Pulmonary edema as a postoperative complication in two obese patients (a horse and a dog)

Longoedeem als postoperatieve complicatie bij twee obese patiënten (een paard en een hond)

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ABSTRACT

In this case series, the development and successful treatment of pulmonary edema are described in two obese animals (a horse and a dog) in the postoperative period. This rare but severe complication is normally fairly easy to diagnose, but the cause is usually multifactorial and difficult to determine. Potentially contributing factors are discussed. Both animals responded successfully to therapy and were discharged without further incidents.

SAMENVATTING

In deze casuïstiek worden het ontstaan en de succesvolle behandeling van longoedeem beschreven bij twee obese dieren (een paard en een hond) in de postoperatieve periode. De diagnose van deze zeldzame maar ernstige complicatie is normaal gesproken eenvoudig, maar de onderliggende oorzaak is vaak multifactorieel en moeilijk exact te identificeren. Mogelijk bijdragende factoren worden besproken. Beide dieren werden met succes behandeld en zonder verdere complicaties ontslagen.

INTRODUCTION

Pulmonary edema (PE) is a rare but serious complication following surgery and anesthesia in both horses (Senior, 2005) and dogs (Boutureira et al., 2007). This condition usually is multifactorial in origin (Wilkins, 2003; Senior, 2005). Two cases (a horse and a dog) are described in the present case series.

CASE HISTORY

Case 1

A 2-year-old, 141 kg miniature horse was referred for cryptorchidism. The day before surgery, the horse received 5 mL tetanus antitoxin (ATS, Intervet, Belgium) subcutaneously (SC), penicillin-procaine (Penikel, Kela, Belgium, 15 mg kg^{-1}) intramuscularly (IM) and fluxinine meglumine (Finadyne, Intervet, Belgium; 1.1 mg kg^{-1}) orally. Preanesthetic examination was normal, apart from obesity (body condition score (BCS) 5/5). The horse was classified as "American Society of Anesthesiologists (ASA) class III", i.e. a patient with severe systemic disease.

After premedication with acepromazine maleate (Placivet, Kela Veterinaria, Belgium; 0.02 mg kg^{-1} IM), the horse was sedated with romifidine (Sedivet, Boehringer Ingelheim, Belgium; 80 µg kg^{-1}) and morphine (Morphine HCl, Belgium; 0.14 mg kg^{-1}) intravenously (IV). The quality of sedation was good. A 14 G catheter (Vasocan Braunüle Luerlock, B. Braun Melsungen AG, Germany) was placed in the jugular vein. Anesthesia was induced with midazolam (Dormicum, Roche, Belgium; 0.06 mg kg^{-1}) and ketamine (Anesketin, Eurovet, Belgium; 2.2 mg kg^{-1}) IV. The induction was smooth and the horse was easily intubated orotracheally (12 mm ID silicone endotracheal tube). The cuff was inflated to a pressure of 80 cmH_2O.

The horse was positioned in dorsal recumbency. Anesthesia was maintained with isoflurane (Isoflo, Abbott Laboratories Ltd, UK) in a mixture of oxygen and air (inspired oxygen fraction $FI'O_2$ 60%), using a rebreathing system (Dräger-AV1, Drager, Belgium) with an out-of-circuit vaporizer (Vapor 19.3, Drägerwerk AG, Germany). A constant rate infusion (CRI) of romifidine (40 µg kg^{-1} h^{-1}) and a lactated polyionic solution (Haemofiltrate, Dirinco, Switzerland; 5 mL kg^{-1} $hour^{-1}$) were infused. Anesthesia was monitored using a Datex Ohmeda S/5 (GE Healthcare, Belgium).

Monitoring included electrocardiography (ECG, apex basis lead), pulseoximetry (SpO_2), measurement of the respiratory rate (RR, min^{-1}) end tidal concentrations of isoflurane (FE´ISO), and carbon dioxide ($FE´CO_2$). A catheter was placed in the facial artery and connected to a calibrated pressure transducer, zeroed to the atmosphere and placed at the level of the right atrium for continuous measurement of the arterial blood pressure (ABP).

The horse was mechanically ventilated (initial tidal volume (TV) 1000 mL; RR 8 min^{-1}) immediately after the induction of anesthesia. After a few breaths, the peak inspiratory pressure (PIP) was observed to be 35 cmH_2O. The tidal volume was reduced to 700 mL, which reduced PIP to 18-19 cmH_2O. The respiratory rate was increased to 16-19 min^{-1}. A heparinized blood sample was withdrawn from the facial artery for immediate blood gas analysis (ABG, ABL5, Radio-meter, Denmark) and the determination of packed cell volume (PCV). The results indicated normocapnia ($PaCO_2$ = 44 mmHg) but borderline hypoxemia (PaO_2 = 60 mmHg; SaO_2 90%). A second sample obtained 15 minutes later revealed a PaO_2 of 54 mmHg (SaO_2 88%). Positive end expiratory pressure (PEEP) was applied at 3 cmH_2O. As the mean arterial pressure (MAP) dropped to 55 mmHg, dobutamine (Dobutrexmylan, Mylan bvba, Belgium) was administered using a syringe driver (Terufusion model STC-526, Terumo, Belgium) at 0.3-0.6 µg kg^{-1} min^{-1}. Twenty minutes later, surgery was terminated, the horse was weaned from the ventilator and the arterial catheter was removed. Romifidine 20 µg kg^{-1} IV was administered before the horse was transported to the recovery box and positioned in left lateral recumbency. The cuff of the endotracheal tube was deflated and oxygen was supplemented at 4 L min^{-1} through the tracheal tube. The horse was extubated 12 minutes after the end of anesthesia, after which oxygen was administered via nasal insufflation. Undisturbed bilateral nasal air flow was observed. The respiratory rate was fast (36 min^{-1}; preanesthetically 24 min^{-1}). No abnormalities were heard on auscultation of the lungs. Slight snoring was audible over the laryngeal area. The horse was manually assisted to sternal recumbency 32 minutes after the end of anesthesia, and stood 10 minutes later. The horse was calm and breathed quietly. He was returned to a box and was fasted for 4 hours postoperatively.

Two hours after standing, the horse showed severe dyspnea (RR 60 min^{-1}) and tachycardia (60 bpm). Crackles could be auscultated over both lung fields, the mucous membranes were cyanotic, CRT was prolonged. Severe generalized PE was suspected based on the clinical signs and thoracic ultrasonography (occurrence of comet tails). Oxygen (6 L min^{-1}) was supplemented for 24 hours while furosemide (1.78 mg kg^{-1} (Dimazon, Intervet Nederland b.v., the Netherlands; repeated 2 hours later; then TID for 1 day and BID on day 2) and dexamethasone 0.1 mg kg^{-1} SID for 3 days (Rapidexon, Eurovet AH, Belgium) were administered IV. Enoxaparine (Clexane, Sanofi-Aventis, Belgium) 0.5 mg kg^{-1} SC was administered SID for 3 days. An aerosol containing clenbuterol 0.8 µg kg^{-1} (Ventipulmin, Boehringer Ingelheim, Belgium) was administered TID for 3 days. Clinically, the horse was much improved after a day of treatment. The oxygenation on room air as assessed by venous blood gas analysis was normal. The horse was discharged six days postoperatively without further complications.

Case 2

A 9-year-old, male, 34 kg English bulldog was referred for exercise intolerance, lethargy and breathing difficulties induced by pericardial effusion. A pericardiocentesis had not resulted in clinical improvement. On clinical examination, the dog was calm, alert and responsive, with a 5/5 BCS. An inspiratory stridor was audible with maximal intensity located over the larynx. Lung sounds were diminished, heart sounds were muffled and the femoral pulse was weak. The abdomen was enlarged and the undulation test seemed positive. On echocardiography, pleural and pericardial effusion were observed. Cardiac tamponade was not present at that time. A mass (2.8 x 2.8 cm) was observed at the base of the aorta. Cardiac contractility and overall function were normal. Preliminary diagnosis was chemodectoma with pericardial, pleural and peritoneal effusion. A partial pericardectomy was scheduled the following day via an abdominal-diaphragmatic approach to minimize the effects of body position and conformation on ventilation.

The next day, the dog was presented for surgery. The owner reported that the complaints worsened overnight. Clinical examination was identical while bloodwork was normal. Electrocardiography showed low voltage QRS complexes and electrical alternans. The dog ("ASA class IV", i.e. a patient with severe systemic disease that is a constant threat to life) was preoxygenated (2 L min^{-1}) by mask for 5 minutes before premedication with fentanyl (Fentadon, Eurovet Animal Health, Belgium; 5 µg kg^{-1} IV) through a 20G catheter placed in the left cephalic vein. The sedated dog was positioned in left lateral recumbency for cardiac ultrasound (which now indicated cardiac tamponade) and pericardiocentesis. Over 300 mL of serohemorrhagic fluid was removed, after which the right ventricle and the atria distended normally again. Contractility and cardiac function appeared to be normal.

Anesthesia was induced (T=0) with fentanyl 5 µg kg^{-1}, followed by midazolam 0.5 mg kg^{-1} and 6 mg etomidate (Hypnomidate, Janssen-Cilag, Belgium) IV. A throat inspection was performed, classifying the dog as having brachycephalic airway obstructive syndrome (BAOS) grade II. The dog was intubated with a cuffed, 8 mm ID silicone endotracheal tube and connected to a circle system supplying isoflurane in oxygen. While the dog was clipped for surgery, a 22G catheter was placed in the left dorsal metatarsal artery for monitor-

ing ABG and ABP. Cefazoline (Cefazoline, Sandoz n.v./s.a, Belgium; 20 mg kg^{-1} IV) was administered and repeated every 2 hours during the surgery. Ringer Lactate (B. Braun Vet Care GmbH, Germany) was infused using an MP-1000 volumetric infusion pump (Medifusion, UK) at 5 mL kg^{-1} h^{-1}.

The dog was transferred to the surgical theatre, positioned in dorsal recumbency (T25) in reverse Trendelenburg position (30°) and connected to a rebreathing system and ventilator (Cicero, Dräger, Germany). A Dräger Ohmeda S/3 Monitor was used for monitoring gas composition, capnography, spiro-graphy (adult D-Lite sensor), tidal volumes, airway pressures, RR and SpO_2. A Cardiocap II (Datex Instrumentarium Corp., Finland) was used for monitoring ECG and ABP. The initial gas flow consisted of 2 L min^{-1} of oxygen mixed with 0.8 L min^{-1} of medical air. Mean FE´ISO was 0.7% during the surgery, with initial $FI'O_2$ 62%. A CRI of fentanyl (5 µg kg^{-1} $hour^{-1}$) was administered, using a Graseby 3400 Syringe Pump (Smiths Medical, Belgium).

Initially, spontaneous ventilation was allowed, until at T10, SpO_2 was 87%. The inspired oxygen fraction was increased to 89% and mechanical ventilation was started. The initial settings limited PIP at 13.3 cmH_2O. The variables were set at PEEP 3.1 cmH_2O, I:E ratio 1:2, frequency 18 min^{-1}, TV 150 mL (= 4 mL kg^{-1}). It was immediately noted that the delivered TV was markedly lower (75 mL) than intended, the maximum set pressure was reached and the total compliance (Crs) was 5 mL cmH_2O^{-1}. Ventilator-patient dyssynchrony was observed and ketamine (0.5 mg kg^{-1}) and fentanyl (2 µg kg^{-1}) were administered IV. Since little improvement was obtained, atracurium besylate (Tracrium, GlaxoSmithKline, the Netherlands; 0.5 mg kg^{-1} IV) was administered while a median laparotomy was performed (T35). The dyssynchrony disappeared, but compliance only improved marginally (6 mL cmH_2O^{-1}). The pressure limitation was increased to 15.3 cmH_2O, but the delivered TV remained constant.

Compliance increased to 8-13 mL cmH_2O^{-1} after the incision of the diaphragm (T45). An ABG was performed, indicating hypoventilation ($PaCO_2$ 88 mmHg) and hypoxemia (PaO_2 60%, SaO_2 80%). As the thorax was now open, PEEP was increased to 7.2 cmH_2O and PIP to 20.5-23.5 cmH_2O. The delivered TV increased to 120-170 mL. As MAP dropped below 60 mmHg (T75), ephedrine 0.1 mg kg^{-1} IV (Ephedrine HCl, Sterop, Belgium) was administered, followed by a CRI of norepinephrine 0.2 µg kg^{-1} min^{-1} (Levophed, Hospira Benelux bvba, Belgium). Normotension was restored quickly. On ABG, both the hypoventilation ($PaCO_2$ 60mmHg) and hypoxemia (SaO_2 99%; PaO_2 171 mmHg) improved. Surgery was uneventful (pericardial window at T55, diaphragmatic closure at T110 and end of surgery at T130). After opening the pericardium, the infusion of Ringer Lactate was increased to 10 mL kg^{-1} h^{-1}.

The dog was placed in sternal recumbency. Spontaneous ventilation was regained after 5 minutes of synchronized intermittent mandatory ventilation. As SpO_2 stayed normal, the $FI'O_2$ was progressively decreased. However, at an $FI'O_2$ of 40%, the saturation dropped (SpO_2 83%), so $FI'O_2$ was increased to 70% (SpO_2 97%). Lung auscultation was performed by several experienced clinicians, but no abnormalities were detected. A nasal catheter was placed for postoperative oxygen supplementation and thoracic radiographs were taken which indicated the presence of PE. Furosemide 2 mg kg^{-1} IV was administered. The dog improved quickly and maintained saturation easily with $FI'O_2$ 40%. Norepinephrine administration was decreased and stopped as ABP improved. Recovery was uneventful. Oxygen was supplemented at 2 L min^{-1} through the nasal catheter. The dog received 1.9 mL kg h^{-1} Hartmann. A second dose of furosemide was administered one hour after the first.

Postoperative analgesia included the administration of methadone (Comfortan, Eurovet Animal Health, Belgium; 0.2 mg kg^{-1} IV every 4 hours) and carprofen (Rimadyl, Pfizer Animal Health, Belgium; 4 mg kg^{-1} IV SID). The dog recovered well and was discharged two days after surgery on oral antibiotics (Rilexine, Virbac, Nederland), carprofen (Rimadyl, Pfizer Animal Health, Belgium) and tramadol (Tramadol; Sandoz, the Netherlands). There were no complications at four-week follow-up.

DISCUSSION

The diagnosis of PE is normally fairly straightforward. In horses, it is usually based on clinical signs, such as tachypnea, dyspnea, excitation and crackles on auscultation and foamy nasal discharge. Arterial blood gas analysis, ultrasonography or thoracic radiography (limited by physical considerations (Koblik and Hornoff, 1985) may usually confirm correct diagnosis (Wilkins, 2003). In small animals, the clinical symptoms are similar and are usually confirmed by thoracic radiographs (Adamantos and Hughes, 2009). The cause of PE is usually multifactorial and difficult to determine (Wilkins, 2003; Senior, 2005), which was also true in the described cases.

Fluid therapy has been classified as a risk during feline anesthesia (Brodbelt et al., 2007) and anesthesia in cardiac disease (Clutton, 2007; Dugdale, 2010). However, it is unlikely that volume overload contributed to the formation of PE in either case. The low compliance present at the start of surgery in the dog indicated that PE had already been present before significant fluid was administered. The horse was anesthetized only for 65 minutes and received 5 mL kg^{-1} fluids, which is within or lower than the recommended rates (Hardy, 2009; Snyder and Wendt-Hornickle, 2013).

Drugs including propofol (Boesch et al., 2009) and ketamine-diazepam (Stegmann, 2000; Boutureira et al., 2007) have incidentally been reported to induce PE in several species. The horse in the present case received intravenous morphine, but whether this may

contribute to PE formation (Kaartinen et al., 2010) or possibly protect against it (Senior, 2005) is presently unknown. An anaphylactic reaction induced by the administration of drugs cannot be excluded in either case.

Systemic inflammatory response syndrome could lead to an increased permeability edema (Adamantos and Hughes, 2009). As this syndrome occurs secondary to other disease processes, such as sepsis, pancreatitis, pneumonia, severe tissue trauma, immune-mediated disease and metastatic neoplasia, this possibility seems unlikely in both cases.

In several case reports in horses, the diagnosis is described as occurring during or directly after recovery (Borer, 2005; Kaartinen et al., 2010). In the horse of the present case, PE was only noticed 2 hours after recovery. As there were no problems visible during or immediately after recovery, catecholamine release due to postoperative stress and excitation cannot be ruled out as a causative factor (Senior, 2005), although the horse appeared to have a calm recovery. An inspiratory stridor of the larynx was observed, and although a negative pressure generated by upper airway obstruction has been described to cause PE (Kollias-Baker et al., 1993; Ball and Trim, 1996; Tute et al., 1996), the authors of the present case consider this to be unlikely, as the nasal air flow after extubation was bilateral, strong and unhindered. In the brachycephalic dog, upper airway obstruction may be a contributing factor to PE, due to increased inspiratory effort against a partially closed airway (Algren et al., 1993).

Central venous air embolism has also been reported as a cause of PE in horses in absence of upper airway obstruction (Holbrook et al., 2007). This seems unlikely in the present case, as the IV catheter was removed before recovery and was not opened to air at any point during the proceedings. Moreover, the horse recovered quickly from the edema without cardiovascular or neurologic sequelae.

Hypoxia has been known to contribute to the formation of PE (Algren et al., 1993; Ball and Trim, 1996; Boutureira et al., 2007). Whether pre-existing hypoxemia contributed to edema formation in the horse of the present case or if the edema caused the observed hypoxemia is unknown. The dog may have been chronically hypoxemic, as he was suspected to have a chemodectoma (not confirmed by biopsy) (Hayes, 1975). Additionally, brachycephalic dogs have been described to have a lower PaO_2 than meso- or dolichocephalic dogs (Hoareau et al., 2012).

Cardiac dysfunction and more specifically, pericardial effusion may induce PE (Dugdale, 2010). On preoperative echocardiographic examination, the cardiac function of the dog appeared to be normal after pericardiocentesis. However, cardiac output and pulmonary vascular pressure were not measured, so a cardiac cause could not be ruled out. No evidence of cardiac problems was found in the horse, neither pre- nor postoperatively.

The origin of the PE in the horse of the present case was potentially ventilator-associated lung injury (VALI). Despite starting mechanical ventilation at 7 mL kg^{-1} (a relatively low TV), PIP was quite high (35 cmH_2O), indicating low respiratory system compliance. A PIP over 40 cmH_2O is potentially harmful to a normal horse lung (Kerr and McDonell, 2009). This pressure level was not reached in the present case, but no data are available on lung dynamics in miniature horses. Direct volutrauma with high PIP is possible, since the obesity in this miniature horse may have induced (micro)atelectasis (Littleton, 2012), resulting in overinflation of open alveoli at relatively low TV's (Syring, 2009). Additionally, secondary atelectrauma (alveolar shear-stress injury, which occurs with repetitive alveolar recruitment and derecruitment) may have occurred (Carney et al., 2005; Syring, 2009).

In the dog of the present case report, VALI may also have occurred, as a relatively high PIP (20.5-23.5 cm H_2O) was reached. However, PEEP was administered continuously, which was part of a pulmonary protective ventilator strategy (Carney et al., 2005). In addition, the measured compliance was already low at the start of mechanical ventilation (before the use of high PIP). According to Bradbrook et al., (2013), normal dynamic compliance of the respiratory system of a healthy dog of this size should be 39 mL cmH_2O^{-1}. It actually varied between 5-13 mL cmH_2O^{-1}. In trying to find a cause for this abnormality, a measurement error should be considered first. However, since the delivered TV was low but resulted in high PIP (as observed on the integrated monitor of the anesthetic machine rather than on the spirometer used) this possibility could be excluded. The high PIP that was reached in the horse when a relatively small TV was administered, suggests the horse also had a decreased compliance.

A decrease in compliance may be caused by restrictive pulmonary, pleural or thoracic disease (Haskins, 2007). Hence, beside PE, several factors could have contributed. First, obesity decreases respiratory system compliance in humans. This is related to a decrease in both lung (an increase in pulmonary blood volume, increased closure of dependent airways and a higher percentage of fibrosis) and chest wall compliance (Pelosi and Gregoretti, 2010). Increased chest wall resistance appears to have been present in the dog, as compliance doubled after opening the thorax. Although the dog was positioned in reverse Trendelenburg position to minimize pulmonary compression due to pleural effusion or abdominal organ pressure (associated with dorsal recumbency), these factors could still have contributed to a decrease in compliance. This is also likely to have occurred in the horse, where obesity and dorsal positioning probably led to increased pressure on the lungs.

In human medicine (primarily in neonates), fentanyl (Vaughn and Bennett, 1981; MacGregor and Bauman, 1996; Fahnenstich et al., 2000; Elakkumanan et al., 2008) and other opiates (Lynch and Hack, 2010; Carvalho et al., 2004; Bennett et al., 1997) have

been described to cause chest wall rigidity, thereby decreasing compliance. This has been reported in pigs (Thurmon and Smith, 2007), but not in dogs or horses.

Severe bronchoconstriction may also lead to decreased compliance (Lumb, 2005a, Boesch et al., 2009). Furosemide has bronchodilating properties (Wilkins, 2003), and as both animals improved quickly after its administration, bronchoconstriction cannot be excluded as a contributing factor to low compliance.

In retrospect, the presence of PE in the dog could have been suspected earlier during anesthesia, as low compliance was present from the start of PPV, and persisted even after opening the thorax. Preoperative thoracic radiographs could potentially have indicated the presence of PE.

Surprisingly, in both cases, the animals did not appear to have wheezing nor crackles on auscultation. As PE was certainly present in the dog at the time of auscultation, which was performed by experienced clinicians, the authors suspect a damping of the lung sounds by body fat surrounding the thorax. This could also contribute to the normal auscultation of the horse. However, another possibility is that the horse was still in an early stage of PE at the time of auscultation (Lumb, 2005b).

Treatment of peri-anesthetic pulmonary edema should be rapid and aggressive, but is mainly supportive (Senior, 2005). If possible, treatment should be adapted to the suspected underlying condition (Adamantos and Hughes, 2009). Oxygen should be supplemented, the airway should be checked for patency, and stress and movement should be minimized (Adamantos and Hughes, 2009). Sedation may be needed (Senior, 2005). Diuretics such as furosemide are especially useful when the edema is cardiogenic, but can aid in non-cardiogenic causes as well. Vasodilators, such as nitroprusside and nitroglycerin, can be used in acute situations to decrease pulmonary hydrostatic pressure (Adamantos and Hughes, 2009). Corticosteroids prevent increases in vascular permeability and like non-steroidal anti-inflammatory drugs may also decrease prostaglandin induced bronchoconstriction (Senior, 2005). Bronchodilators, such as clenbuterol, aminophylline and theophylline, may be useful. Fluid administration should generally be restricted. Severe cases may need PPV (Adamantos and Hughes, 2009).

Treatment in the described cases consisted of oxygen supplementation and the administration of a diuretic. The horse received additional corticosteroids, a bronchodilator to treat the pulmonary edema, and enoxaparin to prevent laminitis. Both animals responded well to therapy.

CONCLUSION

Although the final outcome in both cases was successful, the occurrence of pulmonary edema is a serious adverse peri-anesthetic event. In retrospect, the management of both cases may have been suboptimal. Regarding the dog, preoperative thoracic radiographs would have been justifiable. Pulmonary edema should be included in the differential diagnosis of low compliance. Obese animals should be considered to have an increased peri-anesthetic risk, and conservative ventilation strategies are recommended to manage these patients.

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REFERENCES

Adamantos S., Hughes D. (2009). Pulmonary edema. In: Silverstein D.C., Hopper K. (editors). *Small Animal Critical Care Medicine.* Saunders Elsevier, Canada, p 86-97

Algren J.T., Price R.D., Buchino J.J., et al. (1993). Pulmonary edema associated with upper airway obstruction in dogs. *Pedaetric Emergengy Care 9(6),* 332-337

Ball M.A., Trim C.M. (1996). Post anaesthetic pulmonary oedema in two horses. *Equine Veterinary Education 8(1),* 13-16

Bennett J.A., Abrams J.T., Van Riper D.F., et al. (1997). Difficult or impossible ventilation after sufentanil induced anesthesia is caused primarily by vocal cord closure. *Anesthesiology 87(5),* 1070-1074

Boesch J.M., Gleed R.D., Gagne J.W. (2009). Acute non-cardiogenic pulmonary edema in an anesthetized Nubian goat kid. *Veterinary Anaesthesia and Analgesia 36,* 567-573

Borer K.E. (2005). Pulmonary oedema associated with anaesthesia for colic surgery in a horse. *Veterinary Anaesthesia and Analgesia 32,* 228-232

Boutureira J., Trim C.M., Cornell K.K. (2007). Acute pulmonary oedema after diazepam-ketamine in a dog. *Veterinary Anaesthesia and Analgesia 34,* 371-376

Bradbrook C.A., Clark L., Dugdale A.H.A. (2013). Measurement of respiratory system compliance and respiratory system resistance in healthy dogs undergoing general anaesthesia for elective orthopaedic procedures. *Veterinary Anaesthesia and Analgesia 40(4),* 382-389

Brodbelt D.C., Pfeiffer D.U., Young L.E., et al. (2007). Risk factors for anaesthetic-related death in cats: results from the confidential enquiry into perioperative small animal fatalities (CEPSAF). *British Journal of Anaesthesia 99(5),* 617-623

Carney D., DiRocco J., Nieman G. (2005). Dynamic alveolar mechanics and ventilator-induced lung injury. *Critical Care Medicine 33 (3),* S122-128

Clutton R.E. (2007). Cardiovascular disease. In: Seymour C., Duke-Novakovski T. (editors). *BSAVA Manual of Canine and Feline Anaesthesia and Analgesia*. Second edition, BSAVA, UK, p 200-219

Dugdale A. (2010). Some cardiac considerations. In: *Veterinary Anaesthesia Principles to Practice.* Blackwell Publishing Ltd, UK, p 341-343

Egenvall A., Hansson K., Säteri H. (2003). Pulmonary oedema in Swedish hunting dogs. *Journal of Small Animal Practice 44,* 209-217

Elakkumanan L.B., Punj J., Talwar P., et al. (2008). Atypical presentation of fentanyl rigidity following administra-

tion of low dose fentanyl in a child during intraoperative period. *Paediatric Anaesthesia 18 (11),* 1115-1117

Fahnenstich H., Steffan J., Kau N., et al. (2000). Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants. *Critical Care Medicine 28(3),* 836-839

Hardy J. (2009). Venous and arterial catheterization and fluid therapy. In: Muir W.W., Hubbell J.A.E. (editors). *Equine Anesthesia Monitoring and Emergency* Therapy. Second edition, Saunders Elsevier, USA, p 131-148

Haskins S.C. (2007). Monitoring anesthetized patients. In: Tranquilli W.J., Thurmon J.C., Grimm K.A. (editors). *Lumb & Jones' Veterinary Anesthesia and Analgesia.* Fourth edition, Blackwell Publishing, USA, p 533-560

Hayes H.J. (1975). A hypothesis for the aetiology of canine chemoreceptor system neoplasms, based upon epidemiological study of 73 cases among hospital patients. *Journal of Small Animal Practice 16,* 337-343

Holbrook T.C., Dechant J.E., Crowson C.L. (2007). Suspected air embolism associated with post-anesthetic pulmonary edema and neurologic sequelae in a horse. *Veterinary Anaesthesia and Analgesia 34,* 217-222

Hoareau G.L., Jourdan G., Mellema M., et al. (2012). Evaluation of arterial blood gases and arterial blood pressures in brachycephalic dogs. *Journal of Veterinary Internal Medicine 26*, 897-904

Kaartinen M.J., Pang D.S.J., Cuvelliez S.G. (2010). Post-anesthetic pulmonary oedema in two horses. *Veterinary Anaesthesia and Analgesia 37,* 136-143

Koblick P.D., Hornof W.J. (1985). Diagnostic radiology and nuclear cardiology. Their use in assessment of equine cardiovascular disease. *Veterinary Clinics of North America: Equine Practice 1(2),* 289-309

Kollias-Baker C.A., Pipers F.S., Heard D., et al. (1993). Pulmonary edema associated with transient airway obstruction in three horses. *Journal of American Veterinary Medical Association 202(7),* 1116-1118

MacGregor D.A., Bauman L.A. (1996). Chest wall rigidity during infusion of fentanyl in a two-month-old infant after heart surgery. *Journal of Clinical Anesthesia 8(3),* 251-254

Littleton S.W. (2012). Impact of obesity on respiratory function. *Respirology 17,* 43-49

Lumb A.B. (2005a). Elastic forces and lung volumes. In: *Nunn's Applied Respiratory Physiology*. Sixth edition, Elsevier Limited, USA, p 25-38

Lumb AB. (2005b). Pulmonary vascular disease. In: *Nunn's Applied Respiratory Physiology*. Sixth edition, Elsevier Limited, USA, p 387-396

Lynch R.E., Hack RA. (2010). Methadone-induced rigid-chest syndrome after substantial overdose. *Pediatrics 126,* e232-234

Pelosi P., Gregoretti C. (2010). Perioperative management of obese patients. *Best Practice & Research: Clinical Anaesthesiology 24(2),* 211-225

Senior M. (2005). Post-anaesthetic pulmonary oedema in horses: a review. *Veterinary Anaesthesia and Analgesia 32,* 193-200

Snyder L.B.C., Wendt-Hornickle E. (2013). General anesthesia in horses on fluid and electrolyte therapy. *Veterinary Clinics of North America: Equine Practice29,* 169-178

Syring R.S. (2009). Ventilator-associated lung injury. In: Silverstein D.C., Hopper K. (editors). *Small Animal Critical Care Medicine.* Saunders Elsevier, USA, p 110-113

Thurmon J.C., Smith G.W. (2007). Swine. In: Tranquilli W.J., Thurmon J.C., Grimm K.A. (editors). *Lumb & Jones Veterinary Anaesthesia and* Analgesia. Fourth edition, Blackwell Publishing, USA, p 747-763

Tute A.S., Wilkins P.A., Gleed R.D., et al. (1996). Negative pressure pulmonary edema as a post-anesthetic complication associated with upper airway obstruction in a horse. *Veterinary Surgery 25(6),* 519-523

Vaughn R.L., Bennett C.R. (1981). Fentanyl chest wall rigidity syndrome: a case report. *Anesthesia Progress 28(2),* 50-51

Wilkins P.A. (2003). Lower airway diseases of the adult horse. *Veterinary Clinics of North America: Equine Practice 19,* 101-121