an arterial blood gas sample is given in Table 4.

Oxygen Tension-based Indices

Alveolar to arterial oxygen gradient

Oxygenation of blood occurs following diffusion of air across the alveolar-capillary membrane. However, diffusion in normal animals does not occur to a perfect degree

Table 3 Ventilatory abnormalities	
Hypoventilation: A Decrease in VT or in RR can Lead to an Increase in Pa_{CO_2}	Hyperventilation: An Increase in VT or RR Leads to a Decrease in Pa_{CO_2}
Upper airway obstruction	Pain
Respiratory center depression by anesthetic agents, especially opioids	Anxiety
Respiratory center depression secondary to central nervous system disease	Severe hypoxia
Cervical myelopathy	
Diffuse neuromuscular disease	
Chest wall disease	

Table 4
Steps in the assessment of an arterial blood gas sample

(1) Evaluation of acid-base status

pH

Acidemic (pH<7.35)	Normal (pH 7.35–7.45)	Alkalemic (pH>7.45)
Metabolic acidosis?	No acid-base disorder?	Metabolic alkalosis?
Respiratory acidosis?	Mixed acid-base disorder?	Respiratory alkalosis?
Both?	—	Both?

(2) Examination of alveolar ventilation (Pa_{CO_2})

Increased Pa_{CO_2} (>45 mm Hg)	Decreased Pa_{CO_2} (<35 mm Hg)
Primary respiratory acidosis caused by hypoventilation	Primary respiratory alkalosis
Compensatory response to a metabolic alkalosis	Compensatory response to a metabolic acidosis

(3) Examination of HCO_3- and BE

HCO_3^- increased (>24 mmol/L) or BE positive	HCO_3^- decreased (<18 mmol/L) or BE less than -4
Primary metabolic alkalosis	Primary metabolic acidosis
Compensatory response to a chronic respiratory acidosis	—

Remember that the body never overcompensates. The primary process can usually be determined by evaluating the direction in which the pH is trending from 7.4. If the pH is less than 7.4, then the acidosis is the primary process. If the pH is greater than 7.4, then the alkalosis is the primary process

(4) Evaluation of oxygenation (Pa_{O_2})

In healthy animals, Pa_{O_2} should be about 4–5 times the Fi_{O_2}. When breathing room air (Fi_{O_2} = 0.21), Pa_{O_2} should be close to 100 mm Hg. In patients breathing 100% oxygen, Pa_{O_2} should be approximately 500 mm Hg

When Fi_{O_2} changes, equilibration to a new Fi_{O_2} occurs within minutes. Therefore, representative samples can be obtained approximately 5 or more minutes after changing to a new Fi_{O_2}

When breathing room air, a Pa_{O_2} of 75–90 mm Hg indicates mild hypoxemia, whereas a Pa_{O_2} less than 60 mm Hg indicates severe hypoxemia

because a small amount of blood is shunted to bronchial and pleural vessels, to the coronary venous circulation, and to some areas of dead space ventilation. This normal physiologic difference in the resulting partial pressure of oxygen in the alveoli (P_{AO_2}) and the arterial blood (Pa_{O_2}), namely the alveolar to arterial (A-a) gradient, is about 5 to 7 mm Hg in an animal breathing room air (reference range less than 15 mm Hg).

The P_{AO_2} can be derived from the alveolar gas equation:

$$P_{AO_2} = [(P_B - P_{H_2O})Fi_{O_2}] - [Pa_{CO_2}/RQ]$$

where P_B is barometric pressure (mm Hg), P_{H_2O} is water vapor pressure (mm Hg), and RQ is respiratory quotient (ratio of CO_2 production to O_2 consumption). Pa_{CO_2} is used as an approximation of alveolar CO_2.

Using an atmospheric pressure of 760 mm Hg, water vapor pressure at 37°C of 47 mm Hg, and a typical RQ for a dog eating normal dog food and breathing room air of 0.9, the equation can be simplified as:

$$P(A\text{-}a)O_2 = 150 - 1.1(Pa_{CO_2}) - Pa_{O_2}$$

The alveolar gas equation and A-a gradient provide a clinically useful method to evaluate the degree of pulmonary parenchymal disease, especially in situations in which the Pa_{CO_2} is abnormal or variable when serial blood gases are being compared. Because Pa_{CO_2} is taken into consideration in the equation, hypoventilation or hyperventilation is excluded as a potential cause of hypoxemia. However, VQ mismatch, shunting, and diffusion barriers all cause an increased A-a gradient.

Pa_{O_2}/Fi_{O_2}

The Pa_{O_2}/Fi_{O_2} ratio is another clinically useful indicator of oxygenation status. It is particularly helpful for comparison of Pa_{O_2} values between serial blood gases obtained when a patient is breathing varying concentrations of inspired oxygen. In a normal animal breathing room air with an Fi_{O_2} of 0.21, Pa_{O_2} is between 85 and 100 mm Hg, which results in a Pa_{O_2}/Fi_{O_2} ratio of 500.

Abnormalities in the Pa_{O_2}/Fi_{O_2} ratio can occur with any type of severe pulmonary dysfunction and are not diagnostic for a specific disease. However, this ratio has been used to characterize the severity of lung disease in animals with acute lung injury and ARDS. In the past, a Pa_{O_2}/Fi_{O_2} ratio less than 300 was considered consistent with acute lung injury, whereas a Pa_{O_2}/Fi_{O_2} ratio less than 200 indicated ARDS. More recently, the term acute lung injury is no longer recommended and varying degrees of ARDS have been proposed[26]:

- Mild ARDS: Pa_{O_2}/Fi_{O_2} ratio 200 to 300 with positive end-expiratory pressure greater than 5 cm H_2O
- Moderate ARDS: Pa_{O_2}/Fi_{O_2} ratio 100 to 200 with positive end-expiratory pressure greater than 5 cm H_2O
- Severe ARDS: Pa_{O_2}/Fi_{O_2} ratio less than 100 with positive end-expiratory pressure greater than 5 cm H_2O

Pulse Oximetry

Pulse oximetry is a widely available, noninvasive, indirect method for continuously evaluating oxygenation. Ease of use has ensured that this technique has been extensively used in veterinary medicine, particularly in the setting of intensive care units and during anesthesia. Pulse oximetry can be used for measurement of oxygenation at specified time points, as a continuous real-time monitor during stressful procedures,

or for immediate assessment of interventions such as oxygen supplementation. If arterial blood samples are not available for blood gas analysis, pulse oximetry can be combined with venous blood gas analysis to provide a reasonable estimate of lung gas exchange function for many animals.

The primary principle behind pulse oximetry is that the concentration of any given solute (hemoglobin, in this case) dissolved in any given solvent (plasma, in this case) is proportional to the amount of light it absorbs. A pulse oximeter probe consists of a light source and a sensor, which is placed over any body part of the correct thickness that has pulsatile arterial blood flow. Common probe placement sites in small animals include the tongue, lips, ear pinna, preputial or vulvar folds, or across digits. Two diodes within the light source emit light of 2 different wavelengths (red, $\sim$660 nm; and infrared, $\sim$940 nm) that are specific to preferential light absorption by oxyhemoglobin and reduced hemoglobin. The pulsatile nature of blood flow is detected by the sensor and fluctuations in light absorption cause a rhythmical variation that is then translated into a ratio of oxyhemoglobin to reduced hemoglobin. The hemoglobin saturation of oxygen is calculated from this ratio.[25,27]

A very small amount of oxygen is dissolved in plasma and, in accordance with the Henry law, the relationship is linear. The oxygen content of plasma depends on the Po_2 and the oxygen solubility coefficient (0.0029 mL O_2/dL plasma/mm Hg).[28]

In contrast with the small amount of oxygen dissolved in the plasma, hemoglobin carries most of the oxygen in the blood. The relationship between saturation of hemoglobin with oxygen and Pao_2 is not linear and is shown by the oxyhemoglobin dissociation curve (Fig. 5). Each hemoglobin molecule carries 4 oxygen molecules when fully saturated. Binding of the first oxygen molecule causes a change in conformation of the hemoglobin molecule that allows more rapid binding of the other 3 molecules, thereby contributing to the shape of the curve. This curve is shifted to the right or left by several factors such as temperature, pH, and Pco_2, thus altering the ease with which oxygen is loaded onto or unloaded from
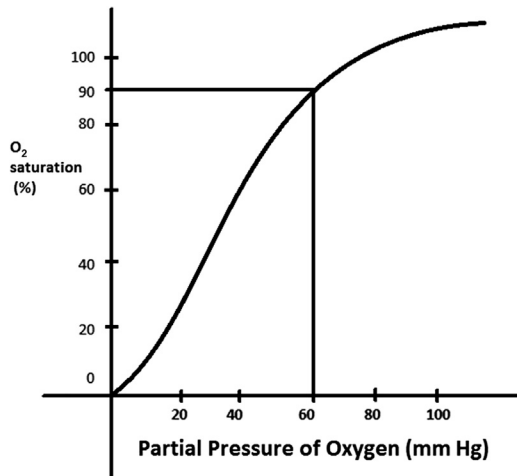
Fig. 5. Oxyhemoglobin dissociation curve. Note that hemoglobin is almost completely saturated with oxygen once the Po_2 is greater than about 70 mm Hg, which creates a safety margin for the patient as hypoxemia develops because of lung disease. However, once the Po_2 decreases to less than 60 mm Hg (which might occur as a result of high oxygen demands associated with stress of handling or transport), severe desaturation is likely.

hemoglobin. The pulse oximeter provides an indirect measure of the saturation of hemoglobin with oxygen.

Although standard pulse oximetry is inexpensive and easy to use and interpret, there are several inherent limitations to the use of this technique. Because only 2 wavelengths are emitted, the device is unable to detect the presence of pathologic variants of hemoglobin dissolved in blood. Any additional hemoglobin species, such as carboxyhemoglobin and methemoglobin, cannot be detected by standard pulse oximeters. This becomes important in the clinical setting in the case of dyshemoglobinemias caused by carbon monoxide toxicity as well as conditions that cause methemoglobinemia, such as acetaminophen toxicity. In recent years, newer pulse oximeters have been developed that emit 4 or more different wavelengths and thus are able to detect additional hemoglobin species that may be present in the blood. These devices are known as pulse CO-oximeters; they measure what is known as fractional saturation, which is oxyHb/(oxyHb + reduced Hb + carboxyHb + metHb), where oxyHb is oxyhemoglobin, Hb is hemoglobin, carboxyHb is carboxyhemoglobin, and metHb is methemogobin.[29] Other factors that decrease the usefulness of pulse oximetry include external motion or noise that causes excessive artifact and signal disruption. Excessive ambient light, especially certain fluorescent lights, can cause erroneous results. Severe anemia can cause erroneously low values, but mild to moderate anemia does not affect the results. Conditions causing decreased perfusion, such as shock or hypothermia, can result in inability to obtain a reading or erroneously low values. In critically ill patients that are anemic, decreased hemoglobin concentration results in markedly decreased total oxygen content of blood. The use of pulse oximetry in these patients can be misleading. Although oxygen saturation might be close to 100%, the total amount of hemoglobin is reduced and the animal can still have extremely low tissue oxygen delivery.[30,31] Pulse oximetry should be interpreted with caution in these animals.

A pulse oximetry reading of 100% correlates with a Pa_{O_2} of about 120 mm Hg,[25] and a pulse oximeter reading more than 95% is considered normal for most animals, correlating with a Pa_{O_2} between 80 and 120 mm Hg. Mild to moderate hypoxemia is indicated by values between 90% and 94%. A pulse oximeter reading of 90% indicates a Pa_{O_2} of about 60 mm Hg. Severe, potentially life-threatening hypoxemia results in Sp_{O_2} readings of less than 90%.

End-tidal Capnography

Measurement of the partial pressure of CO_2 in inhaled and exhaled gases during phasic breathing is known as capnography. This measurement is a noninvasive tool that provides real-time information about ventilatory status, which is particularly valuable for monitoring animals under general anesthesia and for critically ill animals that are intubated and/or being mechanically ventilated.

Commercially available capnometers typically rely on infrared spectroscopy to detect exhaled CO_2 as it flows through a sensor device attached to the endotracheal tube. The amount of CO_2 is estimated by detecting variations in the absorption of light at a specific wavelength (4.26 μm).[32,33] There are 2 main types of capnometers.

Mainstream capnometers

The CO_2 sensor is located directly in the breathing circuit, typically at the hub of the endotracheal tube. Expired air passes directly through the sensor and the CO_2 content is then estimated.

Sidestream capnometers

This device attaches to the end of the endotracheal tube and has a side port through which a small volume of exhaled gas is continuously aspirated. This gas passes through a length of microtubing to a remote sensor in the machine, where the CO_2 content is measured. Sidestream capnographs attached to a nasal catheter have been evaluated in awake, spontaneously breathing dogs, and exhaled CO_2 content correlated well with the Pa_{CO_2}. However, the difference between end-tidal CO_2 (ET_{CO_2}) and Pa_{CO_2} is significantly higher in dogs receiving supplemental oxygen, those with tachypnea, or in dogs that have primary respiratory system disorders.[34,35] Thus, documentation of high ET_{CO_2} values is a specific indication of hypoventilation, but a falsely normal or low reading might occur in some patients, despite the presence of hypoventilation.
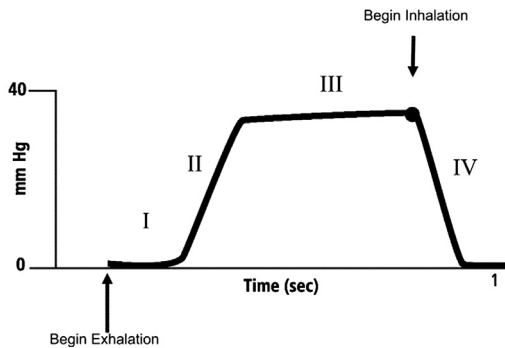
The Capnogram

A typical capnogram consists of 4 distinct phases (Fig. 6)[34]:

1. Beginning of exhalation: zero baseline as CO_2-poor atmospheric air from anatomic dead space is eliminated.
2. Exhalation: as CO_2-rich air from the lower airways begins to mix with dead space air, there is a gradual increase in exhaled CO_2.
3. End-exhalation: the amount of CO_2 in exhaled air reaches a plateau during the last part of exhalation as all exhaled air is coming from the alveoli and lower airways. The CO_2 concentration measured at this plateau is reported by the instrument as ET_{CO_2}.
4. Inhalation: as exhalation ends, the next breath begins and atmospheric air rushes in past the sensor. During this phase, CO_2 levels rapidly decrease and return the baseline to zero.

ET_{CO_2} can be used as an estimate of the pulmonary arterial CO_2 because CO_2 is so highly diffusible, and the alveolar CO_2 concentration is normally close to the CO_2 in the pulmonary arterial blood. A gradient between ET_{CO_2} and Pa_{CO_2} occurs because of the presence of dead space:

Anatomic dead space

There is usually a small difference (about 2–5 mm Hg) between ET_{CO_2} and Pa_{CO_2} in normal animals. This difference is a result of some mixing of alveolar air with CO_2-poor air from anatomic dead space in larger airways.

Fig. 6. Normal capnogram. See text for discussion of the 4 phases of the capnogram. (*From* Krauss B, Hess DR. Capnography for procedural sedation and analgesia in the emergency department. Ann Emerg Med 2007;50(2):174; with permission.)

Physiologic dead space

In animals with significant pulmonary disease, the gradient between $ETco_2$ and $Paco_2$ can be increased because of increased physiologic dead space. This increase occurs because some regions of the lungs can have significant ventilation-perfusion mismatch. High V/Q is seen when regions of lung are hypoperfused. As a result,
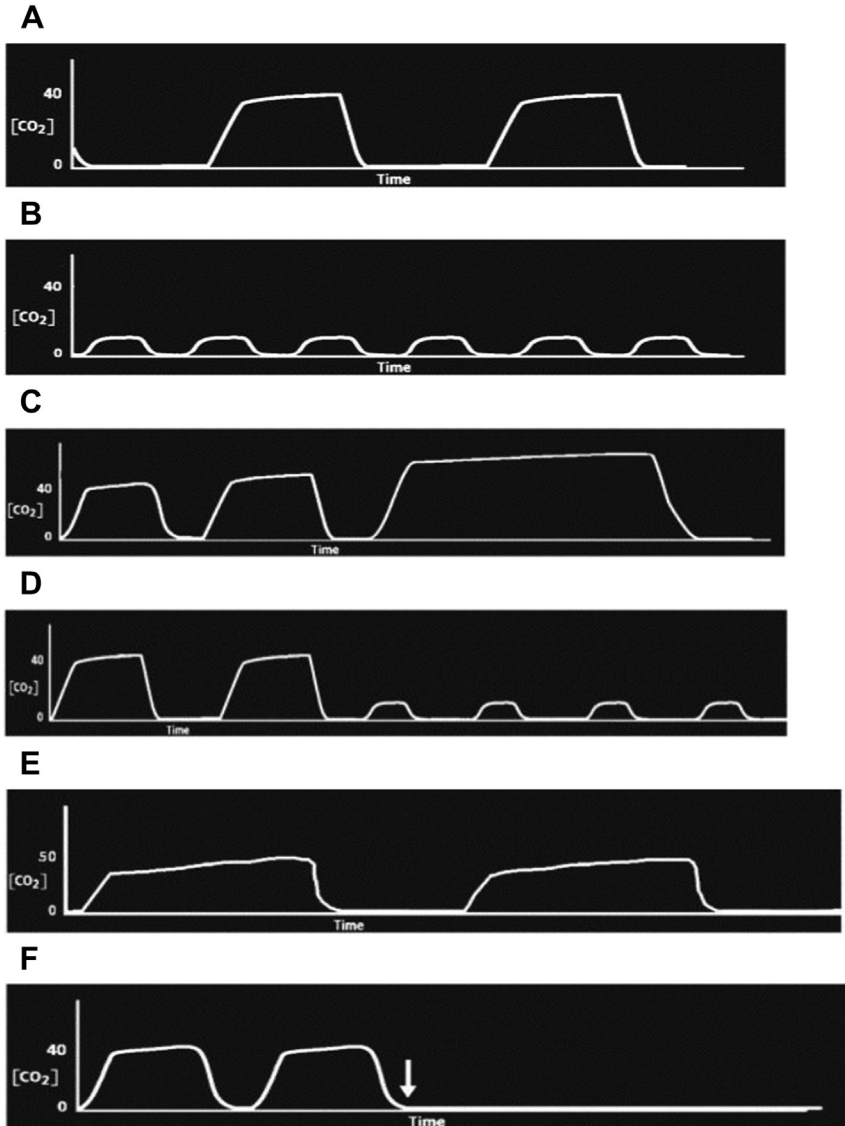
Fig. 7. Capnography during anesthetic monitoring. (*A*) Normal capnogram. (*B*) Hyperventilation. (*C*) Bradypneic hypoventilation. (*D*) Hypopneic hypoventilation. (*E*) Bronchospasm (eg, as can occur during an acute aspiration event). (*F*) Apnea (eg, as can be seen in an intubated patient experiencing a period of respiratory arrest). (*From* Krauss B, Hess DR. Capnography for procedural sedation and analgesia in the emergency department. Ann Emerg Med 2007;50(2):176; with permission.)

less CO_2 is delivered to that area of the lung for elimination, which translates into a low $ETco_2$ relative to the $Paco_2$. Low V/Q results when there are regions of alveolar disease. Decreased alveolar ventilation in these areas relative to perfusion results in inefficient elimination of CO_2 and, ultimately, a low $ETco_2$ relative to the $Paco_2$.

Capnography is an invaluable clinical tool for monitoring ventilatory status. The most common applications of capnography in anesthesia, intensive care, and emergency medicine include:

- Ventilatory monitoring in anesthetized intubated animals[35] (**Fig. 7**)
- Monitoring ventilation in animals with tracheostomies
- Verification of endotracheal intubation during cardiopulmonary resuscitation: attachment of the capnometer to the endotracheal tube after an intubation attempt can help distinguish between accurate endotracheal intubation and a misplaced esophageal intubation because levels of CO_2 in the esophagus are usually negligible, whereas endotracheal intubation should produce a normal capnogram with each breath (either spontaneous or positive-pressure breath)

SUMMARY

PFTs have wide clinical applications and can be used in small animals for evaluation of a wide range of pulmonary conditions. Additional PFTs are commonly used in people but have not found widespread use in veterinary medicine. Impedance oscillometry as a measure of airway function has been widely studied in children with lower airway disease and has potential applications in veterinary medicine because it involves measurements made during normal tidal breathing.

REFERENCES

1. Crapo RO. Pulmonary-function testing. N Engl J Med 1994;331(1):25–30.
2. Morris JF. Spirometry in the evaluation of pulmonary function. West J Med 1976; 125(2):110.
3. Zibrak JD, O'Donnell CR, Marton K. Indications for pulmonary function testing. Ann Intern Med 1990;112(10):763–71.
4. Morris MJ, Lane DJ. Tidal expiratory flow patterns in airflow obstruction. Thorax 1981;36(2):135–42.
5. Carlsen KL, Magnus P, Carlsen KH. Lung function by tidal breathing in awake healthy newborn infants. Eur Respir J 1994;7(9):1660–8.
6. Miller CJ, McKiernan BC, Pace J, et al. The effects of doxapram hydrochloride (Dopram-V) on laryngeal function in healthy dogs. J Vet Intern Med 2002;16: 524–8.
7. Amis TC, Kurpershoek C. Tidal breathing flow-volume loop analysis for clinical assessment of airway obstruction in conscious dogs. Am J Vet Res 1986;47: 1002–6.
8. Amis TC, Smith MM, Gaber CE, et al. Upper airway obstruction: canine laryngeal paralysis. Am J Vet Res 1986;47:1007–10.
9. McKiernan BC, Dye JA, Rozanski EA. Tidal breathing flow-volume loops in healthy and bronchitic cats. J Vet Intern Med 1993;7:388–93.
10. McKiernan BC, Johnson LR. Clinical pulmonary function testing in dogs and cats. Vet Clin North Am Small Anim Pract 1992;22:1087–99.
11. Dye JA, McKiernan BC, Rozanski EA, et al. Bronchopulmonary disease in the cat: historical, physical, radiographic, clinicopathologic, and pulmonary functional

evaluation of 24 affected and 15 healthy cats. J Vet Intern Med 1996;10(6): 385–400.

12. Bark H, Epstein A, Bar-Yishay E, et al. Non-invasive forced expiratory flow—volume curves to measure lung function in cats. Respir Physiol Neurobiol 2007;155:49–54.

13. Rodarte JR, Rehder K. Dynamics of respiration. Comp Physiol 2011;131–44. Available at: http://onlinelibrary.wiley.com/doi/10.1002/cphy.cp030310/abstract.

14. Stahl CA, Moller K, Schumann S, et al. Dynamic versus static respiratory mechanics in acute lung injury and acute respiratory distress syndrome. Crit Care Med 2006;34(8):2090–8.

15. Scanlan CL, Realey A, Earl L, et al, editors. Egan's fundamentals of respiratory care. 8th edition. St Louis (MO): Mosby-Year Book; 2003.

16. Bernstein W. Pulmonary function testing. Curr Opin Anaesthesiol 2012;25:11–6.

17. Rubin BK, Dhand R, Ruppell GL, et al. Respiratory care in review 2010: part 1. Asthma, COPD, pulmonary function testing, ventilator-associated pneumonia. Respir Care 2011;56(4):488–502.

18. Ruppell GL, Enright PL. Pulmonary function testing. Respir Care 2012;57(1): 165–75.

19. Hoffman AM, Dhupa N, Cimetti L. Airway reactivity measured by barometric whole-body plethysmography in healthy cats. Am J Vet Res 1999;60(12): 1487.

20. Hamelmann E, Schwarze J, Takeda K, et al. Noninvasive measurement of airway responsiveness in allergic mice using barometric plethysmography. Am J Respir Crit Care Med 1997;156:766–75.

21. Rozanski EA, Hoffman AM. Pulmonary function testing in small animals. Clin Tech Small Anim Pract 1999;14(4):237–41.

22. Hoffman AM. Airway physiology and clinical function testing. Vet Clin North Am Small Anim Pract 2007;37:829–43.

23. Bedenice D, Rozanski E, Bach J, et al. Canine awake head-out plethysmography (HOP): characterization of external resistive loading and spontaneous laryngeal paralysis. Respir Physiolo Neurobiol 2006;151:61–73.

24. Bedenice D, Bar-Yishay E, Ingenito EP, et al. Evaluation of head-out constant volume body plethysmography for measurement of specific airway resistance in conscious, sedated sheep. Am J Vet Res 2004;65:1259–64.

25. Proulx J. Respiratory monitoring: arterial blood gas analysis, pulse oximetry and end-tidal carbon dioxide analysis. Clin Tech Small Anim Pract 1999;14(4):227–30.

26. Ferguson ND, Fan E, Camporota L, et al. The Berlin definition of ARDS: an expanded rationale, justification and supplementary material. Intensive Care Med 2012;38(10):1573–82.

27. Schnapp LM, Cohen NH. Pulse oximetry–uses and abuses. Chest 1990;98: 1244–50.

28. Habler OP, Messmer KF. The physiology of oxygen transport. Transfus Sci 1997; 18(3):425–36.

29. Yelderman M, New W. Evaluation of pulse oximetry. Anesthesiology 1983;59: 349–52.

30. Hendricks JC, King LG. Practicality, usefulness and limits of pulse oximetry in critical small animal patients. J Vet Emerg Crit Care 1993;3(1):5–12.

31. King GG. Cutting edge technologies in respiratory research: lung function testing. Respirology 2011;16:883–90.

32. Nagler J, Krauss B. Capnography: a valuable tool for airway management. Emerg Med Clin North Am 2008;26:881–97.

33. Sullivan KJ, Kissoon N, Goodwin SR. End-tidal carbon dioxide monitoring in pediatric emergencies. Pediatr Emerg Care 2005;21(5):327–32.
34. Kelmer E, Scanson LC, Reed A, et al. Agreement between values for arterial and end-tidal partial pressure of carbon-dioxide in spontaneously breathing, critically ill dogs. J Am Vet Med Assoc 2009;235:1314–8.
35. Thompson JE, Jaffe MB. Capnographic waveforms in the mechanically ventilated patient. Respir Care 2005;50(1):100–8.