

**Association of
Veterinary Anaesthetists**

Liverpool

April 3rd-5th 2006

Welcome to AVA, Liverpool 2006!

Welcome to Liverpool, the European City of Culture for 2008. In 2006 however, it is the city of veterinary anaesthesia, as we greet delegates to the Spring meeting of the AVA. In particular we would like to offer a very special welcome to our sponsors for this meeting, without whose support it would not be taking place. There are many others we also wish to thank, but there is not enough space to do them all justice here.

From its inception the AVA has been proud to include among its membership a number of interested but unspecialised practitioners. In more recent times we have perhaps projected too rarefied an atmosphere, inhibiting veterinary surgeons in practice from becoming involved. Therefore, in choosing our themes and speakers we have deliberately tried to widen the bounds of the subjects covered, in the hope that our delegates will find the subjects entertaining as well as intellectually stimulating.

Fittingly, at the time the new Animal Welfare Bill is about to embark on its parliamentary journey, the meeting opens with an in-depth consideration of pain recognition in non-verbal species by Professor Flecknell and Dr Nilofer Sabrine. Continuing the analgesia theme, later in the meeting Dr Polly Taylor will present the scientific basis behind the imminent introduction of a new analgesic for use in cats.

The physiological essentials for surviving the extremes of our environment are explored, both in marine mammals and high above the earth in aeroplanes. Putting icing on the cake, several eminent medical anaesthetists will discuss some of the latest developments in anaesthesia. All this after the opening training day for our up-and-coming colleagues, which will leave them all in need of refreshment and should give everyone an appetite for the social highlight of the meeting, the formal Dinner on Tuesday evening.

The Adelphi Hotel has a fascinating history of its own, and is ideally suited for social forays into the city. A wealth of information will be available to ensure that delegates can let their hair down in appropriate fashion.

On behalf of the organizing committee, welcome to Liverpool; enjoy yourselves!

Alex Dugdale Nicky Grint Mark Senior John and Jean Hird

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MONDAY 3rd April

RESIDENTS' TRAINING DAY

0800-0900

REGISTRATION

Breathe Easy

Chaired by Miss Alex Dugdale

0900-1000

Introduction to ventilation and ventilators

Dr Görel Nyman

Sponsor: Vetronics

1000-1100

Ventilation in small animal intensive care

Miss Amanda Boag

Sponsor: Woodley

1100-1130

COFFEE

1130-1230

Ventilation in neonatal foals

Dr Kevin Corley

Sponsor: Abbott

1230-1330

LUNCH

Food for Thought

Chaired by Miss Alex Dugdale

1330-1430

Interpretation of blood gas and electrolyte results

Miss Amanda Boag

Sponsor: Woodley

1430-1530

Nutrition in intensive care patients

Dr Daniel Chan

Sponsor: Abbott

1530-1600

TEA

Write it Right

Chaired by Miss Alex Dugdale

1600-1645

How to please the editor

Prof Jennie Hunter

Sponsor: Pfizer

1645-1715

The graphical presentation of data

Mr Eddie Clutton

Sponsor: Vetoquinol

1715-1800

How to review a manuscript

Mr Eddie Clutton

Sponsor: Boehringer

REGISTRATION will be open from 1900 - 2100 on SUNDAY 2nd April

from 1800

REGISTRATION and WELCOME RECEPTION

TUESDAY 4th April

0800-0900	REGISTRATION	
	Where does it hurt? Sponsor: Alstoe Chaired by Dr Louisa Slingsby	
0900-0945	Pain recognition in non-verbal species - animals Prof Paul Flecknell	
0945-1030	Pain recognition in non-verbal species - neonatal humans Dr Nilofer Sabrine	
1030-1100	COFFEE and POSTERS	
1100-1200	Abstracts 1a Chaired by Nicki Grint	Abstracts 1b Chaired by Briony Alderson
1200-1300	LUNCH -- ECVA AGM	
1300-1400	LUNCH -- ECVA AGM	
	Ready for take-off? Sponsor: Fort Dodge Chaired by Prof Robin Glead	
1400-1445	Flight physiology Gp Capt David Gradwell	
1445-1530	Aeroplane transport of horses Dr Paul van Dijk	
1530-1600	TEA and POSTERS	
	Deep breathing Sponsor: Kruuse Chaired by Mrs Lynne Hughes	
1600-1645	Physiology of diving animals Dr Andy Yule	
1645-1800	Abstracts 2a Chaired by Mark Senior	Abstracts 2b Chaired by Briony Alderson
	Fatty issue Sponsor: Boehringer Chaired by Prof Ron Jones	
1800-1830	Adipokines Prof Martin Leuwer	
1930	FORMAL DINNER at the ADELPHI HOTEL	

WEDNESDAY 5th April

0800-0900	REGISTRATION
	Comparative complications Sponsor: Boehringer Chaired by Prof Yves Moens
0900-0945	Management of difficult human airways Dr Peter Charters & Prof Duncan Gillies
0945-1030	Hyperbaric oxygen therapy Dr John Harrison
1030-1100	COFFEE and POSTERS
	Accidents will happen Sponsor: Pfizer Chaired by Eddie Clutton
1100-1200	How Accidents happen Prof Helen Muir
1200-1230	CEPSAF update Dr David Brodbelt
1230-1400	LUNCH -- AVA AGM
	Some good news Sponsor: Alstoe Chaired by Dr Kathy Clarke
1400-1445	A feline ABC: Analgesia: Buprenorphine: Cat Dr Polly Taylor
1445-1530	A novel approach to reversal Prof Jennie Hunter
1530-1600	TEA and POSTERS
1600-1645	Abstracts 3 Chaired by Nicki Grint
	Some more good news Sponsor: Veterinary Defence Society Chaired by Miss Alex Dugdale
1645-1730	Neurosteroids in veterinary anaesthesia Dr Kirby Pasloske
1730	End of Conference

Breathe Easy

**Chaired by
Miss Alex Dugdale**

**Speakers
Dr Görel Nyman
Miss Amanda Boag
Dr Kevin Corley**

Sponsors



Introduction to ventilation and ventilators

Görel Nyman DVM, PhD, DiplECVA

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Görel Christina Nyman was born in Härnösand, Sweden 1956. Graduated from the Veterinary Faculty in Uppsala and worked in general practice for two years. Then worked at the Department of Surgery at the Swedish University of Agricultural Sciences and gained her PhD in 1987 for a thesis concerning pulmonary function in anaesthetised horses. She had the first ever position as a veterinary anaesthetist in Sweden in 1991 and gained a Research Fellow Award in Uppsala 1995 at the Agricultural University Veterinary School where she was responsible for running the clinical anaesthetic service, teaching undergraduates and post graduates in anaesthesia and for the anaesthesia research programme.

She became a Diplomate of the European College of Veterinary Anaesthesia in 1998. Awarded PhD thesis 1987-1989 in Veterinary Medicine, Society of Veterinary Medical Research in Sweden, 1990 Equine Veterinary Journal Open Award and 2002 Journal of Veterinary Anaesthesia and Analgesia Langley Prize.

Current research interests continue in anaesthesia and physiology. Has published numerous papers on anaesthesia and acted as the main supervisor for six graduate students in veterinary anaesthesia and physiology.

Dr Nyman now works as a freelance consultant in anaesthesia, with work ranging from clinical anaesthetic services, teaching and research.

She also runs a farm with her husband Erik and daughters Emma and Maja. Interests include riding, horse breeding, skiing, music.

Introduction to ventilation and ventilators

A prime requirement during anaesthesia is maintenance of adequate respiratory function and pulmonary gas exchange. The ventilation requirement for oxygen uptake and carbon dioxide elimination varies with the metabolic requirement of the animal, i.e. body size, activity level, body temperature and the depth of anaesthesia. Respiratory dysfunction during general anaesthesia is caused by disruption of physiological mechanisms as well as anatomical and mechanical factors. Although hypoventilation with increased levels of arterial carbon dioxide tensions (PaCO_2) is commonly measured during general anaesthesia, intermittent positive ventilation (IPPV) is often utilized on a "need to" rather than routine basis. For any given metabolic situation PaCO_2 and alveolar ventilation (V_A) are directly and inversely related; if V_A is doubled (by IPPV) PaCO_2 will fall by approximately 50%. However, changes in PaCO_2 will affect the acid-base balance and the cardiovascular function.

The characteristics of the lungs and the chest wall differ in different animals

The thoracic cavity and lungs differ between animal species both in anatomy and function. It is well known that dogs and cats are adapted to rest or sleep in a sternal, lateral and even in supine position whereas larger animals, such as cattle and horses, never sleep on their back. Large animals and some athletic dog breeds have a narrow thorax with a large vertical lung distance. In addition, the diaphragm slopes diagonally downward and forward so that the lungs lie on top of the abdominal cavity when the animal is standing. This anatomical arrangement, with the largest part of the lungs situated in the dorsal part of the thorax with little lung tissue lateral to the heart, may be a functional adaptation in athletic species. Turning these animals upside down during anaesthesia will however reverse the favorable situation, causing the lungs to be squeezed down under the weight of the abdominal viscera. The tracheal dimension in relation to body size also varies amongst species. In flight animals a high flow of air through the airways is efficient for improved ventilation during strenuous exercise. The cost of a wider trachea is a larger dead space ventilation. Dead space ventilation in a giraffe is actually smaller than in a horse, probably due to the relatively longer but narrower trachea in the giraffe.

Although different animal species use different mechanisms to match their ventilation and perfusion, either by collateral ventilation or pulmonary hypoxic vasoconstriction, or a mix of both, healthy animals achieve the same result. The strategy is probably related to the differences in lung structure and function. Cattle and pigs have no collateral ventilation and are dependent on redistribution of blood flow by pulmonary vasoconstriction. Dogs, cats and sheep depend on collateral ventilation with little contribution from hypoxic vasoconstriction whereas the horse primarily depends on hypoxic vasoconstriction with only a small contribution from collateral ventilation.

The mechanics of the respiratory system

The forces that are applied to the respiratory system will determine the ventilation, whether the forces are generated by the respiratory muscles or by an external ventilator. The impedance to breathing consists of two major components, the elastance of the lung and the chest wall, and the resistance to gas flow in airways and to tissue movement. The inverse of elastance (e), compliance (c), is more commonly used in pulmonary physiology and is thus: $c = 1 \div e$. The mechanics variables, compliance and resistance, can also be used to quantify the severity of lung function impairment and they are often used for diagnostic and prognostic evaluations. The recording of compliance is also used in the guidance of the ventilator setting. Compliance is reduced during anaesthesia although the mechanisms are not fully understood. The fall in FRC, the formation of atelectasis and possible decrease in surfactant function may all contribute to the reduced compliance. Almost all anesthetic

Introduction to ventilation and ventilators

agents (halogenated compounds, neuroleptic agents, barbiturates and derivatives), both inhalational and intravenous drugs, reduce respiratory muscle tone. This causes a shift in the balance between the outward forces of the respiratory muscles and the inward forces caused by the elastic recoil of the lung tissue, so that functional residual capacity (FRC) is reduced. The net effect of change in body position and anesthesia is a decrease in FRC from an average of 3.4 to 2.2 liters (example from a 75 kg, 180 cm tall man). The fall is close to what can be reached during maximum expiration, the so-called residual volume. Breathing at this lung volume is highly uncomfortable. Not only will airways close in the anesthetized subject, also alveoli may collapse, so called atelectasis. Atelectasis will occur in the bottommost lung regions and will comprise 10-15% of the total lung tissue in the average subject. It may exceed 30-40% of the lung in what may still be considered an uneventful anesthesia! However, it will cause considerable impairment of oxygenation of blood. There are two prerequisites for atelectasis to develop during anesthesia: 1/ loss of respiratory muscle tone with subsequent fall in lung volume - this promotes airway closure; 2/ ventilation with highly absorbable gas that will easily be taken up by the blood flow so that the gas pocket behind the closed airway is emptied. Thus, ventilation with 100% O₂ causes atelectasis in 5-7 minutes whereas air (the major component (79%) being the poorly soluble gas N₂) takes several hours to absorb and to cause lung collapse. It has indeed been shown that atelectasis in the anesthetized subject occurs already during the induction of anesthesia when pre-oxygenation is provided. If pre-oxygenation is performed with 80% O₂ (makeup gas N₂) much less atelectasis is produced.

Recruitment of collapsed lung increases compliance, reasonably explained by more lung tissue being available for inflation by gas. However, observations in a human study show that this is not the full explanation. Thus, a vital capacity maneuver opened up collapsed lung and increased, as expected, compliance, but during the following hour compliance fell and to the same extent whether lung tissue began to collapse again or if the lung was maintained open. This suggests that another or additional mechanism is of importance, possibly changes in the surfactant properties. Resistance will be elevated in the presence of airway obstruction, for example by bronchospasm as in asthma and by destruction of the airway wall as in chronic bronchitis. Measurements of the respiratory mechanics in the anesthesia and intensive care situation do mostly include all parts of the respiratory system, chest wall and lungs. The measurements are relatively simple in the mechanically ventilated animal, airway pressure and flow measurements providing information for overcoming total impedance. To enable distinction between total respiratory compliance and resistance, end-inspiratory and expiratory pauses are required to produce short moments of zero gas flow. If constant flow is administered during inspiration, the sudden cessation of flow at end-inspiration causes a rapid drop in pressure and this drop divided by inspiratory gas flow will give respiratory resistance. Similarly, compliance will be calculated as the insufflated volume divided by end-inspiratory minus end-expiratory pressure. It is often desirable to make measurements of the compliance and resistance of the lung per se, separate from compliance and resistance of the chest wall. The separate recording of lung and chest wall mechanics requires that pleural pressure, or its substitute, esophageal pressure, be measured. The esophageal pressure is normally recorded with an esophageal balloon catheter that is placed in the lower third of the esophagus.

Ventilation and perfusion distribution

Relatively similar vertical distributions of ventilation and blood flow ensure good matching between them and optimum gas exchange with an arterial oxygen tension (PaO₂) of around 10-13 kPa (75-100 mmHg) with a magnitude of ventilation that causes an arterial carbon dioxide tension (PaCO₂) of around 5.5 kPa (40 mmHg).

In dogs and horses blood flow distribution is more even between upper and lower lung regions than in man. A higher vascular resistance in the lower, anterior lung regions than in upper regions can explain this. An animal that is mostly standing on his four legs (prone) may benefit from this uneven distribution of vascular resistance that causes more even perfusion. Man may not benefit from this since he is moving between different positions so that one optimum posture cannot be identified. With an increase in intrathoracic pressure, as with the application of IPPV and PEEP, the return of blood flow from systemic veins into the thoracic cavity and the right heart is impeded and cardiac output is reduced. Fluid loading of the vascular system and use of vasoactive and cardiovascular stimulating drugs can counter the fall in cardiac output. Moreover, with increase in intrathoracic pressure, blood flow is forced down towards dependent regions, i.e. dorsal regions if the subject or animal is in the supine (dorsal recumbent) position. Already a moderate PEEP of 10 cm H₂O applied to both lungs in the lateral position may force all blood flow to the dependent lung with virtually no perfusion of the upper lung. The distribution of blood flow in the lung is a major determinant of gas exchange and since blood flow can be manipulated both by pharmacological and mechanical means this area can be of considerable interest for animal research.

Pulmonary gas exchange

The gas exchange in the lung is determined mainly by the matching of alveolar ventilation and blood flow (V_A/Q). A good match results in optimal oxygenation. The assessment of gas exchange can be based on an arterial blood gas analysis that provides an overall value (single compartment analysis) or different multicompartment models. The latter will provide better insight in mechanisms behind an impaired oxygenation or CO₂ elimination.

There is considerable difference between different species during anaesthesia.

Dog: The efficiency of oxygenation is slightly decreased in dorsal recumbency during anesthesia. However, VA/Q matching is better than in man with a narrow unimodal distribution of V_A/Q and a small log SDQ. Shunt does not develop, opposite to man. It has also been shown that atelectasis does not develop. However, regions with high V_A/Q develop, in particular when a positive end-expiratory pressure (PEEP) is applied. This is caused by a tiny perfusion of so called corner vessels in the uppermost part of the lung.

Pig: During anaesthesia the V_A/Q matching is less efficient than in the dog with larger scatter of V_A/Q ratios and the pig does also develop some shunt.

Sheep: Sheep have been studied standing in a cradle awake and they show a broad unimodal VQ distribution with a much larger scatter than in waking man. Sheep have well-developed interlobular septa that reduces collateral ventilation and this may explain the poorer V_A/Q match.

Introduction to ventilation and ventilators

There is further slight worsening of the V_A/Q match during anaesthesia in the dorsal recumbent position and shunt is as large as in anesthetized man.

Rabbit: In the anesthetized, mechanically ventilated rabbit in dorsal recumbency a surprisingly large V_A/Q scatter has been found, not the least in view of the small size of the animal with a weight of 3-4 kg and a vertical lung distance of 7-8 cm. However, no or minor shunt was observed. The rabbit has good collateral ventilation, which would also have prevented poor matching. However, it is possible that there are species differences with regard to hypoxic pulmonary vasoconstriction - the rabbit is well known to easily develop hypoxemia during anaesthesia.

Horse: Standing awake horses (trotters) with the weight of approximately 500 kg show a surprisingly good V_A/Q matching, comparable to the healthy awake man and no or minor shunt was noticed. In view of the high vertical lung distance of about half a meter, this might seem surprising, not the least when comparing with the worse matching in standing awake sheep with less than half the vertical lung distance of the horse. Also, the anesthetized rabbit showed considerable mismatch despite much smaller lung distance. A cranial displacement of the diaphragm has been shown in the horse during inhalation anesthesia and spontaneous breathing and a concomitant decrease in FRC to about 50% of the value in standing horse. According to Sorenson and Robinson, closing capacity exceeds FRC in dorsal recumbency, and they suggested that the loss of ventilated lung volume probably was due to compression of the lung by the weight of the thoracic and abdominal viscera. Conventional mechanical ventilation in dorsal recumbency reduces cardiac output and does in general not improve gas exchange compared to spontaneous breathing, except for normalization of PaCO_2 . With the horse in lateral recumbency, conventional mechanical ventilation reduces the venous admixture and improves PaO_2 to some extent but the cardiac output is reduced concomitantly. This may be attributed to impeded venous return to the heart by the increased intrathoracic pressure or to lowered PaCO_2 by improved ventilation.

Giraffe: Gas exchange was studied in a young giraffe with the weight of 500 kg when it was given a light anaesthesia for the application of a plaster in the treatment of a foot fracture. Measurements of the V_A/Q were made during fentanyl anaesthesia in a sitting position with the head kept up in a cradle. During spontaneous breathing a good match of the V_A/Q was seen, better than in anesthetized man. This is surprising in view of the tall lung height of approximately 0,6-0,7 meter. Another unexpected finding was an ordinary dead space ventilation of the same size as in the horse. The airway dead space was calculated to less than one litre and in view of the more than 3-metre long trachea one may have anticipated a larger volume (own unpublished observations). The explanation is that the giraffe has a very narrow trachea, reducing dead space but increasing airway resistance in the event of rapid breathing.

Mechanical ventilation and ventilators

Mechanical ventilation with supplemental oxygen is indicated for patients with life-threatening apnea or when the respiratory system can no longer provide adequate oxygenation and/or alveolar ventilation. However, many veterinarians and nurses do not understand the altered physiology of mechanically ventilated patients. Also, confusion often exists over ventilator terminology and no widely accepted best mode of mechanical ventilation is available. All forms of mechanical ventilation have potential complications, which include barotrauma and reduction of cardiac output. Although today's ventilators are highly reliable, there is no substitute for constant surveillance by competent personnel.

A ventilator is a machine that generates a controlled flow of gas into a patient's airways. Gas is delivered to the patient using one of many available modes of ventilation. The most commonly used modes of ventilation include; control ventilation where the machine initiates and delivers each breath, assist-control ventilation where patient initiates or triggers a machine-delivered breath and intermittent mandatory ventilation where the patient can breathe spontaneously between mandatory ventilator breaths.

The magnitude, rate and duration of flow are determined by the operator. The pattern of flow may be sinusoidal (normal), decelerating or constant. Flow is controlled by an array of sensors and microprocessors of the ventilator. Flow is either volume targeted and pressure variable, or pressure limited and volume variable. In volume controlled modes, a desired tidal volume is delivered at a specific flow (peak flow) rate, using constant, decelerating or sinusoidal flow patterns: the airway pressure generated may be higher than is desirable. In pressure controlled modes, flow occurs until a preset peak pressure is met over a specified inspiratory period. The flow pattern is decelerating in pressure controlled modes but the tidal volume may be lower than that desired and the delivered tidal volume may vary as pulmonary mechanics change over time.

Airway pressures with mechanical ventilation differ from normal breathing. During spontaneous breathing airway pressure alternates between negative pressure on inspiration and positive pressure on expiration. In the most common mode of mechanical ventilation, intermittent positive pressure ventilation (IPPV), airway pressure is positive on inspiration. Exhalation is passive, utilizing the recoil nature of the chest to let air be exhaled, and is physiologically similar as during spontaneous breathing. Therefore, spontaneously breathing animals may maintain cardiovascular function better than anaesthetized animals in which ventilation is controlled.

Ventilator settings

The anaesthetist should be able to comfortably order the following settings. There are other ventilator settings and alarm limits, but the listed are, in my opinion, main and additional settings that the therapists need to be aware of.

1. Mode of ventilation: controlled, assisted or mandatory.
2. Respiratory Rate: Dogs, usually 8-14 breaths/min to start, cats 10-16 breaths/min and horses 6-8 breaths/min.
3. Tidal Volume: Controversial; a safe level is about 10 cc/kg body weight for large animals and 15-20 ml/kg for small animals.
4. FIO_2 : Varies from 0.21 to 1.00, depending on clinical circumstances.
5. I:E ratio: 1:2 or less depending on the respiratory rate. Inspiratory flow rate; generally set between 60 and 100 l/min. This flow rate determines the inspiratory:expiratory time, I:E ratio. The faster the flow rate, the quicker inspiration and the longer the animal has to exhale.

Introduction to ventilation and ventilators

Additional settings:

6. Peak inspiratory pressure limit for patients receiving ventilation. Generally set at 15-20 (30) cm H₂O; above this limit the ventilator "cuts off" and no more volume is delivered
7. Sensitivity level, for animals who can trigger the ventilator; set by an analog-type dial, this allows a slight inhalation to trigger the machine to deliver a full ventilator breath. When the sensitivity dial is turned all the way to the off position, no amount of patient effort will initiate a machine breath, and the machine is in the controlled ventilatory mode. As sensitivity is "dialed in," the ventilator changes to the assist-control mode, and it becomes much easier for the patient to initiate a machine breath. The sensitivity dial is not calibrated in units, but the patient's inspiratory effort will show up as a negative (subatmospheric) deflection on the ventilator's pressure dial, usually between - 0.5 and 2.5 cm H₂O.
8. Positive end- expiratory pressure, PEEP.
On some ventilators, PEEP can be set by dialing to a desired setting. The dial regulates an expiratory resistance valve that keeps airway pressure above atmospheric pressure at endexpiration. PEEP is a method of improving oxygenation that can be used in any ventilatory mode. PEEP can be applied to an intubated, mechanically ventilated patient. If airway pressure remains above the ambient pressure during spontaneous breathing, in this case the technique is called continuous positive airway pressure, CPAP. Applying PEEP may have effects on cardiac output and oxygen delivery. The PaO₂ can increase while cardiac output and arterial oxygen delivery are decreasing. Optimal PEEP for a given patient can only be found by trial and error.
9. Inspiratory plateau or hold. Inspiratory plateau was originally used to improve oxygenation by providing a longer time for gas exchange, but PEEP is now used instead. The inspiratory plateau or hold adds resistance to the expiratory circuit; the effect is to prolong inspiration and create a transient plateau pressure.

Discontinuing Mechanical Ventilation

In general, the PaCO₂ must increase to stimulate breathing or the patient must regain a level of consciousness that promotes spontaneous breathing. Progressive reduction of breaths/minute usually rapidly increase PaCO₂ and stimulates breathing. Assisted ventilation and oxygen should be provided until the respiration rate and tidal volume are adequate.

More details on anaesthesia ventilators for animals will be discussed.

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Introduction to ventilation and ventilators

Introduction to ventilation and ventilators

Ventilation in small animal intensive care

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Lecturer in Emergency and Critical Care Royal Veterinary College

Amanda Boag graduated from Cambridge University in 1998. She then completed rotating Small Animal Internships at both the Royal Veterinary College, London (1998-99) and the Veterinary Hospital of the University of Pennsylvania (1999-2000). She returned to the Royal Veterinary College in September 2000 to pursue a residency in Small Animal Internal Medicine and gained her American Diploma in 2003. She has subsequently completed an alternate track residency in Emergency and Critical Care achieving Diplomate status in Emergency and Critical Care in 2005. She is currently a lecturer in Emergency and Critical Care at the Royal Veterinary College.

Ventilation in Small Animal Intensive Care

In human intensive care units, mechanical ventilation is widely used and a high proportion of critically ill humans will undergo a period of ventilation during their ICU stay. Experience in the veterinary field is more limited; however mechanical ventilation has been increasingly used over the last 15 years in the management of critically ill small animal veterinary patients. Although negative pressure ventilators have been developed and were some of the first mechanical ventilators used on a large scale basis during the human polio epidemics in the early 20th century, they are not routinely used in clinical practice. The focus of this lecture will be on the use of positive pressure ventilation (PPV) in clinical veterinary patients.

Mechanical ventilation is a costly treatment option both in terms of the equipment required and the nursing and veterinary time and expertise involved. For the owner it can be an emotionally draining experience and with no guarantee of a successful outcome. However in certain patient groups it is life saving and offers patients that would otherwise require euthanasia a chance to recover fully. It also represents a humane treatment option in patients with severe dyspnoea that cannot be relieved using less invasive methods.

Candidates for ventilation – how do I decide my patient needs ventilation?

There are two principle groups of patients that may require prolonged ventilation in an ICU representing the two major categories of respiratory failure: those with significant hypoventilation and those with significant hypoxia that is not responsive to less invasive means of oxygen supplementation.

Ventilatory respiratory failure— hypoventilation is defined as a PaCO_2 greater than 45mmHg. Mild hypoventilation is not uncommon especially in patients recovering from anaesthesia and does not usually require specific management. However severe hypoventilation with a sustained PaCO_2 greater than 60 mmHg warrants treatment. The causes of hypoventilation that may require treatment by mechanical ventilation are:-

- Neuromuscular disease e.g.
 - Myasthenia gravis
 - Tetanus/botulism
 - Peripheral polyneuropathy (e.g. tick paralysis)
- Central nervous system disease e.g.
 - Cervical spinal cord disease
- Respiratory muscle fatigue with severe parenchymal disease

It should be remembered that the term hypoventilation does not imply anything about the patient's respiratory rate and effort. Patients with hypoventilation secondary to upper airway obstruction may have significant hypercarbia yet a rapid respiratory rate with significant respiratory effort whereas patients with neuromuscular disease may have the same degree of hypercarbia yet minimal movement of the ventilatory apparatus. Patients with hypoventilation secondary to neurological or neuromuscular impairment may not show overt clinical signs until their PaCO_2 reaches very high levels (80mmHg). At this point they often start to make gasping, open mouth breathing efforts still with minimal chest wall movement. Arterial blood gases should be proactively monitored in patients considered to be at high risk of hypoventilation especially post-operative cervical surgery patients.

Hypoxaemic respiratory failure – hypoxaemia is defined as a PaO_2 less than 80mmHg with severe hypoxaemia being defined as a PaO_2 less than 60mmHg. Although less invasive means of oxygen supplementation (e.g. nasal oxygen catheter, oxygen cage) should always be considered first, some patients will be unable to maintain a $\text{PaO}_2 > 60\text{mmHg}$ despite this and these patients should be considered candidates for ventilation. Not only can high fractional inspired oxygen be reliably achieved but PPV also improves blood oxygenating efficiency which allows for a reduction in the inspired oxygen concentration. Severe hypoxaemia may be seen with any pulmonary parenchymal disease including pulmonary contusions, pneumonia and cardiogenic and non cardiogenic oedema.

An important consideration in the decision to ventilate a hypoxaemic animal is the patient's work of breathing and degree of distress. Although it is difficult to measure objectively in a clinical setting it should be remembered that most parenchymal diseases cause the lungs to have decreased compliance (i.e. they become stiffer) and thus the animal has to work harder and harder to achieve the same degree of oxygenation. In normal animals only about 2% of total oxygen consumption is used by the ventilatory system however this can increase to 25-50% with severe parenchymal

Ventilation in small animal intensive care

disease. Any benefit of improved oxygen uptake may be negated by the increased effort and oxygen consumption used to achieve it! Ultimately the respiratory muscles will fatigue and hypoventilation will ensue further depressing the PaO_2 .

Although the decision to place a patient on the ventilator should not be taken lightly, it should also not be left until the patient is close to respiratory arrest – not only does this lead to increased distress to the patient, it is also likely to lead to a less successful outcome.

The ICU ventilator

A large number of different ventilators are available for use in the ICU and increasingly sophisticated machines are becoming available. Typically ICU ventilators have the option of a number of different ventilatory modes (both controlled and assisted), the ability to alter fractional inspired oxygen concentration and the ability to add positive end expiratory pressure (PEEP).

Generally speaking when ventilating a patient with normal lungs (i.e. ventilatory failure), the initial ventilator settings are chosen to achieve the following:-

- Tidal volume of 8-12 ml/kg
- Peak airway pressure of 10-20 cmH_2O
- Ventilatory rate of 10-20 breaths per minute
- An I:E ratio of 1: 2-3
- End expiratory pressure of zero.

An FiO_2 of 100% is often used whilst the patient is settled onto the ventilator but this is commonly decreased soon afterwards to 30-40%. The aim is to achieve a PaCO_2 of 35-45 mmHg with a PaO_2 of around or just above normal (80-140 mmHg). The above settings are very likely to achieve this in a patient with normal lungs.

When ventilating a patient with diseased lungs, the above settings may be insufficient to maintain oxygenation and ventilation. Although oxygenation can be improved by increasing the FiO_2 , it is not advisable to maintain patients on an FiO_2 greater than 60% for prolonged periods due to the risk of oxygen toxicity. Strategies that can be used for maintaining PaO_2 in this situation include:-

- The addition of PEEP
- Increase in ventilation rate
- Alteration in I:E ratio with increased inspiratory time

Peak airway pressures may also be allowed to climb although should be kept below 35 cmH_2O (dependent on PEEP). It is not advisable to increase the tidal volume significantly as this has the potential to lead to volutrauma - in fact current lung protective ventilatory strategies recommend a smaller than normal tidal volume of 4-8ml/kg. Permissive hypercarbia where a PaCO_2 that is above the normal range is tolerated in order to avoid using more aggressive ventilatory strategies is also currently advocated.

Ventilator modes

A number of different ventilator modes may be utilised and the method chosen will depend on a number of factors including clinician familiarity, the ventilator available, the size of the patient and the nature of its disease and the stage of ventilation (i.e. maintenance vs weaning). Volume control and pressure control modes are both examples of full ventilatory support where the ventilator essentially performs all of the work of breathing. These are most commonly used during the early stages of ventilation. Patient-ventilator asynchrony may develop if the patient attempts to breathe and thus patients are generally kept anaesthetised or heavily sedated. The key difference between volume and pressure support is that in volume support the machine delivers a breath of a preset tidal volume whereas in pressure support the machine delivers a breath with a preset amount of inspiratory pressure.

There are a number of partial ventilatory support modes where the patient is able to provide increasing amounts of the ventilatory effort. In some of these modes ventilatory effort by the patient triggers a machine breath; in others a smaller number of mandatory machine breaths are delivered by the ventilator with the patient able to take their own breaths at other times. Examples of these modes include assist/control, synchronous intermittent mandatory ventilation (SIMV) and pressure support. Continuous positive airway pressure (CPAP) is also considered to be a mode of partial ventilatory support although machine breaths are not delivered. These modes are generally used during the weaning period.

Maintaining an animal on a ventilator

There are a number of important considerations when maintaining a patient on a ventilator. Twenty-four hour care by experienced personnel is essential as issues may arise at any time. The most important considerations are summarised below:

Managing ventilatory settings: the patient's ventilatory and oxygenation status must be closely monitored. End tidal CO_2 and pulse oximetry may be used as continuous monitoring tools but will need to be checked against arterial blood gases at regular intervals. The frequency of arterial sampling will be dependent on the stability of the patient and its disease, but may also be compromised by patient factors such as size and ease of arterial access. Ideally arterial blood gases should be checked every time patient status changes, following significant changes in ventilator settings or if the less invasive monitoring tools show a significant change. The clinician must be prepared to change settings as the patient's status changes. It is also important to have available a manual ventilation source (e.g. Ambu bag) in case it becomes necessary to disconnect the patient temporarily for any reason.

Ventilation in small animal intensive care

Airway maintenance: Most patients are initially managed with an endotracheal tube in place although it may be advantageous to place a tracheostomy tube especially in patients who may require ventilation for several days. Whichever method of airway access is used, the tube must be cuffed and a high volume low pressure cuff is preferred. The cuff should be deflated and the tube position moved at regular intervals (every 4-6 hours) to reduce the risk of tracheal mucosal damage. When using a tracheostomy tube with an inner cannula, the cannula should be removed and cleaned every 4 hours. With endotracheal tubes or tracheostomy tubes without inner cannulas, the tube should be **gently** suctioned intermittently. The frequency of suctioning will be dependent on the amount of secretions produced but starting with every 4-6 hours is reasonable. The entire tube should be replaced by a new sterile tube every 24-48 hours. Hydration of the airways should be maintained by the use of a humidifier system within the ventilator circuit.

Sedation/anaesthesia: Ventilated patients commonly need some form of sedation or full anaesthesia especially when full ventilatory support is being provided or when an endotracheal tube is being used. Patient-ventilator asynchrony ("fighting the vent") has a number of negative effects and should be avoided initially by achieving an appropriately deep plane of sedation. As the patient becomes more conscious (which may well be desirable), the ventilator mode should be tailored to the patient's respiratory pattern. There is no such thing as a perfect sedation protocol for these patients and the patient's cardiovascular status and any comorbidities must be taken into account when deciding on a protocol. Commonly used drugs include opioids, benzodiazepines, barbiturates and propofol. These may be delivered as constant rate infusions or intermittent boluses and a combination approach is often required.

Nutrition: It is important to consider the nutritional needs of ventilated patients so a strategy can be implemented at an early stage. Dependent on the patient, early placement of an enteral feeding tube or parenteral nutrition should be considered. Over feeding should however also be avoided.

Mouth care: Ventilated patients will develop colonisation of their oropharynx commonly with gram negative bacteria and this will predispose to nosocomial infection. They are also prone to developing oral ulcers especially on the tongue if it is left in one position (especially if outside the mouth) for prolonged periods. The mouth and tongue should be gently cleaned every 4 hours with sterile saline followed by a dilute chlorhexidine mouth wash. If the tongue is outside the mouth (as is commonly the case in patients with endotracheal intubation), dessication should be prevented by applying a small amount of glycerine every 4 hours

Body position and physiotherapy: The patient's body position should be changed every 4 hours. There is some evidence that sternal recumbency results in improved oxygenation in patients with parenchymal disease and should be maintained if possible. In patients being ventilated for several days, passive range of movement exercises for the limbs should be initiated. The patient should be monitored closely for the development of any sores or pressure points.

Eye care: The ocular surface can dry rapidly and lubricant eye drops should be instilled every 2-4 hours.

Bladder care: Ventilated patients are unable to urinate normally. The bladder must be checked regularly and may need to be expressed. Strict attention to hygiene is required to prevent urine scalding. In many patients, placement of a urinary catheter aids management. Considering that the catheter is likely to be in place for several days, it must be placed in an aseptic fashion. Monitoring urine output can help to optimise fluid therapy for the patient.

Complications of ventilation

Mechanical ventilation may be associated with a number of complications including:-

- Thoracic bloodflow impairment – venous return to the heart is impaired by the increased intrapleural pressures associated with PPV. Cardiovascular parameters should be closely monitored.
- Pneumothorax – PPV may lead to the development of a pneumothorax following marginal alveolar rupture and should be one of the top rule outs if a patient suddenly becomes hypoxic or develops patient-ventilator asynchrony. If a pneumothorax occurs, a chest drain should be placed and attached to a continuous drainage system.
- Nosocomial pneumonia – this occurs commonly in patients who are ventilated long term. Prophylactic antibiotics are not recommended as they will only predispose to the development of pneumonia with bacteria resistant to those antibiotics. Vigilance is however required and an endotracheal wash with culture performed if the development of pneumonia is suspected. Antibiotic therapy can then be tailored to the specific bacteria involved.

Outcome

There have been several small retrospective veterinary studies looking at the outcome following mechanical ventilation in different populations of dogs (references below). In general patients who are ventilated for ventilatory failure have a better outcome than those ventilated for hypoxaemic respiratory failure. Cats seem to have a worse outcome than dogs which may be related to the nature of the diseases requiring ventilation in the cat or to the difficulties associated with ventilating smaller patients successfully.

Conclusion

Mechanical ventilation represents a viable treatment option for the management of certain diseases conditions in small animal patients. Although demanding on both time and finances, it can be very rewarding and can result in good long term outcomes.

Ventilation in small animal intensive care

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Ventilation in small animal intensive care

Ventilation in small animal intensive care

Ventilation in neonatal foals

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Ventilation in Neonatal Foals

Introduction

Mechanical ventilation is a therapy that is untaken on relatively few foals, as it is only available at a few hospitals in Europe. However, with good patient selection and correct application, mechanical ventilation is both a clinically and financially worthwhile therapy. At the hospitals that I have worked at in Europe and the USA, approximately 5-10% of critically ill foals are ventilated¹.

Clinical indications

Foals that are candidates for mechanical ventilation fall into two broad groups:

- 1) Conditions where there is a failure of neurological control of breathing:
 - Perinatal Asphyxia Syndrome
 - Botulism
 - Prematurity
 - Avermectin (usually moxidectin) toxicity
- 2) Conditions of primary lung pathology:
 - Infectious pneumonia (bacterial or viral)
 - Acute Lung Injury
 - Acute Respiratory Distress Syndrome
 - Neonatal Respiratory Distress Syndrome

Generally, foals that fall into group 1 present with hypercapnia and a relatively normal Alveolar-arterial oxygen gradient. Group 2 foals often present with hypoxaemia that is variably accompanied by hypercapnia.

The prognosis between these two groups is markedly different. Group 1 foals have a good to excellent prognosis (greater than 80% discharge rate from the hospital^{2,3}), providing mechanical ventilation is instituted early. Group 2 foals have a much more guarded prognosis. The timing of institution of mechanical ventilation is vital to success in both groups. There has been a tendency in some clinics to reserve mechanical ventilation for moribund patients, with inevitable poor outcomes.

Preparation for mechanical ventilation

Nasotracheal intubation is greatly preferred for ventilation. Use of a nasotracheal tube (as opposed to an orotracheal tube), allows mechanical ventilation without sedation or anaesthesia – foals tolerate mechanical ventilation remarkably well! The only foals that I have had to sedate are those which are showing jerky muscular movements as part of their disease process (usually foals with perinatal asphyxia syndrome).

Because of the relative ease of placing and maintaining a nasotracheal tube, tracheostomy is only very rarely utilised to ensure an airway. The largest diameter nasotracheal tube that it is possible to pass should be employed – for a term, 45-50kg, Thoroughbred foal it is usually possible to place a 10mm internal diameter, 55cm long cuffed tube.

The foal should be maintained in sternal recumbency on a soft mat, if possible. This is to promote equal ventilation of both lungs. If an active humidifier/warmer is being used in the circuit, the circuit should be pre-warmed if possible to reduce 'rain-out'. I generally use Heat and Moisture Exchange (HME) filters to prevent the problems associated with maintaining an active humidifier.

Ventilation in neonatal foals

Initial settings

Initial settings depend on the underlying disease process, and arterial blood gas values obtained prior to initiation. The mode of ventilation I most commonly use in foals is Synchronised Intermittent Mandatory Ventilation (SIMV) with Pressure Support (**SIMV-PS**). There are two periods within each ventilation cycle in this mode:

- 1) SIMV period
During this period, the machine waits for the foal to trigger a breath (by generating a negative pressure less than the trigger sensitivity). If the foal triggers a breath, a full mechanical breath is delivered according to the settings on the ventilator. After the breath is delivered, the machine switches to the spontaneous period for the rest of the ventilation cycle. If the foal makes no sufficient respiratory effort during the entire SIMV period, a full mechanical breath is delivered at the end of the SIMV period without a foal trigger.
- 2) Spontaneous period
During this period, respiratory efforts by the foal result in supported spontaneous breathing, rather than full mechanical breaths. In SIMV without pressure support, the only support is that the oxygen concentration that the foal breathes in from the circuit may be greater than room air. However, there is some extra work of breathing to overcome the resistance of the circuit.
Pressure support – the foal triggers the breath, set by the trigger sensitivity. During this breath, the ventilator applies a set pressure. When the inspiratory flow reaches a predetermined (usually not user controlled) percentage of the peak flow, the ventilator switches into expiration and the pressure is switched off. In many ventilators, this switch to expiration occurs at 25% of peak flow. The breath rate is used as a safety feature in pressure support, as a time-gate to prevent the ventilator being stuck in inspiration if there is a leak in the circuit and flow does not decelerate. If pressure support is used together with PEEP (positive end-expiratory pressure), it is added to PEEP during inspiration.

'Typical' initial settings:

Mode: SIMV-PS
Tidal Volume: 6-8ml/kg
SIMV breaths per minute: 20-30
PEEP: 5-10cm H₂O
Pressure Support: 10cm H₂O
Trigger Sensitivity: -2cm H₂O
I:E ratio: 1:2
FIO₂: Usually start with 1.0, but rapidly try to decrease below 0.6

Aim for:

Plateau pressures below 30cm H₂O
As low FIO₂ as possible
Good ventilator-patient synchrony

Foals that do not make any respiratory effort are usually ventilated in Assist-Control modes (however this is effectively what SIMV will deliver if the foal makes no spontaneous breath attempts). Occasionally foals with severe hypoxaemia cannot be adequately ventilated with volume-controlled ventilation, and I have had some success with pressure-controlled ventilation and reverse I:E ratios (still not requiring sedation). Other modes of ventilation, such as high-frequency jet ventilation⁴, have been described in the foal, but are not commonly available.

General maintenance activities

- Regular deflation/re-inflation of the cuff
- Respiratory toilet
- Culture respiratory secretions
- Thoracic radiographs
- Naso-tracheal tube exchange

Alternatives or adjuncts to mechanical ventilation

- Intranasal oxygen therapy
- Nebulisation of antimicrobials and bronchodilators
- Methylxanthine derivative therapy
- Sildenafil therapy
- Inhaled nitric oxide

Weaning from mechanical ventilation

Criteria:

- FIO₂ ≤ 0.40
- paO₂ > 60mmHg
- Foal making good respiratory efforts

Ventilation in neonatal foals

Options:

- CPAP
- Pressure Support
- T-piece

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Ventilation in neonatal foals

Ventilation in neonatal foals

Food for Thought

**Chaired by
Miss Alex Dugdale**

**Speakers
Miss Amanda Boag
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Animal Health

Interpretation of blood gas and electrolyte results

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Interpretation of blood gas and electrolyte results

Blood gas analysis, strictly speaking, is the measurement of pH, $p\text{CO}_2$ and $p\text{O}_2$ with calculation of HCO_3^- and base excess (BE). It provides useful information on three physiologic processes namely oxygenation, ventilation and acid base balance. Venous blood can be used for the assessment of acid base balance in the majority of clinical situation and also provides useful information on ventilation however arterial blood is required for assessment of oxygenation. Many blood gas machines also measure other parameters useful in the management of the critically ill patient such as electrolytes, lactate and glucose.

Arterial blood is usually obtained from the dorsal metatarsal artery in patients weighing more than 7kg and from the femoral artery in smaller patients. It can be obtained by single arterial puncture or an arterial catheter can be placed to facilitate sampling at multiple time points. The use of a syringe specifically designed for arterial puncture (e.g. the BD preset produced by BD Vacutainer systems) facilitates arterial sampling. If these are not available, a standard 1ml syringe usually with a 23 or 25G needle may be used. Samples must be handled anaerobically and should be run as soon as possible. Caution should be exercised when considering arterial sampling in patients who are coagulopathic or thrombocytopenic.

Clinical use of arterial blood gas

Although it is usually not challenging to recognise that a patient is in respiratory distress, arterial blood gas analysis can provide a wealth of information about the underlying disease process. It can help the astute clinician to formulate a differential diagnosis list and allows accurate evaluation of the severity of the respiratory impairment and an objective way of tracking patient progression.

Oxygenation

PaO_2 is the partial pressure of oxygen in arterial blood and, with normal lung function, should be in the region of 5 x the fractional inspired oxygen concentration (FiO_2). Thus at room air, the PaO_2 would be expected to be around 100mmHg whereas when intubated and on 100% O_2 , a patient's PaO_2 should be about 500mmHg.

A more familiar way of assessing oxygenation is pulse oximetry and whilst this has its place especially in the monitoring of anaesthetised patients, it has significant limitations. Most importantly, due to the sigmoid nature of the oxyhaemoglobin dissociation curve, pulmonary function may be significantly compromised and PaO_2 may be markedly reduced before the saturation drops to any remarkable extent. Arterial blood gas analysis thus provides a more sensitive and accurate way of determining oxygenation. The table below illustrates the expected relationship between PaO_2 and SaO_2 .

	PaO_2 (mmHg)	SaO_2 (%)
Normal	80-110	98-99
Hypoxaemia	<80	<95
Severe hypoxaemia	<60	<90
Lethal hypoxaemia	<40	<75

Interpretation of blood gas and electrolyte results

Hypoxia can occur secondary to a large number of disease processes but these can be categorised into 4 major groups as below:-

- ❖ **Right to left shunt**
This can be further subdivided into cardiac R→L shunts such as is seen with some congenital cardiac disease or pulmonary R→L shunt which may be seen with severe pneumonia, ARDS or anatomic artery-vein shunt. Patients with hypoxaemia secondary to shunts are not responsive to oxygen supplementation as the shunted blood is never exposed to the higher FiO_2 .
- ❖ **Ventilation-perfusion mismatch**
This is the form of hypoxia seen with most parenchymal diseases such as both cardiogenic and noncardiogenic pulmonary oedema, pneumonia and atelectasis. It is responsive to oxygen and probably the commonest form of hypoxia seen in veterinary patients.
- ❖ **Diffusion barrier**
This form of hypoxaemia occurs when there is a thickening of the blood gas barrier with slowing of diffusion such that equilibrium of oxygen between the alveolus and the blood does not occur. It is a rare form of hypoxia in veterinary medicine but is probably the form shown by breeds such as the West Highland White Terrier with pulmonary fibrosis.
- ❖ **Hypoventilation**
The increased PaCO_2 (and hence PACO_2) that defines hypoventilation will lead to a secondary decrease in PaO_2 according to the alveolar gas equation. This form of hypoxia is usually mild and is easily abolished by oxygen supplementation, however the patient's CO_2 retention may be the more significant clinical problem. Changes in CO_2 must be borne in mind when using arterial blood gas to monitor patients with hypoxia secondary to one of the other causes.

A low fractional inspired oxygen concentration is another potential cause of a low PaO_2 and is relevant in some institutions e.g. Colorado veterinary school – it is unlikely however to be cause for concern in the UK!

As PaO_2 would be expected to change with FiO_2 , the ratio between the two is often used as a marker for the severity of parenchymal disease:-

Normal $\text{PaO}_2/\text{FiO}_2$ ratio ~ 480

Severe lung disease $\text{PaO}_2/\text{FiO}_2$ ratio < 300

Criteria for ARDS $\text{PaO}_2/\text{FiO}_2$ ratio < 200

Ventilation

It should be remembered that the definition of hypo- and hyperventilation are specifically related to the PaCO_2 as shown in the table below:-

PaCO_2 (mmHg)	Condition in blood	State of alveolar ventilation
> 45	Hypercapnia	Hypoventilation
35-45	Eucapnia	Normal ventilation
< 35	Hypocapnia	Hyperventilation

Any combination of respiratory rate, depth and effort can reflect any PaCO_2 value and vice versa.

Similarly a differential list can be generated for hypo- and hyperventilation and is summarised below.

Hyperventilation

- Pain/fear/stress
- Decreased arterial oxygen content (marked)
- Neurological disease
- Hyperthermia
- Compensation for a metabolic acidosis

Hypoventilation

- Airway obstruction
- Depression of respiratory centre (drugs, central neurological disease)
- Neuromuscular disease
- Restrictive defects (severe pleural effusion/pneumothorax)
- Respiratory muscle fatigue

Respiratory muscle fatigue is a major concern in patients with severe parenchymal disease and the increasing CO_2 has the consequence of further depressing PaO_2 . These patients are candidates for mechanical ventilation dependent on underlying disease.

Use of the alveolar gas equation and calculation of the A-a gradient

The alveolar-arterial oxygen difference (often called A-a gradient) represents the difference between the partial pressure of O_2 in the alveoli (PAO_2) and arterial blood (PaO_2). It provides a numerical value that gives an idea of how well ventilation and perfusion are matched in the lungs.

Interpretation of blood gas and electrolyte results

The full equation involves calculation of PAO_2 from

$$PAO_2 = FIO_2 (P_B - P_{H_2O}) - PaCO_2/RQ$$

where FIO_2 = fractional inspired O_2
 P_B = barometric pressure
 P_{H_2O} = water vapour pressure
 RQ = respiratory quotient

On room air at sea level with an estimated RQ of 0.9, the equation is simplified to

$$PAO_2 = 150 - 1.1 \times PaCO_2$$

The PaO_2 can then be subtracted from this to calculate the gradient. Normal values are less than 15 (slightly higher is acceptable in an old animal).

The example below illustrates how the A-a gradient may be used

Dog 1

$PaCO_2$ – 65 mmHg

PaO_2 – 70 mmHg

Dog 2

$PaCO_2$ – 23 mmHg

PaO_2 – 75 mmHg

A-a gradient

$$\{150 - (1.1 \times 65)\} - 70$$

$$= 8.5$$

$$\{150 - (1.1 \times 23)\} - 75$$

$$= 50$$

Although dog 1 has a slightly lower PaO_2 , this is entirely due to hypoventilation and the A-a gradient can reassure the clinician that pulmonary function is normal. Dog 2 however, despite having a slightly better PaO_2 , has a markedly elevated A-a gradient telling us that pulmonary function is severely compromised. If dog 2 develops an increase in $PaCO_2$ (e.g. respiratory muscle fatigue or drug induced), then PaO_2 may drop rapidly to levels incompatible with life.

Acid-base abnormalities

Acid base abnormalities can be assessed on a venous sample in most conditions other than circulatory collapse. Assessment of acid-base can help clinicians develop complete problem and differential diagnosis lists and may aid in the identification of some disorders. They can also be monitored to assess response to therapy (e.g. resolution of a metabolic (lactic) acidosis in a shocked patient with fluid therapy).

Although there are many layers of interpretation, the points listed below should help people as they start interpreting acid-base – as with all things the ability to rapidly and accurately interpret these results improves with practice.

- Using pH, determine if acidaemia ($pH < 7.35$) or alkalaemia ($pH > 7.45$) is present
- If acidaemia is present, determine if it is respiratory or metabolic in origin
 - if $PaCO_2 > 45$ mmHg – respiratory
 - if $BE < -4$ mmol/l (or $HCO_3^- < 20$ mmol/l) – metabolic
- If alkalaemia is present, determine if respiratory or metabolic in origin
 - if $PaCO_2 < 35$ mmHg – respiratory
 - if $BE > +4$ mmol/l (or $HCO_3^- > 26$ mmol/l) – metabolic
- Evaluate for any compensatory changes that may have occurred. For example if a primary metabolic acidosis is present, we would expect there to be a compensatory respiratory alkalosis. Remember the rules of compensation:-
 - a change in the respiratory or metabolic component of the acid/base status will induce an opposite or compensatory response to try to bring the pH back to normal.
 - Lungs (i.e. respiratory) compensate quickly in a matter of minutes
 - Kidneys (i.e. metabolic) compensate slowly starting after several hours but taking 4-5 days to reach maximum compensation
 - The presence or absence of compensation gives some idea of chronicity of the disturbance and potentially also the likelihood of a mixed disorder being present
 - Overcompensation **DOES NOT** occur.

Various published charts are available for the degree of compensation expected however with experience you often can get a good idea of what is going on by eyeballing it.

- To fully assess metabolic acidosis, it is necessary to know electrolytes and consequently anion gap. The assessment of whether it is a normal or high anion gap acidosis helps in diagnosing the underlying cause.

Interpretation of blood gas and electrolyte results

Points to remember

1. More than one primary disorder can exist at once e.g. a dog with severe pneumonia may have a respiratory alkalosis and a metabolic acidosis
2. The pH can be normal and there still be significant acid base disorders going on either because of adequate compensation or because of two primary processes
3. Full interpretation cannot be performed without electrolytes
4. Published data for compensation are not as well studied in dogs as people and are not exactly the same therefore caution is recommended when interpreting compensation

Clinical correlates – differential diagnosis of acid-base abnormalities

Metabolic acidosis

Increased anion gap

Lactic acidosis (principally seen with decreased tissue perfusion)

Uraemic acidosis

Diabetic ketoacidosis

Toxicity

e.g. Ethylene glycol, Salicylate

Normal anion gap

Diarrhoea

Renal tubular acidosis

Dilutional acidosis

Posthypocapnic metabolic acidosis

Drug administration

e.g. Carbonic anhydrase inhibitors

Metabolic alkalosis

Chloride responsive

Vomiting of stomach contents

Diuretic therapy

Posthypercapnia

Chloride resistant

Primary hyperaldosteronism

Hyperadrenocorticism

Miscellaneous

Refeeding after fasting

Alkali administration

Respiratory acidosis

Airway obstruction

Respiratory centre depression (neurologic disease or drugs)

Neuromuscular disease

Restrictive disease (e.g. pneumothorax, pleural effusion etc)

Severe pulmonary disease (pneumonia, asthma, PTE etc)

Inadequate mechanical ventilation

Respiratory alkalosis

Hypoxaemia (severe)

Pulmonary disease independent of hypoxaemia

Pain

Exercise

CNS mediated

Excessive mechanical ventilation

Electrolytes

Electrolytes, notably sodium, potassium and chloride, are commonly measured by the point of care analysers that also measure blood gases. They can be used to calculate the anion gap $\{(Na^+ + K^+) - (Cl^- + HCO_3^-)\}$ which allows a more complete interpretation of the patient's acid base status. It is beyond the scope of these notes to discuss the full differential diagnosis and evaluation of each electrolyte abnormality, however the important points are highlighted below.

Interpretation of blood gas and electrolyte results

Sodium

Although mild changes in serum sodium are commonly present they are usually mild and do not cause clinical signs. Occasionally patients are seen with more dramatic changes in serum sodium and if these occur rapidly patients may demonstrate signs directly referable to these changes which are principally neurological in nature. Conversely, if a patient has developed a sodium abnormality over a prolonged period of time, treatment that rapidly normalises the sodium may actually precipitate neurological signs! As a rule, when treating sodium abnormalities sodium should not change by more than **0.5 mEq/hr** in any direction.

In our practice, significant hyponatraemia occurs most commonly with inappropriate use of hypotonic fluids (especially 0.18%NaCl and 4% dextrose), hypoadrenocorticism and chronic vomiting. Significant hypernatraemia occurs most commonly in cats in association with renal disease.

Potassium

Changes in potassium are the most common electrolyte abnormalities to be associated with significant (and potentially fatal) clinical signs due to potassium's importance in maintaining normal membrane potential differences in all muscle and especially the specialised conduction fibres in cardiac muscle. Marked hyperkalaemia is most commonly seen with urinary tract obstruction, uroabdomen and hypoadrenocorticism. Patients with hyperkalaemia exhibit changes in myocardial conduction with bradycardia and characteristic ECG abnormalities— these may progress to be fatal if left untreated. Emergency medical stabilisation of these patients may be required. Options include:-

- Intravenous calcium gluconate (10%) at 0.5-1.5 ml/kg over 5-10 minutes
- Soluble insulin at 0.5IU/kg IV with a contemporaneous bolus of 0.5g/kg glucose IV and supplementation of the patient's fluids to 2.5% glucose
- Bicarbonate IV (rarely required)

Hypokalaemia is even more common although the clinical signs are not usually as dramatic and consist mainly of muscular weakness. Oral or intravenous potassium supplementation may be used for treatment.

Chloride

Hypochloraemia most commonly occurs either with severe vomiting or frusemide administration. It is often accompanied by, and acts to perpetuate, a metabolic alkalosis. When treating patients with intravenous fluid therapy, the presence of hypochloraemia may prompt the clinician to consider 0.9%NaCl as the replacement fluid of choice. This will lead to more rapid resolution of the accompanying acid-base abnormality. Hyperchloraemia most often accompanies hypernatraemia which is of greater clinical significance.

Interpretation of blood gas and electrolyte results

Interpretation of blood gas and electrolyte results

Nutrition in intensive care patients

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Dan qualified as a veterinary surgeon at the School of Veterinary Medicine at Cornell University in 1998. He then completed a small animal internship at Animal Medical Center in New York City. This was followed by a dual residency in Emergency and Critical Care and Clinical Nutrition at the Cummings School of Veterinary Medicine at Tufts University, after which he served as a Research Assistant Professor for two years. Dan was board certified by the American College of Veterinary Emergency and Critical Care in 2004, and by the American College of Veterinary Nutrition in 2005. He now serves as a lecturer in Emergency and Critical Care and as a Clinical Nutritionist at The Royal Veterinary College. His main interests are in critical care nutrition, glucose metabolism, coagulation and sepsis.

Nutrition for Intensive Care Patients

Critically ill animals undergo several metabolic alterations which put them at high risk for the development of malnutrition and its subsequent complications. During periods of nutrient deprivation, a healthy animal will primarily lose fat. However, sick or traumatized patients will preferentially catabolise lean body mass when they are not provided with sufficient calories. This loss of lean body mass reduces the animal's strength, immune function, wound healing, and overall survival. Inadequate calorie intake is commonly due to a loss of appetite, an inability to eat or tolerate feedings, vomiting, or dehydration that accompanies many disease processes. Because malnutrition can occur quickly in these animals, it is important to provide nutritional support by either enteral or parenteral nutrition if oral intake is not adequate. The goals of nutritional support are to treat malnutrition when present but, just as importantly, to prevent malnutrition in patients at risk. Whenever possible, the enteral route should be used because it is the safest, most convenient, and most physiologically sound method of nutritional support. However, when patients are unable to tolerate enteral feeding or unable to utilise nutrients administered enterally, parenteral nutrition should be considered. Ensuring the successful nutritional management of critically ill patients involves selecting the right patient, making an appropriate nutritional assessment and implementing a feasible nutritional plan.

Nutritional Assessment

As with any medical intervention, there are always risks of complications. Minimising such risks involves appropriate patient selection and patient assessment. The first step in designing a nutritional strategy for a patient involves making a systematic evaluation of the patient, and this is termed **nutritional assessment**. Nutritional assessment identifies malnourished patients that require immediate nutritional support and also identifies patients at risk for developing malnutrition in which nutritional support will help to *prevent* malnutrition.

Indicators of overt malnutrition include recent weight loss of at least 10% of body weight, poor haircoat, muscle wasting, signs of poor wound healing, hypoalbuminemia, lymphopenia, and coagulopathies. However, these abnormalities are not specific to malnutrition and are not present early in the process. In addition, fluid shifts may mask weight loss in critically ill patients. Factors that predispose a patient to malnutrition include anorexia lasting longer than three days, serious underlying disease (eg, trauma, sepsis, peritonitis, pancreatitis, and significant gastrointestinal surgery), and large protein losses (eg, protracted vomiting, diarrhea, or draining wounds). Nutritional assessment also identifies factors that can impact the nutritional plan, such as cardiovascular instability, electrolyte abnormalities, hyperglycaemia, and hypertriglyceridaemia or concurrent conditions such as renal or hepatic disease that will impact the nutritional plan. Appropriate laboratory analysis should be performed in all patients to assess these parameters. Before implementation of any nutritional plan, the patient must be cardiovascularly stable, with major electrolyte, fluid, and acid-base abnormalities corrected.

Goals of Nutritional Support

Even in patients with severe malnutrition, the immediate goals of therapy should focus on fluid resuscitation, stabilisation, and identification of primary disease process. As steps are made to address the primary disease, formulation of a nutritional plan should strive to prevent (or correct) overt nutritional deficiencies and imbalances. Placement of feeding tubes (which require anesthesia) should only be performed once the patient is deemed stable.

By providing adequate energy substrates, protein, essential fatty acids, and micronutrients, the body can support wound healing, immune function, and tissue repair. A major goal of nutritional support is to minimize metabolic derangements and catabolism of lean body tissue. During hospitalization, repletion of body weight is not a priority as this will only occur when the animal is recovering from a state of critical illness. Therefore gain of body weight is not a goal whilst the animal is hospitalized for the majority of cases. However, continued weight loss during hospitalisation is of particular concern and should be addressed. The ultimate goal of nutritional support is to have the patient eating adequate amounts of food in its own environment.

Nutrition in intensive care patients

Nutritional Plan

Proper diagnosis and treatment of the underlying disease is the key to the success of nutritional support. Based on the nutritional assessment, a plan is formulated to meet energy and other nutritional requirements of the patient and at the same time address any concurrent condition requiring adjustments to the nutritional plan. The anticipated duration of nutritional support should be determined and factored into the plan. This will largely depend on clinical familiarity with the specific disease process and sound clinical judgment. For each patient, the best route of nutrition should be determined – enteral versus parenteral nutrition. This decision should be based on the underlying disease and the patient's clinical signs. Whenever possible, the enteral route should be considered first. If enteral feedings are not tolerated or the gastrointestinal tract must be bypassed however, parenteral nutrition should be considered. Nutritional support should be introduced gradually and reach target levels in 48-72 hours.

With regards to appetite stimulants, it is the author's opinion that they have no place in the nutritional management of hospitalised critically ill patients. The only means of insuring adequate caloric intake is through nutritional support (i.e. tube feeding or parenteral nutrition). Appetite stimulants could be used once the patient is recovering from its disease and at home.

Calculating Nutritional Requirements

The patient's resting energy requirement (RER) is the number of calories required for maintaining homeostasis while the animal rests quietly. The RER is calculated using the following formula:

$$\text{RER} = 70 \times (\text{body weight in kg})^{0.75}$$

For animals weighing between 2 and 30 kg, the following linear formula gives a good approximation of energy needs:

$$\text{RER} = (30 \times \text{body weight in kg}) + 70$$

Traditionally, the RER was then multiplied by an illness factor between 1.1-2.0 to account for purported increases in metabolism associated with different conditions and injuries. Recently, there has been less emphasis on these subjective illness factors and current recommendations are to use more conservative energy estimates to avoid overfeeding. Overfeeding can result in metabolic and gastrointestinal complications, hepatic dysfunction, increase carbon dioxide production, and weaken respiratory muscles. Of the metabolic complications, the development of hyperglycaemia is most common, and possibly the most detrimental. Recent findings suggest that the development of hyperglycaemia in the setting of critical illness could negatively impact outcome.

Currently, the RER is used as an initial estimate of a critically ill patient's energy requirements. It should be emphasized that these general guidelines should be used as starting points, and animals receiving nutritional support should be closely monitored for tolerance of nutritional interventions. Continual decline in body weight or body condition should prompt the clinician to reassess and perhaps modify the nutritional plan (e.g., increasing the number of calories provided by 25%).

While definitive studies determining the actual nutritional requirements of critically ill animals have not been performed, general recommendations can be made. Currently, it is generally accepted that hospitalized dogs should be supported with 4-6 grams of protein/100 kcal (15-25% of total energy requirements), while cats are usually supported with 6 or more grams of protein/100 kcal (25-35% of total energy requirements). Patients with protein intolerance, e.g., hepatic encephalopathy, severe azotaemia should receive reduced amounts of protein. Similarly, patients with hyperglycaemia or hyperlipidaemia may also require decreased amounts of these nutrients. Other nutritional requirements will depend upon the patient's underlying disease, clinical signs, and laboratory parameters.

Enteral Nutrition

The enteral route of nutritional support is usually the preferable route. Enteral nutrition is safer and less expensive than parenteral nutrition, and helps to maintain intestinal structure and function. Even with the use of feeding tubes, patients can easily be discharged for home-care with good owner compliance. The majority of complications with feeding tubes include tube occlusion and localised irritation at the tube exit site. More serious complications include infection at the exit site or rarely, complete tube dislodgment and peritonitis if the tube was a gastrostomy or jejunostomy tube. Complications can be avoided by using the appropriate tube, proper food selection and preparation and careful monitoring.

Although the enteral route should be utilized if at all possible there are contraindications to its use. Contraindications include persistent vomiting, severe malabsorptive conditions, and an inability to guard the airway. If the enteral route is chosen for nutritional support, the next step is selecting the type of feeding tube to be used (Box 1). Feeding tubes commonly used in dogs and cats include nasoesophageal, oesophagostomy, gastrostomy, and jejunostomy tubes. Once the desired feeding tube is placed, radiography or fluoroscopy should be used to confirm satisfactory tube placement.

Based on the type of feeding tube chosen and the disease process being treated, an appropriate diet should be selected. This will also depend upon the animal's clinical parameters and laboratory results. The amount of food is then calculated and a specific feeding plan devised (Box 2). Generally, feedings are administered every 4-6 hours and feeding tubes should be flushed with 5-10mls of water after each feeding to minimize obstruction of the tube. By the time of hospital discharge however, the number of feedings should be reduced to 3-4 times/day to facilitate owner compliance. Commercially-available veterinary liquid diets should be used for nasoesophageal and jejunostomy tube feedings as these tubes are too small to accommodate any other type of diet. Jejunostomy tubes are primarily for in-hospital use because they require administration of a liquid diet by continuous rate infusion and this feeding via this route also requires more vigilant monitoring. Oesophagostomy and gastrostomy tubes are generally larger (> 12 Fr for oesophagostomy and > 20 Fr for gastrostomy tubes) and allow for more calorically-dense, diets to be administered. This decreases the volume of food necessary for each feeding. These tubes can be used for long-term enteral feeding. In the author's opinion, mastering the placement of oesophagostomy feeding tubes is essential in the management of critically ill animals and this technique should be adopted in almost all practices. A step-by-step description of this technique is outlined in **Box 3**. A volume of **5-10 ml/kg** per individual feeding is generally well tolerated but this may vary with the individual patient. In patients that are generally healthy but cannot consume food orally, e.g., jaw fracture, larger volumes of food per feeding (15-20 ml/kg) may be tolerated. As enteral diets are mostly composed of water (most canned food are already >75%

Nutrition in intensive care patients

water) the amounts of fluids administered parenterally should be adjusted accordingly to avoid volume overload. Prevention of premature removal of tubes can be accomplished by using a buster collar and by wrapping the tube securely. Care should be taken to avoid wrapping too tightly as this could lead to patient discomfort and even compromise proper ventilation.

Parenteral Nutrition

Parenteral nutrition (PN) is more expensive than enteral nutrition and is only for in-hospital use

Indications for parenteral nutrition include vomiting, acute pancreatitis, severe malabsorptive disorders, and severe ileus. While terminology of parenteral nutrition can be confusing there are two major types. Total parenteral nutrition (TPN) is typically delivered via a central venous (jugular) catheter and provides all of the energy requirements of the patient. With partial parenteral nutrition (PPN) only a portion of the animal's energy requirements are met (40-70%) but because of the lower osmolality of the solution, it can usually be administered through a large peripheral vein such as the lateral saphenous in dogs and femoral vein in cats (hence PPN is sometimes referred to as Peripheral Parenteral Nutrition). Because PPN only provides a portion of the patient's requirements, it is only intended for short-term use in a non-debilitated patient with average nutritional requirements. Regardless of the exact form of PN, intravenous nutrition requires a dedicated catheter that is placed using aseptic technique. Long catheters composed of silicone, polyurethane, or tetrafluoroethylene are recommended for use with PN to reduce the risk of thrombophlebitis. Multi-lumen catheters are often recommended for PN because they can remain in place for longer periods of time as compared to normal jugular catheters and provide other ports for blood sampling and administration of additional fluids and IV medications. Most parenteral nutrition solutions are composed of a carbohydrate source (dextrose), a protein source (amino acids), and a fat source (lipids). Vitamins and trace metals can also be added.

Due to the high osmolality of the TPN solution (usually 1100-1500 mOsm/L), it must be administered through a central venous (jugular) catheter. PPN is formulated so that it can be administered through a peripheral catheter but, because it is more dilute, it can only provide a portion of the patient's energy requirements. Formulation of TPN and PPN solutions can be individualised to each patient and the reader is referred to some of the recommended references to further details. In most cases, it is easiest to have a local human hospital formulate TPN and PPN.

Monitoring and Reassessment

Body weights should be monitored daily with both enteral or parenteral nutrition. However, the clinician should take into account fluid shifts in evaluating changes in body weight. For this reason, body condition scores are important as well. The use of the RER as the patient's caloric requirement is merely a starting point. The number of calories provided may need to be increased to keep up with the patient's changing needs, typically by 25% if well tolerated. In patients unable to tolerate the prescribed amounts, the clinician should consider reducing amounts of enteral feedings and supplementing feeds with PPN.

Possible complications of enteral nutrition include mechanical complications such as obstruction of the tube or early tube removal. Metabolic complications include electrolyte disturbances, hyperglycaemia, volume overload, and gastrointestinal signs (eg, vomiting, diarrhoea, cramping, bloating). In critically ill patients receiving enteral nutritional support, the clinician must also be vigilant for the development of aspiration pneumonia. Monitoring parameters for patients receiving enteral nutrition include body weight, serum electrolytes, tube patency, appearance of tube exit site, gastrointestinal signs (eg, vomiting, regurgitation, diarrhea), and signs of volume overload or pulmonary aspiration.

Possible complications with PN include sepsis (low risk), thrombophlebitis, and metabolic disturbances such as hyperglycaemia, electrolyte shifts, hyperammonaemia, and hypertriglyceridaemia. Avoiding serious consequences of complications associated with PN requires early identification of problems and prompt action. Frequent monitoring of vital signs, catheter-exit sites, and routine biochemistry panels may alert the clinician of developing problems. The development of persistent hyperglycaemia during nutritional support may require adjustment to nutritional plan (e.g., decreasing dextrose content in PN) or administration of regular short-acting insulin. This obviously necessitates more vigilant monitoring.

With continual reassessment, the clinician can determine when to transition patient from assisted feeding to voluntary consumption of food. The discontinuation of nutritional support should only begin when the patient can consume approximately 75% RER without much coaxing. In patients receiving TPN, transitioning to enteral nutrition should occur over the course of at least 12-24 hours, depending on patient tolerance of enteral nutrition.

Special Nutrients

In recent years, there has been particular focus in the pharmacological role of nutrients in modulating disease in people. "Immune-enhancing diets" often include nutrients such as glutamine, arginine, omega-3 fatty acids, antioxidants, and nucleotides. In certain populations of critically ill human patients, these strategies (singly or in combination cocktails) provide significant benefits in reducing complications and even decreasing mortality. Unfortunately, no such benefits have been documented in veterinary patients. Documentation of depletion of these key amino acids in animals with naturally-occurring disease is also lacking. While such nutrients may indeed confer health benefits to veterinary patients, studies confirming these benefits are unlikely to be forthcoming. As the majority of veterinary patients are only hospitalized for a short term (relatively low percentage are hospitalized for more than 10 days), pharmacological effects of nutrients will be difficult to discern. While risk of side-effects from these therapies are likely low, the added cost of such supplements in the face of little supporting evidence in veterinary patients may make use of such products unwarranted at this time. As nutrient requirements vary considerably among species, it is likely that the same holds true in respect to the pharmacological effects of nutrients. Determination of minimal dosages for each nutrient necessary to achieve desired biological effects may be warranted as the next step.

Nutrition in intensive care patients

Summary

While critically ill patients are often not regarded as in urgent need of nutritional support given their more pressing problems, the severity of their injuries, altered metabolic condition, and necessity of frequent fasting, place these patients at high risk of becoming malnourished during their hospitalisation. Proper identification of these patients and careful planning and execution of a nutrition plan can be key factors in the successful recovery of these patients.

Recommended Reading

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Box 1: Feeding tube selection			
Feeding tube	Duration	Advantages	Disadvantages
Nasoesophageal	Short-term (< 5 days)	Inexpensive Easy to place No anesthesia required	Requires liquid diet Some animals will not eat with an NO tube in place
Oesophagostomy	Long-term	Inexpensive Easy to place Can use calorically-dense diets	Requires anesthesia Cellulitis can occur if tube is removed early
Gastrostomy			
Percutaneous endoscopically-guided (PEG)	Long-term	Easy to place Can use calorically-dense diets	Requires anesthesia Requires endoscope
Surgically-placed	Long-term	Can use calorically-dense diets	Requires anesthesia and laparotomy
*For all the gastrostomy tubes, peritonitis is a possible complication if the tube leaks or is removed early			
Jejunostomy	Long-term	By-passes stomach and pancreas Can be used in patients with pancreatitis	Requires anesthesia and laparotomy For in-hospital use Requires continuous rate infusion Requires liquid diet Peritonitis can occur if tube is removed early

Nutrition in intensive care patients

Box 2: Worksheet for calculating enteral nutrition

1. Resting Energy Requirement (RER)

$$\text{RER} = 70 \times (\text{current body weight in kg})^{0.75}$$

or, for animals weighing between 2 and 35 kg:

$$\text{RER} = (30 \times \text{current body weight in kg}) + 70 = \text{_____ kcal required/day}$$

2. Product selected _____

Contains _____ kcal/ml

3. Total volume to be administered per day

$$\frac{\text{kcal required/day}}{\text{kcal/ml in diet}} = \text{_____ ml/day}$$

4. Administration schedule

$$1/2 \text{ of total requirement on Day 1} = \text{_____ ml/day}$$

$$\text{Total requirement on Day 2} = \text{_____ ml/day}$$

5. Feedings per day

Divide total daily volume into 4-6 feedings (depending on duration of anorexia, patient tolerance)

$$= \text{_____ feedings/day}$$

6. Calculate volume per feeding

Total ml/day

$$\text{Number of feedings/day} = \text{_____ ml/feeding (Day 1)}$$

$$= \text{_____ ml/feeding (Day 2)}$$

*Be sure to adjust the animal's intravenous fluids according

Diet options

Oesophagostomy and gastrostomy tubes

Eukanuba High Calorie canned

Combine 1 can with 50 ml water. [1.6 kcal/ml]

Hill's a/d canned

Combine 1 can with 25 ml water. [1.1 kcal/ml]

Royal Canin **Canine** Sensitivity Control (Duck and Rice)

Combine 1 can with 150 ml of water in blender for 5 minutes. [0.75 kcal/ml]

Royal Canin **Canine** Digestive Low Fat

Combine 1 can with 200 ml water in blender for 5 minutes. [0.56 kcal/ml]

Royal Canin **Canine** Renal

Combine 1 can with 200 ml water in blender for 5 minutes. [0.74 kcal/ml]

Royal Canin **Feline** Instant Convalescence Support

Mix 125 ml of water to 50 grams of LCD powder [1.37 kcal/ml] – suitable for 5 kg cat

Royal Canin **Canine** Instant Convalescence Support

Mix 225 ml of water to 150 grams of LCD powder [1.75 kcal/ml] – suitable for 20 kg dog

Nasoesophageal and jejunostomy tubes

Fortal C+ Liquid diet [0.9 kcal/ml]

Nutrition in intensive care patients

Box 3: Oesophagostomy tube placement

1. Proper placement of an oesophagostomy feeding tube requires the distal tip to be placed in the distal oesophagus at the level no further than the 9th intercostal space. This may require premeasuring the tube. Rather than cutting the distal tip and creating a sharp edge, the exit side hole should be elongated using a small blade.
2. The patient should be anaesthetised and preferably intubated. While in right lateral recumbency, the left side of the neck should be clipped and a routine surgical scrub should be performed.
3. A curved Rochester Carmalt is placed into the mouth and down the oesophagus to the midcervical region. The jugular vein should be identified and avoided.
4. The tip of the Carmalt is then pushed dorsally, pushing the oesophagus towards the skin.
5. The tip of the Carmalt is palpated over the skin to confirm its location and an incision is made through the skin into the oesophagus directly over the tips of the instrument. The mucosa of the oesophagus is relatively more difficult to incise than the skin.
6. The tip of the instrument is gently forced through the incision when the mucosa is finally incised with the blade. The incision can be slightly enlarged to allow opening of the tips of the Carmalt and placement of the oesophagostomy tube within the tips.
7. The Carmalt is then clamped closed and pulled from the oral cavity.
8. Disengage the tips of the Carmalt and curl the tip of the tube back into the mouth and feed into oesophagus. As the curled tube is pushed into the oesophagus, the proximal end is gently pulled outwards simultaneously. This will result in subtle “flip” as the tube is redirected within the oesophagus. The tube should easily slide back and forth a few centimeters, confirming that the tube has straightened.
9. Visually inspect the oropharynx to confirm that the tube is no longer present within the oropharynx.
10. The incision site should be briefly re-scrubbed before a purse-string suture is placed followed by a “Chinese finger trap,” further securing the tube in place.
11. A light wrap is applied to the neck.
12. Correct placement should be confirmed with either radiography or fluoroscopy.

Nutrition in intensive care patients

Nutrition in intensive care patients

Write it Right

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How to please the editor

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Professor Hunter graduated with commendation from the University of St. Andrews in 1971 and then embarked upon her career in anaesthesia. She soon gained her Fellowship of The Royal College of Anaesthetists, and went on to complete a PhD entitled 'Pharmacodynamics and pharmacokinetics of neuromuscular blocking drugs in health and disease.' Professor Hunter is a world-renowned expert in this field, and has been honoured with many prestigious awards including the Gold Medal of The Royal College of Anaesthetists in 2004, and the Featherstone Award of the Association of Anaesthetists of Great Britain and Ireland in 2005. Amongst her many honorary appointments, she was Editor-in-Chief of the British Journal of Anaesthesia from 1997-2005, and now chairs the Board of the BJA. She is extremely active in the world of anaesthesia and has recently become Chairman of the Scientific Programme Committee of the European Society of Anaesthesiology. Professor Hunter has worked and taught in the Royal Liverpool University Hospital since it opened in 1978, and was awarded a Personal Chair at the University of Liverpool in 2000.

How To Please The Editor

Scientific writing is a discipline, which takes years to perfect; few have a natural talent for it, and most of us must spend many hours culturing our skills. Attention to basic detail is the essence of success when preparing a manuscript for submission to a scientific journal.

Guidelines to Authors

Always study the Guidelines to Authors for the journal you are submitting to. Read them over and over again. (Adhering to such instructions is the path to an editor's heart). Pay absolute attention to the details listed in the Guidelines. Develop an obsessional approach to your work. Always supply the number of copies required, including the required copies of any figures, and a disk if necessary. Provide your full address, including your fax and telephone numbers, and email address. If you are submitting a manuscript electronically, follow the step-by-step guidelines on the website carefully.

Summary

Be concise in this section; most journals limit the number of words in it, for indexing purposes. Give facts and values, only reporting your findings (not others). Structure it, if the journal requires, and provide some key words. No references should be added to this section.

Introduction

This should be relatively short - usually about one side of A4 (double-spaced). It should outline the reasons for setting out on the study, and end with a short description of the work you are reporting. A few, relevant references should be added.

Methods

This section should start, if appropriate, by acknowledging that ethical approval and informed consent have been obtained. The methods must be reproducible, detailing any equipment used, including information about manufacturers, pharmaceutical companies etc. Sub-sections may be useful e.g. *Patient Details, Anaesthetic Technique, Plasma Sampling, Pharmacokinetic Analysis, Statistics, etc.*

Statistics

These are usually detailed at the end of the Methods section. Name the tests you have used. Reference any unusual tests (try not to be too esoteric in the ones you select). Name any software packages employed. Explain which sets of data each test has been used to compare (a common pitfall).

Results

Be systematic and succinct, possibly using the same sub-headings used in the Methods section. Do not simply repeat the data provided in the tables and figures. No discussion must be included in this section - a common fault.

Tables and Figures

These are expensive to produce. Only use them if your data cannot be easily included in the text. Limit the number of them as much as possible. They should not be too small e.g. two lines, or too large e.g. cover two sheets of A4 paper. Make sure that you mention the figures and tables in the text. Mark in the text where the table or figure should appear.

Tables should be well laid out and spacious. An adequate, stand alone legend should be provided with them. Explain the statistical symbols you have used in the table, in the legend. Make clear which sets of data are being compared.

How to please the editor

Figures must be large enough to reproduce. They should not be cluttered with information. Nor should figures be smudged or blurred. A proper key should be provided of the symbols. It should be placed in some white space on the figure, or in the legend. The relevant statistical findings should be added to the figure, if appropriate.

Discussion

Open this section with a sentence or two summarizing your findings. Compare and contrast your results with those reported elsewhere. Give values for the variables reported in each instance. Try to explain the differences noted, and indeed your own results. Do not simply repeat the results (a common weakness). Search the recent literature in depth to improve your discussion. Do not insist that you are the first to report such findings - you rarely are! You must not be obsequious or slanderous in this section. There is no need for a long concluding paragraph at the end of the discussion. Try to limit this section to, at the most, three sides of double-spaced A4 paper.

References

Always use the format required by the journal to which you are submitting your manuscript. Make absolutely sure that the references are correct and correlate with the text. Do not just quote your own work, (which is a foible directly correlated with age!). There is no need to use several references to highlight one point.

Declarations of Interest

These should be made in detail on the front page of the manuscript. All grants and other financial support should be listed.

Revisions

Always follow the Editor's instructions when preparing your revision. In your reply, answer each of the assessors' points in order. Check that the tables and figures are still numbered correctly: you may have changed the order in your revised version. Do not be tempted to submit a revised version with hardly any changes to it: it will irritate the Editor profusely!

General Points

Develop an 'eye' for the layout of your manuscript, paying attention to headings and sub-headings, as recommended by the journal. Aim for symmetry in the layout of tables and figures. Paginate your article. Use paragraphs appropriately; one sentence per paragraph, which is another common fault, is rarely apposite. Check that there is no repetition in your manuscript; it can be difficult to avoid. There is no excuse (whatsoever) for spelling errors in a scientific manuscript (or American use of English!). Do not be tempted to send the same manuscript to more than one journal at a time. Editors do not like it, and they find out!

Expect to do several drafts of your manuscript; go over it, again and again. Always ask an experienced research worker to read your manuscript, however senior you are. Never be too proud to do so. This is creative work, which requires extraordinary effort. Take pride in your manuscript, remembering that,

"A thing of beauty is a joy forever." J. Keats, 1817

How to please the editor

How to please the editor

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The graphical presentation of data

R. E. Clutton BVSc MRCVS DVA DipECVA MRCA

Graduated (BVSc [hons]) from the University of Liverpool 1981. Stayed three years in the Department of Anaesthesia, The Royal Liverpool Hospital, with Ron Jones. Awarded Cert VA (RCVS) in 1983 and the DVA in 1988. Worked in the University of Virginia – Maryland, USA for 5 years as assistant professor in Veterinary Anaesthesiology. Head of anaesthesia in R(D)SVS (Edinburgh) since 1990. Became Diplomate European College of Veterinary Anaesthesia in 1996. Member of the Royal College of Anaesthetists, the Animal Welfare Science, Ethics and Law Veterinary Association and the Veterinary History Society.

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How to review a manuscript

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Where does it hurt?

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Pain recognition in non-verbal species - animals

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Paul Flecknell qualified from Cambridge Veterinary School in 1976. He holds the Diploma in Laboratory Animal Science of the Royal College of Veterinary Surgeons and is also a Diplomate of the European College of Veterinary Anaesthesia and the European College of Laboratory Animal Medicine. He was awarded the Livesey Medal by the Royal College of Veterinary Surgeons in 1986, the BVA Dalrymple-Champneys Cup and Medal for contributions to animal welfare in 2004 and the International Academy of Animal Pain Management Pfizer Award in 2005. He is currently Director of the Comparative Biology Centre at the University of Newcastle. His main clinical and research interests are anaesthesia and analgesia of all species of animals, the veterinary care of small mammals, and the development of training materials in these fields.

Assessing Pain in Animals

(Amended and updated from Flecknell, P.A and Roughan, J.V., 2004,
Assessing Pain in Animals – putting research into practice. Animal Welfare, 13 (Suppl) S71-S75)

Introduction

The last decade has seen a growing concern over the issue of pain and distress in animals. This concern has been reflected in a steady increase in interest in pain assessment and pain management amongst veterinary surgeons and others. Despite this increased interest and concern, the management of animal pain remains poor. For example the use of post-operative pain in companion animals is low (Dohoo and Dohoo, 1996, Capner et al, 1999, Lascelles et al, 1999, Raekallio et al, 2003). Even if analgesic use were to increase, pain management is likely to remain poor as we still have virtually no practically applicable means for evaluating the degree of pain, and hence the effectiveness of our analgesic therapy, in any species. In a recent informal survey of veterinary surgeons and nurses attending anaesthesia CPD meetings, less than 1% used any structured pain assessment system (>400 participants). Without a method of assessing pain, we cannot determine the efficacy of analgesic therapy in individual animals, nor determine when therapy can be discontinued.

Pain Assessment in Farm Animals

Behavioural and endocrine indicators of pain in lambs, cattle and pigs have been established by a number of different research groups (Lester et al, 1996, Mellor and Stafford 2000, Molony et al, 2002, Noonan et al, 1994). These have been developed largely to aid in the evaluation of the welfare benefits of modifying standard agricultural practices such as tail docking, castration and dehorning. It has been repeatedly demonstrated that use of local anaesthetics, either alone or in conjunction with modifications to the techniques commonly used, can reduce pain-related behaviours in lambs and cattle. Regrettably, economic considerations have limited widespread application of the results of these studies. Recently, the practical application of improved methods of docking and castration has been demonstrated (Kent et al, 2003), and pain scored in a “field” situation. The improved techniques increased the time taken for castration and docking, and required purchase of an additional piece of equipment. It seems likely that widespread application of the improved methodology will require that these economic issues are addressed.

Since additional interventions, such as administration of additional analgesics, is rarely contemplated following these husbandry procedures, there has been less need to develop a robust pain assessment system for general use on farms. It is worth noting, however, that in the study quoted above (Kent et al, 2003), shepherds were able to use Visual analogue scoring (VAS) to correctly identify lambs experiencing less pain as a result of improved techniques. In some circumstances, identification of pain would lead to a modification of clinical practice, for example after Caesarian section in cattle. Although a high percentage (68%) of specialist cattle veterinarians administer analgesics after Caesarian section, attempts to develop practical pain scoring schemes have not proven successful (Watts, 2001). This is largely because of the very considerable difficulties entailed in developing such schemes, and this is discussed further below. Despite these difficulties, it is encouraging to note that several pharmaceutical companies are now actively marketing NSAIDs for use in presumed painful conditions in farm animals.

Pain assessment in companion animals

Two well documented schemes for pain assessment in dogs have been developed (Firth and Haldane, 1999; Holton et al, 2001). In addition numerous studies using pain scoring systems based on Visual Analogue Scoring, Numerical Rating Systems, or Simple Descriptive Scores, or using a mixture of all 3 approaches have been published (Brodbeck et al, 1997, Mathews et al, 2001). The different approaches adopted in these different studies highlight many of the problems involved in developing pain assessment schemes (Holton et al, 1998). In their original study, Firth and Haldane (1999) carried out detailed behavioural assessments of dogs, both before and after surgery, and identified behaviours that were probable indicators of pain. However, when these criteria were used to identify animals that should have been experiencing pain (as they had undergone surgery and had not received an analgesic), the confidence intervals on the measures were wide. In addition, since only animals undergoing a single type of surgical procedure (ovariohysterectomy) were included, the broader applicability of the scheme cannot be properly evaluated. A different

Pain recognition in non-verbal species - animals

approach was adopted by Holton et al (2001). This group sought to identify descriptors of pain by consulting with experienced small animal clinicians, and then used sophisticated analytical techniques to reduce these descriptors to a set of words or phrases. These descriptors were then developed into a multi-dimensional pain scale. Validation of this scheme, by using it to correctly identify animals with varying degrees of pain relief following surgery has not yet been undertaken. Until this validation has been completed it is difficult to judge the reliability of the scoring system. What is required is a randomised, blinded, placebo-controlled trials, but these certain ethical and practical difficulties (see below). Despite these problems, this system has been developed further and combined with the Firth and Haldane scheme and proposed as a tool suitable for clinical use (Hellyer, 2002).

Ethical and other problems with pain assessment schemes

A large number of other pain scoring schemes have been described, but virtually none of these have been properly validated. Indeed, the descriptions of the scales used in some studies is so brief it is not possible to make a judgement as to how useful the scoring system would have been. In general, these schemes suffer from a number of problems:

- 1) The assessment criteria used are frequently highly subjective
- 2) The study designs do not include untreated (surgery and no analgesia) controls
- 3) The study designs do not include anaesthesia and analgesia (and no surgery) control groups.

Since many schemes include some behavioural assessments, and anaesthetics and analgesics, notably opioids, can markedly change behaviour in normal, pain-free animals, lack of appropriate controls makes the results obtained questionable.

Including such control groups can cause significant ethical problems to those undertaking pain assessment studies. The majority of these studies are carried out in veterinary schools in which students are taught that animals experience pain, and that analgesics should therefore be administered. Deliberately withholding analgesics in circumstances thought likely to result in pain may therefore be considered unacceptable. This problem is addressed in studies of pain in human subjects by implementing an intervention analgesia protocol. If the subject is assessed as experiencing pain above a certain level, they are removed from the study and given an analgesic. This assessment can be carried out by someone not directly involved in the study. This approach has been used successfully in a number of veterinary clinical studies (Lascelles et al, 1995, Grisneux et al, 1999) and in laboratory animals (Roughan and Flecknell, 2003).

Other problems remain, however. In addition to poor study design, few scales have demonstrated linearity – ie is a score of 4 twice as painful as a score of 2? Few have addressed the problems of between-observer variation in applying the scoring system. However, it is encouraging that when placebo controls are included, it is possible to demonstrate significant effects of analgesic administration (eg Lascelles et al, 1997), suggesting that some elements of the scale used are indicators of pain. Considerable additional work is required before any of these schemes could be considered sufficiently reproducible or robust for use in veterinary clinical practice. The assessment schemes have also only examined pain in dogs and cats – pain in birds, rabbits, small mammals, reptiles, amphibians and fish, all of which may undergo surgery in veterinary practice, have received virtually no attention.

Pain Assessment in Laboratory Animals

It might be thought that pain assessment in this group of animals would be the most highly developed, given the great public concern regarding their welfare. Although suggestions for assessing pain have been published (Flecknell, 1984), these were largely based on subjective clinical criteria that had not been subjected to any form of validation. A proposal to develop more robust scoring schemes was published by Morton and Griffiths (1985), but attempts to apply this were largely unsuccessful (Beynen et al, 1987), primarily because the variables selected for inclusion were not fully identified, and the scales used (0-3) not sufficiently well characterised. The scheme has proven much more successful when applied as a means of developing more humane endpoints for studies. These problems were identified by the original authors, but indiscriminate application of the system seems to have led to failure in identifying animals in pain, and to some units abandoning its application. This is to be regretted, since when applied carefully, the scheme provides a structured method for assessing animals, and can be a useful aid for developing end-points in a range of different situations.

Other potential indicators of pain have included general locomotor activity and changes in food and body weight (Flecknell and Liles, 1991, Liles and Flecknell, 1993, Liles et al, 1998). These latter measures are objective, and have been used to assess analgesic drug efficacy. However, they are retrospective measures and so could not be used to modify analgesic therapy for a particular animal. They can, however, be used as a simple measure of post-operative recovery, and as a means of adjusting future analgesic regimens for similar animals undergoing similar surgical procedures.

Other pain assessment systems have aimed at identifying acute and chronic pain states for research purposes (eg Dubuisson and Dennis SG, 1977, D'Amour and Smith, 1941, Gyires and Torma 1984), and these have limited application in assessing pain in other situations. A range of different techniques have been developed for assessing the likely efficacy of analgesics. In many instances, these involve the application of a brief noxious stimulus, followed by quantification of the animals' response. Administration of analgesics usually modifies this response, for example by prolonging the latency of withdrawal of a limb or tail from the noxious stimulus. In addition to their primary use as a means of screening for potential analgesics in drug discovery programs, the results of these tests have been used to estimate dose rates of analgesics for clinical use (Flecknell, 1984). Such extrapolations must be made with caution. For example, estimates of appropriate doses of buprenorphine based on tail flick tests resulted in a recommended dose of 0.5mg/kg in rats (Flecknell, 1984), 10 times higher than the dose shown to be effective using post-operative pain scoring systems (Flecknell et al 1999, Liles and Flecknell 1993). Since high doses of this agent can have undesirable side-effects, it is important that care is taken when making these extrapolations. Although results of these types of test may not predict clinical efficacy, they do illustrate the very wide variation in response that can be encountered between different strains of rodent (Morgan et al, 1999). This reinforces the importance of developing

Pain recognition in non-verbal species - animals

pain scoring systems. If appropriate pain scoring schemes cannot be used, then dose rates are probably best estimated from the results of tonic analgesiometric tests such as the late-phase formalin test or the writhing test (Roughan and Flecknell, 2002).

Recently, we have developed a behaviour-based scheme for assessing pain in laboratory rats following abdominal surgery (Roughan and Flecknell, 2001). During initial development of the scheme, the behaviour of rats was evaluated following a mid-line laparotomy with appropriate untreated, and non-surgery analgesic treated controls included. An initial study using buprenorphine as the analgesic was inconclusive, because of the marked effects of this opioid on normal behaviour (Roughan and Flecknell, 2000). A subsequent study using carprofen and ketoprofen successfully identified a series of behaviours that differentiated rats which had received analgesics following surgery from those which had not. These studies required detailed analysis of considerable periods of video-taped behaviour, and filming at night under red light. So although the scoring criteria were suitable as a research tool, they did not form a practically useful scoring system.

Following completion of this study, the more general utility of the system was assessed in another strain of rat undergoing surgery as part of an unrelated research project. In these studies, the animals were placed in an observation cage for a 10 minute period, and the frequency of the pain-related behaviours assessed. It proved possible to differentiate animals receiving analgesics from untreated controls, and to demonstrate a dose-related effect of the NSAID, meloxicam (Roughan and Flecknell, 2003a). Re-analysis of all of the behaviours shown by these rats confirmed that the same behaviours as those seen in our previous investigations were most useful for developing a clinically applicable pain scoring scheme (Roughan, personal communication).

When experienced staff (animal technicians, research workers and veterinarians) viewed selected video recordings from these animals, they were unable to correctly identify the treatment groups. After viewing a short recording illustrating the key behaviours, their ability to identify animals that had, or had not, received analgesics greatly improved (Roughan and Flecknell, 2006). These studies suggested that the key behaviours could be identified, and used to score pain following one type of surgical procedure in rats. Most recently, we have used the scoring system to assess the relative efficacy of different analgesics and their duration of action (Roughan and Flecknell, 2004). In addition, the scoring system has been applied to rats undergoing a different surgical procedure, bilateral adrenalectomy. These animals perform a very similar range of behaviours to animals undergoing laparotomy, but there are differences in the frequency of particular behaviours, with back-arching being more frequent after mid-line laparotomy, and belly pressing more frequent after bilateral adrenalectomy. This is similar to results of behavioural studies of different methods of castration and tail docking in lambs (Molony et al, 2002), in that different types of abnormal behaviour are seen after the different procedures. What is uncertain is whether behavioural changes in rats after various surgical procedures will differ greatly in type, or whether they will be drawn from a common group of abnormal, pain-related behaviours.

A further problem that is becoming apparent is that all of the animals studied have been anaesthetised with isoflurane, a very short acting anaesthetic that results in rapid recovery of consciousness. When recovery is delayed, or is associated with prolonged sedation, then animals may fail to express pain behaviour. At present it is not certain whether this is because the animals are not experiencing pain, or whether the heavy sedation prevents them showing signs of pain. The scoring system may also be influenced by other factors, such as fear and apprehension, and unexpected variations in behaviour between different strains of animal may be encountered. Nevertheless, this approach offers a step forward in developing a practically useful scoring system for use after at least some types of surgery in rats. What is not yet known is whether similar systems can be developed in other laboratory species, or whether a similar approach can be used to develop means of identifying and quantifying other types of pain in animals, including chronic pain states.

Practical applications

Given the current poor state of our ability to assess pain, it is unsurprising that practical application of any of these schemes remains very limited. Considerably more research is needed to develop appropriate tools for many species, and it is essential that we evaluate current schemes critically. If we do not, and they are promoted widely and then prove to be unreliable, then this will dissuade clinicians from applying assessment schemes. A second problem that is emerging is that applying scoring schemes in either veterinary clinical practice or in research facilities or farms will take a significant amount of time. Taking the assessment scheme for rats as an example, at least 5-10 minutes per animal is required, and subsequent assessment, for example at 1-2 hourly intervals should be made, in order to monitor the animals adequately. If 20-30 animals are involved, this can easily develop into a full time role for a member of staff. It is important that such schemes are developed and promoted, however, as if we do not have clear means of identifying animal pain, then analgesic use will continue to be restricted. It is difficult to assess the overall level of analgesic use in laboratory species. Although a recent survey indicates that provision of post-surgical pain relief may be widespread in the UK (Hawkins, 2002), this survey was made in a highly selected group of facilities and may not reflect practice elsewhere. Reviewing research publications involving surgery in rodents highlights some worrying trends – analgesic use is almost never mentioned in some journals, despite the papers describing invasive surgical procedures (Richardson and Flecknell, 2005). In several recent publications, the authors stated that analgesics were not given because the animals showed no apparent signs of pain (Grau & Steiniger, 2003, Labat et al, 2002, Lawson et al, 2001), reinforcing the need to provide simple means of identifying pain.

Conclusions

The recent significant increase in interest in animal pain and its prevention and alleviation is to be welcomed. We must appreciate, however, that we currently have a very limited ability to assess pain intensity accurately. This limits our ability to prevent and alleviate pain. We must strive to develop robust, practically useful assessment schemes for a wide range of different species of animals. We must do this for different types of both acute and chronic pain. If we can make progress with this goal, we will be able to manage animal pain far more effectively than is possible at present.

For those with an interest in developing research in this field, I would encourage you to join the newly formed special interest group (SIG) of the International Association for the Study of Pain, by contacting Duncan Lascelles, (duncan_lascelles@ncsu.edu).

Pain recognition in non-verbal species - animals

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Pain recognition in non-verbal species - animals

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Pain recognition in non-verbal species - animals

Pain recognition in non-verbal species - animals

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Pain recognition in non-verbal species - neonatal humans

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Born in the Midlands, spent 21 years in North West, (Bolton).

Graduated in Medicine from Sheffield Medical School 1989.

Commenced paediatrics in 1991 and moved to Newcastle upon Tyne.

Now married with 3 young children, and Senior Registrar in neonatology, currently taking 'time out' as 'Honorary Research Associate' with Professor Paul Flecknell, looking at post-operative pain behaviour in neonates and infants up to 3 months old.

Pain Recognition in Human Neonates

Despite significant advances in the management of pain in older children and adults, the assessment and treatment of pain in infants remains an extremely difficult and challenging area. Over the last twenty years there has been a significant change in attitude to infant pain, most importantly the recognition by clinicians that infants from as young as twenty-two weeks gestational age are able to demonstrate behavioural responses to noxious stimuli.

Large numbers of infants pass through neonatal intensive care units where they may be subjected to numerous invasive and painful procedures (Barker and Rutter 1995; Johnston, Collinge et al. 1997). Despite widespread acceptance that infants and neonates experience pain, recent studies have shown that the use of procedural analgesia remains much lower in these groups when compared with older children and adults undergoing the same procedures (Hall 1995; Wilkinson, Coulson et al. 2003).

The present disparity in provision of pain relief is probably not due to a belief that infants and other neonates cannot experience pain, but rather a result of their inability to communicate their sensations of pain and our current limited ability to recognize it.

Aside from causing distress and fear, unalleviated pain has numerous other long and short term consequences. Without reliable techniques for assessing pain severity and duration, it is impossible to determine the most appropriate analgesic therapy or to adjust the dosage regimen to meet the individual infant's needs.

The past 10 to 15 years have seen numerous attempts to develop such methods for assessing pain in infants. A range of techniques has been used including analysis of cry patterns (Grunau, Johnston et al. 1990), facial expressions (Grunau and Craig 1987), and body posture (Rushforth and Levene 1994), (Guinsburg, Kopelman et al. 1998). Other authors have assessed physiological responses such as heart rate, respiratory rate, blood pressure and changes in skin conductance (Abad, Diaz et al. 1996; Craig, Whitfield et al. 1993).

There is now a large body of literature on the assessment of pain in infants and neonates. Despite the growing awareness of the need to alleviate pain in infants, there is little data concerning the assessment and measurement of post-operative pain which is likely to be both qualitatively and quantitatively different.

Pain recognition in non-verbal species - neonatal humans

Pain recognition in non-verbal species - neonatal humans

Theme

Equine Anaesthesia

Chaired by
Nicki Grint

- 11.00am** **S Picek, K Kalchofner, A Fürst, J Price, R Bettschart-Wolfensberger**
Zurich, Switzerland
“Comparison of cardiovascular function of isoflurane/medetomidine anaesthetised horses under conditions of controlled or spontaneous ventilation”
- 11.15am** **H Rohrbach, U Schatzmann, T Korpivaara, C Spadavecchia**
Berne, Switzerland
“Modulation of the Nocioceptive Withdrawal Reflex and Temporal Summation: Comparison of the effects of the alpha-2 agonists detomidine, romifidine and xylazine”
- 11.30am** **C Stratford, R Vogt, S Picek, R Bettschart-Wolfensberger**
Zurich, Switzerland
“Effects of acepromazine in horses on peri-operative packed cell volume and recovery quality from general anaesthesia”
- 11.45am** **G Haddon, A Dugdale, C Proudman, M Senior**
Liverpool, UK
“Is first recorded mean arterial blood pressure (1st MAP) linked to mortality in horses undergoing colic surgery?”

Abstracts – Equine Anaesthesia

Comparison of cardiovascular function of isoflurane/medetomidine anaesthetised horses under conditions of controlled or spontaneous ventilation

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This study investigated cardiovascular function under controlled (CV) and spontaneous (SV) ventilation in horses anaesthetised using isoflurane/medetomidine.

Sixty horses were randomly assigned to one of two groups, CV and SV. Horses were sedated with medetomidine $7 \mu\text{g kg}^{-1}$ IV and anaesthesia was induced with 2 mg kg^{-1} ketamine and 0.02 mg kg^{-1} diazepam IV. Anaesthesia was maintained with isoflurane in oxygen/air and medetomidine CRI ($3.5 \mu\text{g kg}^{-1} \text{ h}^{-1}$ IV). 0.03 mg kg^{-1} acepromazine IM was administered five minutes after induction. In the CV group (Bird ventilator, PIP_{max} 20 mm Hg), IPPV maintained Et CO_2 at 5.3 – 7.99 kPa. Heart rate, respiratory rate and arterial blood pressures were recorded every 5 minutes. Arterial blood gas values were recorded at 30 minute intervals. Cardiac output was measured 45 minutes following anaesthesia induction and hourly thereafter. Dobutamine was infused to maintain mean arterial blood pressure (MAP) between 70 – 80 mmHg.

Cardiopulmonary data was averaged over time and groups were compared using independent t-tests ($p < 0.05$).

There were no significant differences between the groups in age, body weight, anaesthesia duration [mins] (CV: 126.3 ± 32.2 , SV: 123.5 ± 36.4), recumbency position, heart rate [beats min^{-1}] (CV: 32.8 ± 4.5 , SV: 32.2 ± 5.3), mean arterial blood pressure [mmHg] (CV: 83.8 ± 7.4 , SV: 83.6 ± 8.1), cardiac index [$\text{ml kg}^{-1} \text{ min}^{-1}$] (CV: 53.64 ± 4.55 , SV: 61.9 ± 8.9), quantity of dobutamine infused [$\text{ml}^{-1} \text{ kg}^{-1} \text{ min}$] (CV: 0.29 ± 0.24 , SV: 0.43 ± 0.30), p_aO_2 [kPa] (CV: 15.72 ± 4.51 , SV: 17.85 ± 7.29) and p_aCO_2 [kPa] (CV: 7.23 ± 0.84 , SV: 7.0 ± 0.67). Respiratory rate [breaths min^{-1}] (CV: 9.12 ± 0.92 , SV: 6.05 ± 1.96) was significantly higher in the CV group.

In healthy horses anaesthetised with medetomidine-isoflurane, under conditions of mild hypercapnia, ventilation mode does not affect cardiovascular function.

Abstracts – Equine Anaesthesia

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Abstracts – Equine Anaesthesia

Modulation of the Nociceptive Withdrawal Reflex and Temporal Summation: Comparison of the effects of the alpha-2 agonists detomidine, romifidine and xylazine

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Department of Clinical Veterinary Science, Anesthesiology Section, Vetsuisse Faculty, University of Berne, Berne, Switzerland

The modulatory effects of three alpha-2 agonists on nociceptive withdrawal reflex (NWR) and temporal summation were compared in a cross-over fashion in 10 healthy standing horses.

Single electrical stimulations (train-of-five 1-ms pulses, 200Hz, constant-current) on digital nerves to evoke NWR and repeated electrical stimulations (10 stimuli, 5 Hz) to obtain temporal summation were applied to the left forelimb and hindlimb of each horse¹. Electromyographic reflex activity was recorded from the deltoid, the common digital extensor, the biceps femoris and the cranial tibial muscles¹. After baseline measurement equisedative dosages of intravenous (IV) detomidine (20 $\mu\text{g}\cdot\text{kg}^{-1}$), romifidine (80 $\mu\text{g}\cdot\text{kg}^{-1}$, IV) and xylazine (1 $\text{mg}\cdot\text{kg}^{-1}$, IV)^{2,3} were administered with a 2-week-interval. Determinations of NWR and temporal summation thresholds were repeated at 10, 20, 30, 40, 60, 70, 90, 100, 120 and 130 minutes after test-drug administration on forelimb or hindlimb alternatively. Depth of sedation was assessed and scored before measurements at each time point. During stimulation, behavioural reaction was observed and recorded. To compare baseline values with single time points after test-drug administration, Wilcoxon's signed rank-test was used.

Detomidine, romifidine and xylazine significantly increased the current intensities necessary to evoke NWR and temporal summation in forelimbs (median baseline 2.6 mA(2-4 mA)) and hindlimbs (median baseline 6.3 mA(3-10 mA)) of all horses. NWR threshold values were significantly higher than baseline values at 60, 100 and 120 minutes after administration of xylazine, detomidine and romifidine, respectively. Sedation scores higher than baseline were obtained at 40 minutes after administration of xylazine and at 100 minutes after administration of detomidine and romifidine.

Detomidine, romifidine and xylazine administered intravenously at equisedative dosages significantly increased NWR and temporal summation thresholds suggesting a strong antinociceptive action. Maximum increase of NWR and temporal summation thresholds were comparable for all three drugs.

1. Spadavecchia, C et al (2005) Effect of romifidine on the nociceptive withdrawal reflex and temporal summation in conscious horses. *Am J Vet Res*, 66, 1992-1998.
2. Hamm, D and Turchi, P (1995) Sedative and analgesic effects of detomidine and romifidine in horses. *Vet Rec*, 136, 324-327.
3. England et al (1992) A comparison of the sedative effects of three alpha 2-adrenoceptor agonists (romifidine, detomidine and xylazine) in the horse. *J Vet Pharmacol Ther*, 15, 194-201.

Acknowledgements: ORION Pharma for financial support and drug delivery.

Local ethical committee approval was gained for this study.

Abstracts – Equine Anaesthesia

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Abstracts – Equine Anaesthesia

Effects of acepromazine in horses on peri-operative packed cell volume and recovery quality from general anaesthesia

C. Stratford, R. Vogt, S. Picek, R. Bettschart-Wolfensberger

University of Zürich, Winterthurerstrasse 260, 8057 Zürich, Switzerland.

Acepromazine (ACP) premedication may improve anaesthesia recovery quality. However, its action of lowering packed cell volume (PCV) decreases oxygen carrying capacity. This study investigated ACP premedication on these parameters in horses undergoing general anaesthesia.

Twenty-four horses (ASA I, II) were randomly assigned into two groups, Group A premedicated with 0.03 mg kg⁻¹ ACP by intramuscular injection 30 minutes prior to induction and Group C control. Anaesthesia was induced using medetomidine (7 mcg kg⁻¹), followed by ketamine (2 mg kg⁻¹) and diazepam (0.02 mg kg⁻¹) intravenously (IV). Anaesthesia was maintained with isoflurane in oxygenated air (mean FiO₂=61%) and a medetomidine constant rate infusion (3.5 mcg kg⁻¹ hr⁻¹). Ventilation was spontaneous. Horses received Ringers Lactate (10 ml kg⁻¹ hr⁻¹) IV and dobutamine IV as required to maintain mean arterial pressure above 70mmHg. Six jugular blood samples were taken for PCV and total protein (TP) analysis; these samples were collected at baseline, 30 minutes post ACP, before ketamine, 30 minutes post induction, end of surgery and 4 hours after surgery. PCV and TP were measured in 10 (A) and 11 (C) horses. Recovery quality (n=24) was scored from 1 (best) to 5 (worst) by a scorer blinded to the protocol. Areas under the curve (AUC), representing both PCV and TP trends were compared between groups using t-tests (p<0.05) as were anaesthetic and recovery durations. A Fischer's exact test compared recovery scores.

	Group A	Group C
*PCV AUC	145.7 (15.3)	154.5 (17.5)
*TP AUC	293.5 (27.9)	297.6 (28.3)
*Recovery length (min)	55.3 (22.2)	52.8 (14.8)
⁺ Recovery quality	2 (1-3)	1 (1-2)

* Data presented as mean (SD), ⁺Data presented as median (range)

There were no significant differences in PCV AUC, TP AUC or anaesthetic duration between groups. Recoveries were of similar lengths but quality was statistically significantly better in group C than in group A.

The conclusion was ACP did not alter PCV. Sample size was deemed insufficient to yield meaningful recovery data.

Abstracts – Equine Anaesthesia

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Abstracts – Equine Anaesthesia

Is first recorded mean arterial blood pressure (1st MAP) linked to mortality in horses undergoing colic surgery?

Haddon G, Dugdale AHA, Proudman CJ & Senior JM

Philip Leverhulme Equine Hospital (PLEH), Department of Veterinary Clinical Sciences, Faculty of Veterinary Science, University of Liverpool, CH64 7TE.

This study investigated the effect of first recorded mean arterial blood pressure (1st MAP) on intraoperative and postoperative mortality in colic cases.

Anaesthesia records were retrospectively examined and the 1st MAP noted for 679 colic cases between March 1998 and August 2003. Intraoperative and postoperative mortality during hospitalisation were recorded. Long-term survival data was acquired by owner-initiated reporting and by telephone questionnaires every three months for the first year following discharge and every six months thereafter. Recovery from general anaesthesia was defined as the horse walking out of the recovery box postoperatively. Horses that died or were euthanased during surgery or recovery from anaesthesia were classed as intraoperative death. Horses were euthanased when the clinician considered a successful outcome to be unlikely or when the owner refused to allow the horse to undergo further necessary surgery. In most cases this resulted in the horse undergoing euthanasia shortly before it would have died.

Seventy eight horses died or were euthanased intraoperatively. Two hundred and eighty one horses subsequently died during the 5 year study period. 1st MAP for horses that did or did not die intraoperatively was compared using two sample t-tests. The same comparison was made for horses that did or did not die postoperatively. Data for 1st MAP were then categorised to create four similarly sized groups [$>15-43\text{mmHg}$ ($n=176$), $>43-57\text{mmHg}$ ($n=174$), $>57-69\text{mmHg}$ ($n=164$), $>69-178\text{mmHg}$ ($n=165$)]. Cross-tabulations and Chi² tests were performed considering both outcomes. $P<0.05$ was considered significant. 1st MAP was significantly linked to intraoperative (t-test $p=0.01$, Chi² test $p=0.025$) but not postoperative death. 1st MAP was then included in a generalised linear model built using variables which have been linked to intraoperative mortality in colic cases¹ and showed a distinct linear correlation of greater 1st MAP and higher intraoperative survival rate when 1st MAP was between 15-100mmHg.

1. Proudman, C.J., Smith, J.E., Edwards, G.B., French, N.P. (2002) Long term survival of equine surgical colic cases. Part 2: Modelling post-operative survival. *Equine Vet J* 34, 438-443

Abstracts – Equine Anaesthesia

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Theme Small Animal Local Anaesthetic Techniques

**Chaired by
Briony Alderson**

- 11.00am** **V Bubalo, Y Moens, A Holzmann**
Vienna, Austria
“Isoflurane sparing effect and autonomic responses during canine ovariohysterectomy following local anaesthesia of the ovarian pedicle”
- 11.15am** **V Martin-Bouyer, S Schauvliege, L Duchateau, F Gasthuys, I Polis**
Ghent, Belgium
“Cardiovascular effects after epidural injection of romifidine in isoflurane anaesthetized dogs”
- 11.30am** **P Franci, J Brearley**
Animal Health Trust, UK
“Epidural catheter placement using the paravertebral approach with cephalad angulation: a preliminary study”
- 11.45am** **J Paterson, N Caulkett, G Muir, T Chu**
Saskatchewan, Canada
“Determination of the analgesic efficacy of maxillary incisor suprapariosteal articaine injection and palatine infiltration in dogs using reflex-evoked digastricus muscle potentials”

Abstracts - Small Animal Local Anaesthetic Techniques

Isoflurane sparing effect and autonomic responses during canine ovariohysterectomy following local anaesthesia of the ovarian pedicle

V. Bubalo¹, Y. Moens¹, A. Holzmann²

¹Clinic of Anaesthesiology and Perioperative Intensive Care, ²Clinic for Obstetrics, Gynaecology and Andrology, University of Veterinary Medicine, Veterinärplatz 1, A-1210 Vienna, Austria.

Local anaesthesia of the ovarian pedicle during canine ovariectomy is poorly documented. This study evaluates the isoflurane sparing effect of this technique and the influence on autonomic responses.

Twenty dogs scheduled for ovariohysterectomy were premedicated with 0.02 mg kg⁻¹ acepromazine and 0.1 mg kg⁻¹ methadone intramuscularly. They were randomly allocated to receive an infiltration of the ovarian pedicle with lidocaine (group L, n=10) or NaCl (group N, n=10). Anaesthesia was induced with intravenous propofol and maintained with isoflurane in oxygen. Heart rate (HR), respiratory rate (RR), invasive blood pressure (BP) and end-tidal isoflurane concentration (E'_{iso}) were continuously measured. Infiltration was performed with 2 mg kg⁻¹ lidocaine 2%. Depth of anaesthesia was adjusted by the stepwise reduction in E'_{iso} until HR, RR or BP showed increases of > 20 %. Measurements before (T1) and after (T2) pedicle infiltration and the time period from start to end of excision of both ovaries (T3, mean value) were used for analysis. The formation of post-infiltration haematoma was noted. Data are presented as mean $\pm$ SD. Statistical analysis was done using ANOVA and unpaired t-tests; $p < 0.05$ was considered significant.

In group L, BP was higher at T3 (12.8 ± 1.7 kPa) compared to T1 and T2 (7.7 ± 1.1 kPa and 10.6 ± 1.2 kPa respectively, $p < 0.05$). In group N, BP was higher at T3 (12.4 ± 1.9 kPa) compared to T1 (8.6 ± 2.6 kPa, $p < 0.05$). There were no significant changes in HR nor RR within the groups. There were no statistically significant differences for measured parameters between the groups at any time point. Six dogs in group L developed a haematoma in the mesovarium compared to one in group N.

Neither an isoflurane sparing effect nor an obtunded autonomic response to surgery could be demonstrated in Group L compared to Group N, but there was an increased risk of haematoma formation.

Abstracts - Small Animal Local Anaesthetic Techniques

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Abstracts - Small Animal Local Anaesthetic Techniques

Cardiovascular effects after epidural injection of romifidine in isoflurane-anaesthetized dogs

V. Martin-Bouyer¹, S. Schauvliege¹, L. Duchateau², F. Gasthuys¹, I. Polis³

¹ Department of Surgery and Anaesthesiology of Domestic Animals, ² Department of Physiology and Biometrics, ³ Department of Medicine and Clinical Biology of Small Animals, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium.

The cardiovascular effects of epidural romifidine were investigated in isoflurane anaesthetized dogs.

Anaesthesia was induced in six healthy beagles (12.5 ± 1.4 kg) with propofol (6 to 9 mg kg⁻¹) and maintained with 1.8-1.9% end tidal (ET) isoflurane in O₂. ET CO₂ was maintained between 4.66 and 5.99 kPa. The dorsal pedal artery was used for measurement of arterial blood pressure (AP) and blood sampling. Heart rate (HR) and cardiac output (CO) were determined with a combined LiDCO and PulseCO monitor (LiDCO-Plus®). Stroke volume index (SI) and systemic vascular resistance (SVR) were calculated. After baseline measurements, either 10 µg kg⁻¹ romifidine (R) or saline (S) (total volume of 1 ml per 4.5 kg) was injected into the lumbosacral epidural space. At least 1 week elapsed between protocols. Data were recorded every 5 minutes for 1 hour. Statistical analysis was based on a mixed model with dogs as the random effect and treatment and time as categorical fixed effects (F-tests at 5% significance level).

After epidural injection of romifidine, overall significant decreases were detected for HR (R group 95 ± 22 versus S group 129 ± 22 bpm, $p < 0.0001$), mean AP (R group 81 ± 12 versus S group 89 ± 12 mmHg, $p = 0.0002$), CO (R group 1.58 ± 0.88 versus S group 3.27 ± 0.88 L min⁻¹, $p < 0.0001$), SI (R group 28.90 ± 9.46 versus S group 47.67 ± 9.46 L min⁻¹m⁻², $p < 0.0001$) while significant increases for SVR (R group 4878 ± 1066 versus S group 2122 ± 1066 dynes.sec cm⁻⁵, $p < 0.0001$) were observed.

Epidural injection of 10 µg kg⁻¹ romifidine in isoflurane anaesthetised dogs induced significant decreases in HR, AP, CO and an increase in SVR similar to the demonstrated effects after systemic administration of romifidine¹.

1. Pypendop BH, Verstegen JP (2001) Cardiovascular effects of romifidine in dogs. Am J Vet Res 62 (4), 490-495.

Ethical Committee approval : 2005/33

Abstracts - Small Animal Local Anaesthetic Techniques

[illegible]

Abstracts - Small Animal Local Anaesthetic Techniques

Epidural catheter placement using the paravertebral approach with cephalad angulation: a preliminary study

P Franci, JC Brearley.

Centre for Small Animal Studies - Animal Health Trust Lanwades Park Kentford

Newmarket Suffolk CB8 7UU

The paravertebral approach¹ for introducing epidural catheters (EC)s may allow easier and more cranial placement. This study describes the technique and its use in 4 animals.

EC placement was performed in animals in severe pain and with owner consent. Placement was attempted in three dogs (body mass 11, 27 and 31 kg) and one cat (4.5 kg). Exclusion criteria included contraindications for epidural injection and/or the possibility of catheter dislodgement due to surgery. No more than three attempts to place the EC were allowed. Once anaesthetized, the animals were positioned in right or left lateral recumbency. A 20G Tuohy needle (Perfix Paed, B-Braun) was inserted paravertebrally at the level of the caudal margin of the spinal process of the vertebral caudal to the interspace at which the EC was to be introduced. The needle was directed cranio-medially and when it struck the vertebra lamina it was redirected cranially aiming for the interspace. The epidural space was identified with loss of resistance technique². A 24G EC was advanced through the needle. Catheter placement was confirmed radiographically.

EC placement was successful in three dogs but not in the cat. One dog had the EC placed at the first attempt at T12-T13, with the tip at T9. The second had the EC placed at the second attempt at L1-L2, with the tip at T12, the third had the EC placed at third attempt at the same interspace with the tip at L1.

Despite the limited number of cases, this appears to be a relatively simple technique, allowing the EC to be advanced more easily than the traditional midline approach at the L7-S1 space. EC placement was straightforward in two dogs, while body dimensions made placement difficult in the other dog (31 kg) and impossible in the cat within the number of attempts permitted.

1. Armitage EN (2003) Lumbar and thoracic epidural block. In: Principles and Practise of Regional Anaesthesia. (3rd edn) Wildsmith JAW, Armitage EN, McClure JH (eds) Churchill Livingstone, UK, 147-149.

2. Armitage EN (2003) Lumbar and thoracic epidural block. In: Principles and Practise of Regional Anaesthesia. (3rd edn) Wildsmith JAW, Armitage EN, McClure JH (eds) Churchill Livingstone, UK, 146.

Acknowledgements to **B-Braun** for the donation of Perfix[®] Paed set for continuous epidural anaesthesia/analgesia.

Abstracts - Small Animal Local Anaesthetic Techniques

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Abstracts - Small Animal Local Anaesthetic Techniques

Determination of the analgesic efficacy of maxillary incisor suprapariosteal articaine injection and palatine infiltration in dogs using reflex-evoked digastricus muscle potentials.

J.M. Paterson, N.A. Caulkett, G.D. Muir, and T. K. Chu

Department of Small Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4, Canada

Maxillary suprapariosteal injection is the most frequently employed local anesthetic technique in humans for achieving pulpal anesthesia in maxillary teeth¹, but it has never been investigated in dogs. This study examined whether suprapariosteal articaine infiltration of maxillary incisors would abolish reflex-evoked digastricus muscle action potential (REMP) in dogs during non-invasive stimulation of tooth pulp.

Anesthesia was induced with propofol (6mg kg⁻¹) and maintained with halothane (1.37–1.46%) and 100% oxygen in nine adult mixed breed dogs. REMP was recorded using a previously described method². A suprapariosteal injection (SPI) of 1.2 ml 4% articaine (1:200 000 epinephrine) was administered in a left maxillary incisor and the corresponding right incisor was injected with 1.2 ml saline 2 min later. Stimulation was applied over 40 min; every 2 min for the first 10 min and every 10 min thereafter. Palatine infiltration (PI) was added as an augmentation technique, either with SPI, or at 40 min if SPI failed to abolish REMP. An infraorbital nerve block (IOB) was performed if both blocks failed. End tidal (ET) halothane and CO₂, oxygen saturation, heart and respiratory rate, and indirect systolic, diastolic, and mean arterial blood pressures were recorded at each time point. Physiological responses over time and between treatments were compared with one and two-way ANOVA and a Bonferroni's post hoc test. $P < 0.05$ was considered significant. Abolishment of REMP for each technique was calculated as a percent.

The success of abolishing REMP was: SPI (11%), SPI + PI (60%), SPI ± PI + IOB (100%). There were no significant differences between treatments for ET halothane or any physiological parameter.

Suprapariosteal injection, with or without palatine infiltration, is an unreliable technique for provision of maxillary incisor analgesia in dogs. Infraorbital nerve blocks remain the gold standard for providing reliable anesthesia to maxillary incisors in dogs.

1. Haglund, J., and H. Evers. 1986. Incisors and canines. In: Haglund, J., and H. Evers. Local anesthesia in dentistry, 7th ed. Astra Lakemedel., Sodertalje, Sweden. Pp. 31-39.
2. Gross, M.E., E.R. Pope, D. O'Brien, et al. 1997. Regional anesthesia of the infraorbital and inferior alveolar nerves during noninvasive tooth pulp stimulation in halothane-anesthetized dogs. J Am Vet Med Assoc. 211: 1403-1405.

Acknowledgements: Funding for this study was provided by the Western College of Veterinary Medicine Companion Animal Health Fund.

This study was approved by the University of Saskatchewan Animal Care Committee, protocol number 20010128.

Abstracts - Small Animal Local Anaesthetic Techniques

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Ready for take-off?

**Chaired by
Prof Robin Gleed**

**Speakers
Gp Capt David Gradwell
Dr Paul van Dijk**

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Direct Medical Supplies

Flight physiology

David Peter Gradwell BSc PhD MB DAvMed FRCP FRAeS RAF

David Gradwell is a Group Captain in the Royal Air Force Medical Service, and holds the post of Consultant Adviser in Aviation Medicine. After gaining a BSc(hons) in Physiology in 1976, he trained in Medicine, graduating in 1981.

After three years working in the National Health Service, he joined the Royal Air Force to specialise in Aviation Medicine, completing his PhD in High Altitude Physiology and being appointed to a Consultant in 1993.

He took up his present appointment in 1998. He also holds a visiting Senior Lecturer appointment at King's College, London and is the Aviation Medicine Adviser to the Royal College of Physicians.

David is a Fellow of the Royal College of Physicians, the Royal Aeronautical Society and the Aerospace Medical Association in the USA. He is co-editor of the forth-coming fourth edition of the UK Standard Textbook of Aviation Medicine, and in 2005 was awarded the Louis Bauer Founders Award by the Aerospace Medical Association for his contributions to aerospace medicine.

He is married, to a consultant anaesthetist in the Royal Navy.

Flight physiology

Flight physiology

Aeroplane transport of horses

Paul van Dijk DVM PhD DiplECVA

Head of the clinical section of equine anaesthesia and intensive care of the Department of Equine Science, Veterinary Faculty, Utrecht University.

Beside the clinical work Dr. van Dijk is involved in education and research. The main research programme includes aspects of equine endotoxaemia. At the moment he is co-supervisor in a PhD programme regarding the immunomodulatory effects of ketamine in equine endotoxaemia.

A second field of his interest is: Stress and stress behaviour in horses. One of the topics is the effect of air transport on horses. A great opportunity to perform some work in this area of research is the cooperation with Dr. Jan-Willem de Gooijer (KLM veterinarian) and the staff of KLM Cargo.

Aeroplane Transport of Horses

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Aeroplane transport of horses

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Deep breathing

**Chaired by
Mrs Lynne Hughes**

**Speaker
Dr Andy Yule**

Sponsor



Physiology of diving animals

Andrew Bruce Yule BSc PhD

Lecturer in Marine Biology, School of Ocean Science, UW Bangor.

1977 Scientific Officer in the N.E.R.C. Unit of Marine Invertebrate Biology, Marine Science Labs., Menai Bridge. Personal Assistant to the Director, Prof. D.J.Crisp,

1983 Promoted to Higher Scientific Officer.

1983 *Transferred, on closure of the N.E.R.C. Unit, to the academic staff of the Marine Biology Department, UCNW. Appointed as Research Officer, Grade 1A.*

1988 Promoted Research Fellow Grade 2A

1994 Redesignated to Lecturer.

Research Interests: *I have a wide range of research interests covering most areas of marine Biology and I have published in the fields of biophysics, materials technology, zooplankton and rocky shore ecology, larval biology, statistics and animal physiology. I have worked in the areas of antifouling technology, aquaculture physiology, zooplankton energetics and animal behaviour for most of my working life.*

Diving in Marine air breathers

Evolution of life from the sea to the land was a highly improbable event. Only a small fraction of the earth's animal Phyla succeeded. Returning to the sea from a terrestrial existence is equally improbable. Pre-adaptation is the key to successful evolution and the current air breathing divers in the marine environment have made the transition by virtue of many characteristics already exhibited by their terrestrial relatives. The diving reflex and lactate tolerance are central to the success of deep divers yet these physiological characteristics can be found in virtually all mammals (for example). Behaviour, morphological modification of the trachea and increased myoglobin concentrations eliminate the problems of the bends and oxygen toxicity so acutely experienced by human divers. Extreme lactate tolerance and rapid repayment of oxygen debt complete the list of tools required for very deep diving over long periods. Our understanding of how these organisms cope with the extreme pressures at great depth, which must have profound consequences for membrane and enzyme function, is currently very limited.

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Physiology of diving animals

Physiology of diving animals

Theme

Equine Anaesthesia & Analgesia

**Chaired by
Mark Senior**

- 4.45pm** **S Robertson, L Sanchez, C Cole, L Maxwell**
Florida, USA
“Effect of fentanyl on somatic and visceral nociception in conscious horses”
- 5.00pm** **M Martin-Flores, R Gleed, L Campoy**
Cornell, USA
“Comparison between acceleromyography and visual assessment of train-of-four for monitoring neuromuscular blockade in horses”
- 5.15pm** **S Schauvliege, L Duchateau, A Van den Eede, F Gasthuys**
Ghent, Belgium
“Cardiovascular effects of enoximone in anaesthetised ponies”
- 5.30pm** **I Iff, M Mosing, Y Moens**
Vienna, Austria
“Epidural pressure in standing horses: preliminary results”

Abstracts – Equine Anaesthesia & Analgesia

Effect of fentanyl on somatic and visceral nociception in conscious horses.

SA Robertson¹, L C Sanchez¹, C Cole¹, L Maxwell²

¹University of Florida College of Veterinary Medicine, Gainesville, FL and ²Oklahoma State University, Stillwater, OK, USA

Transdermal fentanyl has been used clinically in horses based upon pharmacokinetic data¹ and its anti-nociceptive effect in other species. The aim of this study was to evaluate the effect of fentanyl infusion on visceral and somatic nociception in conscious horses.

Visceral nociception was evaluated using two methods of threshold detection, colorectal distention (CRD) and duodenal distention (DD). Each employed a Mylar® balloon and a computer-controlled barostat for distention. A probe containing a heater element and adjacent temperature sensor placed on the withers was used for thermal stimulation to assess somatic nociception. Nose-to-ground height was used to assess sedation. Heart and respiratory rates were determined by manual count. All variables were measured before treatment then at 15 minute intervals except for DD and CRD which were measured every 30 minutes. Treatments were administered as an intravenous bolus followed by continuous rate infusion for a total of two hours (equal volumes for all treatments). Treatments included four doses of fentanyl (F1-4), saline (negative control), and xylazine (positive control). Six horses were used and each horse received each treatment in a randomized order with at least 7 days between treatments. Serum fentanyl concentrations were analysed by a LC/MS/MS method. All data were analysed by means of a three-factor ANOVA (SAS Proc Mixed) followed by either a simple t test or a Bonferroni t test for multiple comparisons.

Approximate mean serum fentanyl concentrations (ng ml⁻¹) for each treatment were as follows: F1 peak of 0.3, F2 peak of 1.0, F3 peak of 4, maintenance of 2.5, F4 peak of 10, maintenance of 6. Two horses in the F4 group became agitated and tachycardic (HR of 60 and 84) during the first 15 minutes of treatment.

Fentanyl administration did not result in significant changes in DD, CRD, NTG, or RR. TT was increased at 15 and 30 minutes for the F4 group.

Fentanyl did not produce a significant anti-nociceptive effect at the chosen doses, at serum concentrations above those shown to produce analgesia in other species.

1. Maxwell LK, Thomasy SM, Slovis N, Kollias-Baker C. Pharmacokinetics of fentanyl following intravenous and transdermal administration in horses. Equine Vet J 2003;35(5):484-490.

Acknowledgements: this study was supported by the Grayson-Jockey Club Research Foundation.
This study was approved by the University of Florida's Animal Care and Use Committee

Abstracts – Equine Anaesthesia & Analgesia

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Abstracts – Equine Anaesthesia & Analgesia

Comparison between acceleromyography and visual assessment of train-of-four for monitoring neuromuscular blockade in horses.

M. Martin-Flores, R. D. Gleed, L. Campoy

Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY, USA.

Residual neuromuscular blockade is a frequent anaesthetic complication in people¹. The use of acceleromyography (AMG) decreases its incidence from 62% to 3.5%². The objective of this study was to compare AMG with visual assessment of train-of-four (TOF) in terms of their ability to detect residual paralysis in horses.

Nine horses, ASA physical status 1-2, undergoing general anaesthesia for various surgical procedures were included in this prospective study. After induction of general anaesthesia and final positioning of the patient a nerve stimulator and an acceleromyography sensor (TOF Watch, Organon) were placed on the hind limb to stimulate the peroneal nerve and record evoked movement of the hoof. The anaesthetic protocol was selected independently. The anaesthetist visually assessed hoof movement and was unaware of the AMG reading. A single dose of intravenous atracurium besylate, 0.15 mg kg⁻¹ was administered after baseline assessment. At one minute intervals the anaesthetist recorded the number of twitches (0-4) observed visually and whether fade could be detected between the first and fourth twitch. At the same time another observer recorded AMG readings for later comparison.

During recovery from blockade, all twitches first appeared to be of similar amplitude by visual inspection 48 (39, 68) [median (min, max)] minutes after atracurium administration. At that time the TOF ratio (peak acceleration of fourth twitch divided by peak acceleration of the first twitch) measured by AMG was only 53 (43, 68) %. TOF ratio determined by AMG did not equal or exceed 90 % until 56 (48, 110) minutes (Wilcoxon signed rank test, p=0.0092).

We conclude that: 1) TOF ratio by acceleromyography is a more sensitive indicator of residual neuromuscular blockade than is visual assessment of TOF in horses, and 2) when visual assessment of TOF indicates complete recovery from neuromuscular blockade induced by atracurium, there may be substantial residual blockade.

1. Murphy, G.S., Szokol, J.W., Marymont, J.H., et al. (2005). Residual paralysis at the time of tracheal extubation. *Anesth Analg*, 100. pp 1840-1845.

2. Baillard, C., Clec'h, C., Catineau, J., et al (2005). Postoperative residual neuromuscular block: a survey of managements. *BJA* 95(5). Pp 622-626.

Abstracts – Equine Anaesthesia & Analgesia

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Abstracts – Equine Anaesthesia & Analgesia

Cardiovascular effects of enoximone in anaesthetised ponies

S. Schauvliege¹, L. Duchateau², A. Van den Eede¹, F. Gasthuys¹

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Cardiovascular depression is one of the major problems associated with equine anaesthesia. Therefore, the effects of the inodilator enoximone (phosphodiesterase III inhibitor¹), were examined in anaesthetised ponies.

Five ponies, weighing 293 ± 45 kg, were sedated with intravenous (IV) romifidine ($80 \mu\text{g kg}^{-1}$). Anaesthesia was induced with midazolam ($0.06 \text{ mg kg}^{-1}\text{IV}$) plus ketamine ($2.2 \text{ mg kg}^{-1}\text{IV}$) and maintained with isoflurane in oxygen (Et Iso 1.7%). The ponies' lungs were ventilated to maintain eucapnia (PaCO_2 4.66-6.00 kPa). Each pony was anaesthetised twice with an interval of 3 weeks, receiving enoximone $0.05 \text{ mg kg}^{-1}\text{IV}$ (E) or saline (S) 90 minutes post induction. Heart rate (HR), arterial (AP) and central venous pressure (CVP) were measured before treatment, every 5 minutes between T0 (treatment) and T30 and every 10 minutes between T30 and T120. Cardiac index (CI) measurements (lithium dilution technique) and blood gas analysis (arterial and mixed venous samples, obtained from the carotid artery and right atrium respectively) were performed before treatment and at T5, T10, T20, T40, T60, T80, T100 and T120. Stroke volume index (SI), systemic vascular resistance (SVR), venous admixture (VA) and oxygen delivery (DO_2) were calculated. Statistical analysis was based on a mixed model with treatment, time and their interaction as fixed categorical effects and pony as random effect comparing the two treatments both globally (at $\alpha=0.05$) and at T10, T20, T40, T80 and T120 (at Bonferroni-adjusted $\alpha=0.01$).

Table 1: Mean $\pm$ standard deviation for the two treatments (saline (S) or enoximone (E)) and P-value for the difference between the two treatments at different timepoints and overall.

Time (min)		T-10	T10	T20	T40	T80	T120	Overall
HR (BPM)	S	39 $\pm$ 1.4	37 $\pm$ 1.9	36 $\pm$ 2.3	36 $\pm$ 3.2	34 $\pm$ 2.1	34 $\pm$ 1.5	35.37 $\pm$ 1.68
	E	39 $\pm$ 2.9	43 $\pm$ 3.4	42 $\pm$ 2.6	39 $\pm$ 1.6	36 $\pm$ 0.8	35 $\pm$ 0.7	38.56 $\pm$ 1.68
			P<0.0001	P<0.0001	P=0.0065	P=0.1680	P=0.5386	P=0.0230
MAP (mm Hg)	S	60 $\pm$ 6.8	59 $\pm$ 4.0	63 $\pm$ 7.4	68 $\pm$ 9.7	66 $\pm$ 10.7	67 $\pm$ 4.6	65 $\pm$ 3.3
	E	64 $\pm$ 6.4	69 $\pm$ 11.3	69 $\pm$ 12.8	70 $\pm$ 12.7	77 $\pm$ 4.1	72 $\pm$ 8.0	72 $\pm$ 3.6
			P=0.1048	P=0.1846	P=0.6652	P=0.0643	P=0.3874	P=0.1834
CI (mL kg ⁻¹ min ⁻¹)	S	44 $\pm$ 9.4	40 $\pm$ 8.0	38 $\pm$ 10.0	37 $\pm$ 8.5	31 $\pm$ 9.6	33 $\pm$ 7.7	35.58 $\pm$ 6.57
	E	49 $\pm$ 11.2	63 $\pm$ 11.1	59 $\pm$ 10.9	53 $\pm$ 7.8	41 $\pm$ 4.8	39 $\pm$ 5.2	50.41 $\pm$ 6.60
			P<0.0001	P=0.0004	P=0.0057	P=0.0980	P=0.2767	P=0.0224
SVR (dyne.sec.cm ⁻⁵)	S	270 $\pm$ 55	312 $\pm$ 85	351 $\pm$ 91	416 $\pm$ 147	451 $\pm$ 106	451 $\pm$ 137	393 $\pm$ 67
	E	279 $\pm$ 77	247 $\pm$ 62	269 $\pm$ 89	299 $\pm$ 76	424 $\pm$ 97	413 $\pm$ 152	336 $\pm$ 80
			P=0.2723	P=0.1625	P=0.0504	P=0.6404	P=0.5175	P=0.2195
VA (%)	S	24 $\pm$ 5.9	26 $\pm$ 6.0	32 $\pm$ 22.4	23 $\pm$ 4.3	20 $\pm$ 7.3	23 $\pm$ 3.1	24 $\pm$ 4.0
	E	26 $\pm$ 7.2	47 $\pm$ 27.2	33 $\pm$ 5.7	46 $\pm$ 18.8	22 $\pm$ 5.8	36 $\pm$ 16.9	35 $\pm$ 4.0
			P=0.0109	P=0.9881	P=0.0047	P=0.7898	P=0.0936	P=0.0261
DO ₂ (L min ⁻¹)	S	1.6 $\pm$ 0.30	1.4 $\pm$ 0.31	1.4 $\pm$ 0.48	1.4 $\pm$ 0.49	1.1 $\pm$ 0.36	1.1 $\pm$ 0.30	1.23 $\pm$ 0.30
	E	1.9 $\pm$ 0.46	2.3 $\pm$ 0.33	2.3 $\pm$ 0.42	1.9 $\pm$ 0.28	1.7 $\pm$ 0.46	1.4 $\pm$ 0.37	1.82 $\pm$ 0.30
			P<0.0001	P<0.0001	P=0.0008	P=0.0017	P=0.0850	P=0.0008

During the 120 minute time period following treatment, enoximone induced significant increases in HR, CI, SI, VA and DO_2 and a significant decrease in CVP. No significant differences were detected for AP, SVR and blood gases. No cardiac arrhythmias or other side effects were observed. The results suggest enoximone has beneficial effects on CI and SI without significant changes in blood pressure. Despite increases in VA, DO_2 was improved.

1. Vernon M.W., Heel R.C., Brogden R.N. (1991) Enoximone, a review of its pharmacological properties and therapeutic potential. *Drugs* 42 (6), 997-1017

This study was approved by the local Ethical Committee (EC 2005/48).

Abstracts – Equine Anaesthesia & Analgesia

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Abstracts – Equine Anaesthesia & Analgesia

Epidural pressure in standing horses: preliminary results

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Epidural pressures and the epidural pressure profile following epidural injection have not been previously documented in standing horses.

Epidural puncture was performed in ten adult horses weighing 527 ± 63 kg (mean $\pm$ SD). An 18 G Tuohy needle was inserted into the first or second inter-coccygeal vertebral space. The needle was connected via a fluid filled line to a pressure transducer to measure epidural pressure. The transducer was zeroed at the base of the tail. The needle was inserted until a distinct “give” was felt. Lack of resistance to injection of 0.012 ml kg^{-1} of saline was tested. If no resistance was felt, lidocaine 1% (0.2 mg kg^{-1}) was injected over two minutes. Correct epidural administration of lidocaine was verified by evaluation of tail flaccidity, reaction to clamping of the perianal region and observation of areas of increased sweating. Epidural pressure was recorded after penetration of the epidural space (baseline), after local anaesthetic injection and for the following ten minutes. Descriptive statistical analysis was used for evaluation of the data and a paired t-test was used to compare epidural pressures before and after epidural injection and at the end of the measurement period respectively. A P value of < 0.05 was considered significant.

Correct epidural drug administration was confirmed in all ten horses. Mean epidural pressure after puncture was -1.48 ± 1.06 kPa. One horse had a positive epidural pressure of 1.33 kPa. Immediately after the epidural injection the pressure increased to a maximum of 5.04 ± 3.16 kPa. Ten minutes after injection mean epidural pressure decreased to 0.79 ± 1.77 kPa. The maximal pressure after injection and the pressure after ten minutes were statistically significantly different from baseline.

Epidural space pressure is sub-atmospheric in most horses. Following fluid injection epidural pressure rises significantly and becomes positive. Epidural pressure is still elevated ten minutes after epidural injection.

This experimental study has institutional approval and meets the Austrian national regulations on animal experiments.

Abstracts – Equine Anaesthesia & Analgesia

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Theme

Small Animal Analgesia & Analgesiometry

**Chaired by
Briony Alderson**

- 4.45pm** **A Bergadano, O Andersen, L Arendt-Nielsen, U Schatzmann, C Spadavecchia**
Berne, Switzerland
“Evaluation of the short and long term stability of the nociceptive withdrawal reflex threshold in beagle dogs”
- 5.00pm** **A Bergadano, O Andersen, L Arendt-Nielsen, U Schatzmann, C Spadavecchia**
Berne, Switzerland
“Does acepromazine modulate the nociceptive withdrawal reflex characteristics in dogs?”
- 5.15pm** **P Steagall, P Carnicelli, P Taylor, S Luna, M Dixon**
São Paulo, Brazil
“Pressure and thermal thresholds in cats after administration of methadone, morphine, buprenorphine or saline”
- 5.30pm** **S Luna, A Babilio, P Steagall, L Machado, F Moutinho, C Brandao**
São Paulo, Brazil
“Long term safety of carprofen, etodolac, meloxicam, flunixin and ketoprofen in dogs”
- 5.45pm** **A Shih, S Robertson, N Isaza, L Pablo, W Davies**
Florida, USA
“A comparison between buprenorphine and carprofen alone or in combination for post-operative pain after ovariohysterectomy in dogs”

Abstracts – Small Animal Analgesia and Analgesimetry

Evaluation of the short and long term stability of the nociceptive withdrawal reflex threshold in beagle dogs.

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The nociceptive withdrawal reflex (NWR) has been described as a new non-invasive model to investigate nociception in dogs ¹. If within-subject changes in NWR threshold (I_t) are to be attributed to drugs designed to modulate nociception or to change central excitability, it is important to show that I_t remains stable over time ². To demonstrate the reliability of I_t in dogs we analyzed its within-session and intersession variability.

Surface electromyograms evoked by transcutaneous electrical stimulation of the ulnar nerve (ramus dorsalis) were recorded from the deltoid muscle of the forelimb in 8 healthy, male beagle dogs. A train-of-5 pulses was used; current intensity was stepwise increased to reach I_t (minimum stimulus intensity evoking EMG activity from the deltoid muscle in a 20- to 100-millisecond epoch with an amplitude > 10 times the EMG background activity, lasting > 10 milliseconds, and accompanied by a flexion of the carpus). The I_t was determined as the mean of three assessments. The I_t was re-determined within-session at 20, 60, and 100 min (short-term stability) and after 1 week (intersession, long-term stability). Repeated measures ANOVA on ranks was used to analyze within-session I_t and Wilcoxon test for intersession I_t variability ($p < 0.05$ significant). Results are expressed as median (range).

The I_t was 2.7 mA (1.8-7), 2.8 (1.8-7.2), 2.6 (1.8-7), 2.7 (1.8-7) at baseline, 20, 60 and 100 min, respectively without any statistical differences ($p = 0.43$). After 1 week the I_t was 2.4 mA (2-7.4) again without any difference compared to the previous measurement ($p = 0.84$).

The present findings provide important evidence which supports the short- and long-term temporal stability of the NWR thresholds. This allows the application of the model in canine studies examining the antinociceptive effects of drugs over time or the individual changes in I_t as an objective tool to investigate chronic pain³.

1. Bergadano A, Andersen O, Arendt-Nielsen L, et al. Quantitative assessment of nociceptive processes in conscious dogs by use of the nociceptive withdrawal reflex. A methodological study. Am J Vet Res 2005. in print

2. French DJ, France CR, France JL, et al. The influence of acute anxiety on assessment of nociceptive flexion reflex thresholds in healthy young adults. Pain 2005;114:358-363.

3. Curatolo M, Petersen-Felix S, Arendt-Nielsen L, et al. Central hypersensitivity in chronic pain after whiplash injury. Clin J Pain 2001;17:306-315.

Acknowledgments: this study has been funded by a Vetsuisse research grant

The experiments were approved by the committee for animal experimentation of the canton Basel- city, Switzerland (approval number 2090).

Abstracts – Small Animal Analgesia and Analgesiometry

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Abstracts – Small Animal Analgesia and Analgesiometry

Does acepromazine modulate the nociceptive withdrawal reflex characteristics in dogs?

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The nociceptive withdrawal reflex (NWR) has been described as a non-invasive model to investigate nociception in dogs¹. To implement NWR in clinical patients, tranquillization could facilitate the measurements. We hypothesised that a low-dose of acepromazine ² wouldn't affect NWR characteristics.

Surface electromyograms evoked by transcutaneous electrical stimulation of the ulnar nerve (ramus dorsalis) were recorded from deltoid muscle in 8 male beagles. Current intensity was increased to reach NWR threshold (I_t); latency and amplitude were analysed. Behavioural response (0-6 scale; no movement-vocalisation) and sedation (0-8 scale; awake-deep sedation) were scored. Dogs received in a randomized, double-blinded, cross-over fashion 10 mcg kg⁻¹ acepromazine (ACP-group) or saline IV (PLB-group) at 1 week interval. Measurements were done before (Baseline) and 20, 60, 100 min after drug administration. Repeated measures ANOVA on ranks was used to analyze I_t , latency, amplitude, behavioural response and sedation scores over time; Wilcoxon-signed-rank test to compare drug's effect ($p < 0.05$ significant). Results are median (range).

Group	NWR	Baseline	20	60	100
ACP	I_t (mA)	2.4 (2-7.4)	2.8 (2-6.4)	2.8 (1.6-6.8)	2.8 (1.6-4.8)
	Latency (ms)	22 (13.7-24.5)	22 (13.7-24.5)	23.5 (13.7-25.4)	22 (15.4-23.5)
	Amplitude	24.5 (15.1-38.3)	28.1 (16.4-41.5)	20.1 (13.1-32.7)	16.5 (12.8-35)
	Behavior	2 (1-3)	1 (0-2)	1 (1-2)	1 (0-2)
	Sedation	0 (0-1)	2 (1-6) ^{°*}	2 (1-4) [°]	2.5 (0-5) [°]
PLB	I_t (mA)	2.7 (1.8-7)	2.8 (1.8-7.2)	2.6 (1.8-7)	2.7 (1.8-7)
	Latency (ms)	22 (20.5-30.3)	21.5 (20.5-25.4)	20.5 (13.7-24.5)	21.5 (13.7-25.4)
	Amplitude	22.1 (12.6-31.9)	18.6 (10.7-40.7)	13.5 (10.83.4)	19.5 (11.5-40)
	Behavior	1 (1-2)	1.5 (1-3)	1 (1-2)	1.5 (1-2)
	Sedation	0 (0-0)	1 (0-3) [°]	2 (0-4) [°]	0.5 (0-3) [°]

There was no significant difference in I_t , latency, amplitude, behavioral response scores between groups. Sedation scores at 20, 60, 100 min were significantly higher[°] than Baseline in both groups while ACP versus PLB only at 20 min ($p = 0.016$)*.

Low-dose acepromazine exerted a minimal tranquillization and facilitated instrumentation/measurements without affecting NWR characteristics or behavioural responses. Acepromazine can be used to reduce anxiety in dogs without altering the validity of this model.

1. Bergadano A, Andersen O, Arendt-Nielsen L, et al. Quantitative assessment of nociceptive processes in conscious dogs by use of the nociceptive withdrawal reflex. A methodological study. Am J Vet Res 2005. (In Press)
2. Plumb D. Veterinary Drug Handbook. 4 ed. White Bear Lake Minnesota: PharmaVet Publishing, 2002.

Acknowledgments: this study has been funded by a Vetsuisse research grant

The experiments were approved by the committee for animal experimentation of the Canton Basel- city, Switzerland (approval number 2090).

Abstracts – Small Animal Analgesia and Analgesiometry

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Abstracts – Small Animal Analgesia and Analgesimetry

Pressure and thermal thresholds in cats after administration of methadone, morphine, buprenorphine or saline.

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Opioids are widely used for treatment of acute and postoperative pain. This study compared the pressure¹ and thermal thresholds after administration of methadone, morphine, buprenorphine, and saline in cats.

Eight cats (3.0 – 4.9 kg) were studied. Pressure stimulation was performed via a plastic bracelet (5 gm) taped around the forearm. Three 2.4 mm diameter ball-bearings, in a 10mm triangle, were advanced against the dorsolateral surface of the forearm by manual inflation of a modified blood pressure sensing bladder. Pressure in the cuff was recorded at the end point (leg shake and head turn). Thermal threshold was tested as previously reported².

After four baseline threshold recordings, each cat received subcutaneous methadone 0.2 mg kg⁻¹, morphine 0.1 mg kg⁻¹, buprenorphine 0.02 mg kg⁻¹ or saline 0.3 ml in a four period cross-over study with a week interval. Measurements were made at 15, 30, 45 minutes and at 1, 2, 3, 4, 8, 12 and 24 hours after the injection. Data were analysed by ANOVA (p<0.05).

There were no significant changes in thermal threshold after saline or buprenorphine and in pressure threshold after saline. Thermal threshold increased 1h after methadone (3.08±1.56 °C) and 1h and 4h (2.96±2 °C) after morphine. Pressure threshold increased 1h after methadone (255±232mmHg). Pressure threshold increased 30min and 1h (237±205mmHg) after buprenorphine and between 45min (244±207mmHg) and 1h after morphine.

Morphine was the most effective in increasing thermal and pressure thresholds. Buprenorphine's limited effect compared with previous studies is probably related to the route of administration, as when given transdermally, it did not produce thermal antinociception in cats³.

1. Dixon et al (2005) Development of a pressure threshold testing devices for evaluation of analgesics in cats. Proceedings of the Association of Veterinary Anaesthetists Autumn Meeting, Newmarket, UK. 76

2. Dixon MJ, Taylor PM, Robertson SA (2002) ResVetSci 72 205-210

3. Murrell et al (2006) Vet Rec (In Press)

Acknowledgments: The Feline Advisory Bureau and FAPESP for funding the project

This study was approved by the Local Animal Care Committee under protocol number 62/2005.

Abstracts – Small Animal Analgesia and Analgesiometry

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Abstracts – Small Animal Analgesia and Analgesimetry

Long term safety of carprofen, etodolac, meloxicam, flunixin and ketoprofen in dogs.

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NSAIDs can be used to prevent and treat acute, chronic and postoperative pain because of their analgesic and anti-inflammatory effects. This study evaluated the safety of long term use of NSAIDs in dogs.

Thirty-six adult dogs (15 – 25 kg; 1-3 years old) were divided into six groups. CBC, urinalysis, serum urea, creatinine, ALT, ALP, GGT, total protein, albumin, globulin, occult blood in faeces, clotting and bleeding time (internal side of the ear) were measured before and at 7, 30, 60 and 90 days after SID treatment with one of the following drugs: lactose 1 mg kg⁻¹, etodolac 15 mg kg⁻¹, meloxicam 0.1 mg kg⁻¹, carprofen 4 mg kg⁻¹, ketoprofen 2 mg kg⁻¹ for four days, followed by 1 mg kg⁻¹ daily thereafter or flunixin 1 mg kg⁻¹ for three days with four day intervals. Gastrosocopy was performed before and at 90 days. Data were analysed by ANOVA ($p < 0.05$).

There were no differences in cell counts and biochemical profiles. GGT was increased compared to baseline at day 30 in animals treated with meloxicam (8.8 ± 1.9 iu L⁻¹). Bleeding time increased after carprofen at 30 (60 ± 30 seconds - basal 35 ± 8 s) and 90 days (60 ± 19 s). Except for ketoprofen, clotting time increased when compared to baseline in all groups of animals treated with NSAIDs (maximum value 15 ± 3 minutes for carprofen at 90 days). None of the animals treated with lactose, four with etodolac, three with ketoprofen, two with meloxicam, one with carprofen and four with flunixin showed gastric lesions. At the end of the study, animals treated with carprofen had the lowest incidence of occult blood in faeces (50%), compared to the other NSAIDs, which ranged from 83 to 100%.

With respect to gastrointestinal effects, carprofen was the safest NSAID for long term use, followed by meloxicam. Monitoring of side effects should be considered when NSAIDs are used to treat chronic pain in dogs.

This study was approved by the Animal Research Ethical Committee of the School of Veterinary Medicine and Animal Science, University of São Paulo State, Brazil, under the protocol number of 094/2002.

Abstracts – Small Animal Analgesia and Analgesiometry

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Abstracts – Small Animal Analgesia and Analgesimetry

A comparison between buprenorphine and carprofen alone or in combination for post-operative pain after ovariohysterectomy in dogs.

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This study compared the intra- and post-operative effects of buprenorphine (B) and carprofen (C) alone or in combination in dogs undergoing ovariohysterectomy.

Sixty dogs (17 ± 6 kg) were randomized to receive simultaneously during premedication: buprenorphine 0.02 mg kg^{-1} intramuscularly (IM) (Group B); carprofen 4 mg kg^{-1} subcutaneously (SQ) (Group C); or both drugs (Group CB). All dogs received 0.05 mg kg^{-1} acepromazine IM. Anesthesia was induced with propofol and maintained with isoflurane. A dynamic interactive visual analogue scale (DIVAS) and short form Glasgow Composite pain scale (GCS) were used to evaluate analgesia and sedation before surgery (baseline, 0) and at 2, 4, 6 and 24 hours after endotracheal extubation. Intervention analgesia was provided with buprenorphine (0.02 mg kg^{-1}) if any observer felt the animals were uncomfortable. The wound was measured in millimeters using electronic calipers (WM) and photographed for visual assessment (VIS) immediately after surgery and at 2, 4, 6 and 24 hours. Parametric data was compared by one-way ANOVA, and a split plot repeated measures ANOVA used for variables with multiple measurements over time. $P < 0.05$ was considered significant.

Group C required a higher dose of propofol ($5.0 \pm 1.37 \text{ mg kg}^{-1}$) compared to B (3.3 ± 1.14) and CB (3.2 ± 0.74). Intervention analgesia was required 10 times (9 dogs) (Table I). Group B had a higher DIVAS score at 2, 4 and 6 hours (Table II) and higher GCS at 6 hours (4.45 ± 3.49) when compared to C (1.03 ± 1.29) and CB (1.47 ± 1.39). Group C had a lower sedation score at 2 hours (42.9 ± 23.62) when compared to B (68.5 ± 32.1) and CB (68.9 ± 22.1). Group B had higher WM score at 2 hours ($2.58 \pm 0.81 \text{ mm}$) compared to C (1.82 ± 0.64) and at 6 hours (2.80 ± 1.06) when compared to C (2.23 ± 0.76) and CB (2.19 ± 0.75). VIS was not different between groups.

Table I - Number of animals receiving intervention analgesia over time:

GROUP	1h	2h	4h	6h	24h
B	1	1	-	3	-
C	1	1	-	-	-
CB	-	2	1	-	-

Table II – DIVAS over time:

GROUP	0h	2h	4h	6h	24h
B	0	27.81 ± 20.48	19.14 ± 16.70	$22.53 \pm 22.47^*$	0
C	0	19.40 ± 15.43	16.42 ± 11.84	5.72 ± 7.32	0
CB	0	21.73 ± 13.6	17.43 ± 5.23	7.94 ± 10.69	0

*Statistically significant

C and CB were superior to B with respect to pain scores and wound swelling.

No synergistic effect was noticed when both drugs were used.

Abstracts – Small Animal Analgesia and Analgesiometry

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Fatty issue

**Chaired by
Prof Ron Jones**

**Speaker
Prof Martin Leuwer**

Sponsor



**Boehringer
Ingelheim**

Martin K. Leuwer Dr.med., Dr.med.habil, FRCA

Professor of Anaesthesia University of Liverpool

M. Leuwer graduated from the Johann Wolfgang Goethe University in Frankfurt/Main in 1979 and began his career in anaesthesia and intensive care medicine in Giessen. From 1982, he worked in the University Hospitals of Frankfurt/Main and Hannover and was appointed to the Chair of Anaesthesia at the University of Liverpool in 2000. He gained his MD from the Johann Wolfgang University, Frankfurt/Main in 1982 and his PhD (Pharmacodynamics of Neuromuscular Blocking Agents in Neonates and Infants) from the Medizinische Hochschule Hannover in 1994 where he was appointed to a Personal Chair in Anaesthesia and Intensive care in 1999. His interests span from the interactions of anaesthetic drugs with ion channels in neurons and cardiac muscle to many aspects of human sepsis, including the role of white adipose tissue. Keeping strong research links with colleagues in Europe, and as Editor of the European Journal of Anaesthesiology, Professor Leuwer strives to facilitate good communication of new information to anaesthetists and intensivists throughout Europe.

The Role of White Adipocytes in Sepsis

Martin K. Leuwer and Paul Trayhurn

Background and Goal of Project

1. Sepsis

Severe sepsis is a major public health concern. In the United States, approximately 750,000 patients fall ill from severe sepsis. In Germany, this figure is approximately 240,000. The mortality rate approaches 40% in the elderly and the incidence is projected to increase by 1.5% to 9% per annum, due to the growing elderly population. The pathophysiology of sepsis is complex and still poorly understood but involves activation of a huge variety of pro-inflammatory signals. Clinically, there is a significant correlation between the body mass index and sepsis mortality.

2. White Adipose Tissue

It has recently been established that white adipose tissue, besides its metabolic function in storing and releasing fatty acids, has a major role in secreting a variety of hormones and protein factors which are referred to as adipokines. In particular, it has been suggested that adipose tissue releases pro-inflammatory cytokines, e.g. IL-6, in response to hypoxia. Thus, we felt tempted to investigate whether adipokine expression relates to sepsis in an animal model.

Methods

After obtaining a Home Office Licence, we investigated sixteen healthy, non-obese male mice (body weight 25 – 28 g). Eight animals served as controls; in another eight animals, sepsis was induced by intra-peritoneal LPS injection. Twenty-four hours after induction of sepsis, the experimental animals were killed and RNA extracted from the epididymal fat pads. Real time PCR was used to quantify expression of IL-6, IL-18, MCP1, nerve growth factor (NGF), hypoxia-induced factor (HIF1 α) adipisin and adiponectin, in comparison to controls.

Preliminary Results

Twenty-four hours after induction of sepsis, real time PCR revealed substantial increases in the expression of IL-6 (500-fold), MCP1 (55-fold), NGF (10-fold), TNF α (5-fold), and HIF1 α (3-fold), while there were significant decreases in the expression of IL-18 (2.5-fold), adipisin (6-fold), and adiponectin (5-fold).

Conclusions and Working Hypothesis

These preliminary results show that white adipose tissue is an organ system which responds to sepsis by a marked increase in the expression of pro-inflammatory cytokines. At the same time, the expression of anti-inflammatory cytokines, as well as the expression of adipisin and adiponectin (anti-inflammatory) is reduced. Thus, we propose the hypothesis that white adipose tissue may be an important contributor to the pathophysiology of sepsis and that this may relate, at least in part, to hypoxia within the tissue.

Adipokines

Adipokines

Comparative complications

**Chaired by
Prof Yves Moens**

**Speakers
Dr Peter Charters
Prof Duncan Gillies
Dr John Harrison**

Sponsor



**Boehringer
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Management of difficult airways

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Although I graduated in Medicine from Liverpool (1971), I did manage to spend a large part of my postgraduate training outside the city. After obtaining MRCP and FRCA, my clinical commitments have been to Intensive Care and Anaesthesia for major Head and Neck Surgery. Because I have always been a clinician first, I came late to research but did manage a part-time degree in Pure and Applied Maths with the OU. Research interests have mainly concerned difficult airway problems and mathematical modelling. Some early work on 2-dimensional modelling of difficult intubation was the basis for my association with Duncan Gillies and the collaborative venture with his Department is now in its tenth year. My OU experience prepared me for the problems inherent in this sort of association where clinical trials need a lot of forethought and planning to be relevant temporally to the pure scientist's needs.

Duncan Gillies MA MSc PhD

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Duncan Gillies graduated from Cambridge University with a degree in Engineering Science in 1971. He worked for three years as a control engineer in industry, before returning to full time study and obtaining a PhD in the area of artificial intelligence from Queen Mary College London. After teaching for six years at the Polytechnic of the South Bank, he moved to the Department of Computing at Imperial College in October 1983 where he is now Professor of Biomedical Data Analysis. He has worked in the areas of computer graphics and vision, and their applications in the medical field, and in probabilistic inference, particularly Bayesian networks and classifiers. His current work is concerned with biomedical modelling and its application in clinical practice.

Management of difficult human airways

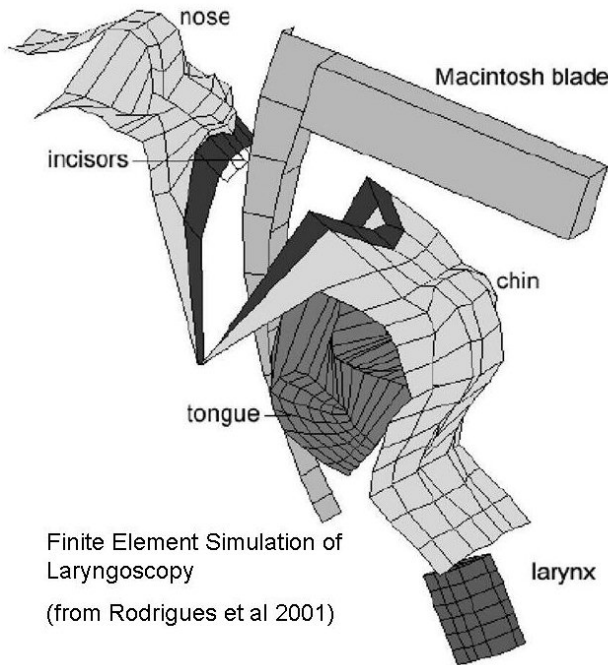
The management of difficult human airways during operations is one of the most problematic areas in anaesthesia. Serious problems can occur in difficult patients including damage to the upper incisor teeth, lesions of upper airway tract, oesophageal trauma, hoarseness and laryngeal injury and even cardiac arrest with brain damage. In the most serious cases, failed intubation may be the cause of death of a patient. Clearly any method that can reliably predict patients that are likely to present difficulties would be an important factor in increasing the safety of anaesthesia.

We have approached this problem by using computer methods to model the upper human airway. Our long-term aim is to create a generic model of the airway that will replicate the geometric, kinematic and mechanical properties of the real human airway. A generic model can be made patient specific by setting a relatively small number of parameters and then could be used for pre-operative assessment of patients, warning of difficulties that could be encountered during anaesthesia or surgery and indicating the best choice of airway instruments to use. A generic model of the upper airway will also have considerable value to surgeons specialising in ear nose and throat and maxillary-facial areas, and medical instrument designers. Most fundamentally it will contribute to the understanding of the structure and function of the airway, and the factors that determine airway patency. It will provide new interactive ways of exploring and visualising the airway in the different head and neck configurations used during intubation and surgical procedures. It could be used to determine the accessibility of tumours destined for surgical removal, or to design implants to replace damaged or diseased bone. It could be incorporated in simulation training systems, replacing the current plastic models, which are inflexible and unrealistic. It could be used for the design of new airway instruments, providing vital information about accessibility and ergonomics. Since the model would be able to replicate the full diversity of the human airway, putative instruments could be tested thoroughly and optimised before expensive clinical trials are begun.

The creation of a generic model of the airway is a difficult task, and many research issues remain unaddressed. The problems result from the complexity of the airway, both in its geometric shape, its physical properties and its moving parts. The geometry shows considerable variation from subject to subject, not merely in size but also in subtle variations of shape. The rigid parts defined by the bones of the mandible and maxilla can be readily identified in CT images, and can be encoded into shape models. However, softer parts such as the soft palate and epiglottis are harder to identify in the images and to characterise. Little information has been published about the physical properties of the deformable parts of the airway, in particular the tongue. What is known is that its deformation is highly non-linear. Initially it behaves in an elastic manner as the blood is squeezed from it, then it becomes almost incompressible. To make things more complex the tongue displays a phenomenon known as stress relaxation. That is after deformation, for example with a laryngoscopic blade, it can be maintained in the deformed position with a force that decreases with time. All these natural properties make it very difficult to apply engineering methods, such as the finite element modelling method to model the deformation. Lastly, the airway contains a number of mobile parts, which are constrained in complex ways. The mandible is the simplest and is hinged in a well-

Management of difficult airways

understood manner. There is however a complex system comprising the floating hyoid bone and the epiglottis. The anaesthetists know its behaviour in practice, since the epiglottis may be raised, revealing the vocal chords by pushing the hyoid bone with the tip of a laryngoscope blade. The nature of this kinematic system is, however, not sufficiently understood to encode it in a computer model. Another moving part is the larynx, which, apart from being highly mobile during swallowing, is also elevated forward with the epiglottis during laryngoscopy.



Although the difficulties are considerable, progress on some of the modelling issues over the last ten years has been encouraging, and has been greatly aided by the considerable increase in computer power and memory size. Our earliest work in this field modelled just the rigid parts of the airway. A model of the osseous factors that can contribute to difficult intubation was proposed by Charters (1994), and later incorporated in a computer model for predicting the best view of the larynx that could be obtained during laryngoscopy (Gillies et al 1997). Although the osseous factors are important it was realised that the size and mechanical properties of the tongue are also important factors determining airway patency, thus the next stage of our work was to model the effect of the deformation of the tongue. For this we used the technique of finite elements. A two dimensional simulation was tried first but was limited in accuracy (Rodrigues et al 1998). The usual method of rigid blade laryngoscopy involves displacement of the tongue to the left, and can only be represented in a full three-dimensional model. Studies using 3D finite element modelling, demonstrated that it is possible to simulate, with a reasonable degree of accuracy, the behaviour of the tongue as it is displaced by a laryngoscope blade, and hence predict whether the vocal cords can be seen (Rodrigues et al 2001).

A major difficulty in using the physical model of the tongue is data acquisition. It is necessary to begin with a magnetic resonance scan of the upper airway, from which the geometry of the tongue and mandible are segmented, then converted into a form where finite element modelling can be performed. This is a time consuming task requiring considerable specialist knowledge and expertise. Ideally, anaesthetists would like to be able to take a relatively small number of "bedside" measurements from a patient, enter these into a computer system and receive a rapid assessment of intubation difficulty. Despite an enormous amount of work by many other groups in recent years this has continued to be an elusive goal. Accordingly, the next phase of our work concerned generic modelling of the shape of the airway. To do this we adopted the technique of active shape modelling which has previously been investigated in the context of creating brain atlases, active appearance models and models of bone development. Our work focussed on the mandible. We developed a 3D shape model in which the main modes of variation can be visualised in three dimensions and studied. (Lam et al 2002, 2004) The model, which is controlled by a small number of parameters, was created using CT scans of dry human mandible specimens. One of the ten sets was selected as a base, and the other nine were registered to it. The registration process deforms an image set so that it matches the base set. The correspondence between each surface point of an image set and the base image set can then be found. The surface geometry of the base image set was encoded as a set of triangles that represents the geometry accurately. Each co-ordinate of each vertex of this set is taken as a variable, and principal component analysis is used to find the main modes of variation in the set. The principal components can be used to reconstruct any mandible shape that is a linear combination of the others. The largest mode of variation in the data sets was due to the different sizes of the specimens. However, shape changes, such as elongation could also be observed. Some smaller modes of variation were caused by the shape, position or absence of teeth. To achieve accurate results the teeth had to be removed by hand segmentation. The work clearly demonstrates the potential of shape models to encode the geometry of the human mandible in a quantitative form suitable for use in accurate simulation of the human airway. In our studies to date we have found that just four principal components are needed to capture the majority of the variance in the set (approximately 94%). This further strengthens the argument that accurate patient specific geometry can be determined from simple bedside measurements.

The ability of the mandible model to match a specific patient was also tested. High reconstruction accuracy could be achieved in the majority of cases, with the average error at corresponding surface points being less than 1.7 mm. The data set that we were using was small and this level of accuracy could not be obtained on mandibles that were outliers of the set used to create the model.

Currently we are continuing the work on two fronts. The first is to investigate the accuracy with which an unseen patient mandible can be replicated using simple bedside measurements to tailor the generic model. Results using measurements from the CT scans demonstrate the feasibility of the method and we are currently addressing practical issues such as the effect of measurement accuracy on the accuracy of reconstruction. Our longer-term aim is to integrate the mechanical model of the tongue with the shape model of the mandible. To this end we are investigating whether we can use a single set of finite elements to represent the natural variability found in practice and whether there are simple measurements that will allow us to make this model patient specific. We hope to begin some further validation studies using real patient data drawn from clinical cases.

Management of difficult airways

One interesting long-term possibility would be to extend the ideas to veterinary medicine. It is possible that many of the problems encountered in human anaesthesia and surgery also exist in operations on animals. A study extending the work to veterinary medicine could therefore throw light on the functional anatomy of the airway and its evolution and adaptation.

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Management of difficult airways

Management of difficult airways

Hyperbaric oxygen therapy

John Harrison

Hyperbaric oxygen therapy

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Hyperbaric oxygen therapy

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Hyperbaric oxygen therapy

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Accidents will happen

**Chaired by
Eddie Clutton**

**Speakers
Prof Helen Muir
Dr David Brodbelt**

Sponsor



How accidents happen

Prof Helen Muir

How accidents happen

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How accidents happen

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How accidents happen

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Dave Brodbelt graduated from the Cambridge Vet School in 1993 and then undertook a residency in veterinary anaesthesia at Cambridge. In 1998 he gained his RCVS Diploma in Veterinary Anaesthesia and became a Diplomate of the European College of veterinary Anaesthesia. He then went into practice for three years, before taking up a PhD at the Animal Health Trust in the Epidemiology Unit, looking at perioperative complications in small animals (The Confidential Enquiry into Perioperative Small Animal Fatalities, CEPSAF). He is now Lecturer in Veterinary Anaesthesia at the Royal Veterinary College. He is particularly interested in anaesthetic complications and practice based research.

CEPSAF Update Results from the Confidential Enquiry into Perioperative small animal fatalities (CEPSAF)

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Introduction

The last UK study evaluated complications in small animal practices in the UK between 1984 and 1986 (Clarke and Hall 1990). They found that approximately one in 679 healthy dogs and cats died (1 in 870 dogs, 1 in 552 cats) as a result of anaesthesia. More recent international work suggested a perioperative death risk of nearer 1 in 1000 dogs and cats undergoing operations in practice (Dodman and Lamb 1992; Rintasalo and Vainio 1995; Dyson and Pettifer 1997; Joubert 2000). Though better than the reported risk in horses of approximately 1 in 100 (Johnston, Taylor et al. 1995; Johnston, Eastment et al. 2002), it is substantially higher than mortality risks reported in man, where about one in 2,000 – 5,000 people die of an anaesthetic-related death (Lunn and Mushin 1982; Tikkanen and Hovi-Viander 1995; Eagle and Davis 1997; Suan, Perez-Torres et al. 1997; Biboulet, Aubus et al. 2001; Kawashima, Seo et al. 2001). Since these small animal studies, new drugs, monitoring and techniques have been introduced into UK practice, making it an appropriate time to re-evaluate the situation in practice in the UK.

A prospective large-scale multi-centre study, the Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF), was undertaken to re-evaluate the risk of anaesthetic-related death in the UK. Endorsed by the AVA, BSAVA and the BVHA, its aims were to establish the current perioperative death risks in small animals undergoing anaesthesia and sedation, to identify risk factors associated with the risk of anaesthetic-related death in dogs, cats and rabbits and to make recommendations to improve practice-based anaesthesia.

This presentation will briefly highlight the general method of the study and then will present some of the results of the study. In particular it will describe the trends in anaesthetic practice of the participating practices, it will present the estimated risks of anaesthetic-related death in small animals and it will describe characteristics of the anaesthetic-related death in dogs and cats.

Methods

A prospective observational study was undertaken over two years between June 2002 and June 2004. Participating practices recorded brief details of all small animal anaesthetics and sedations and patient outcome in case diaries supplied by the study, allowing the calculation of perioperative death risks (cohort study). Anaesthetic-related death was defined as perioperative death (including euthanasia) within 48 hours of termination of the procedure, except where death or euthanasia was due solely to surgical or pre-existing medical conditions, such that anaesthesia could not be reasonably excluded as a contributory factor. Details of patient, procedural, anaesthetic management, and personnel factors were recorded using detailed questionnaires for all animals that died of an anaesthetic-related death (cases) and randomly selected animals that recovered normally (controls) (case-control study). Comparing cases to controls allowed the identification of risk factors associated with anaesthetic-related death.

Results

Trends in Anaesthesia

One hundred and seventeen centres participated in the study between June 2002 and June 2004 and included centres from Jersey to Aberdeen, and included 83 small animal practices, 28 mixed practices and 6 veterinary institutions. Premedication of patients prior to anaesthesia was routinely undertaken with acepromazine combined with an opioid in dogs and cats in approximately 90% of centres. Around 10% of practices routinely used medetomidine combinations for premedication prior to anaesthesia. Four centres did not routinely premedicate cats prior to anaesthesia and eight centres regularly used atropine as part of a premedication in cats.

Anaesthesia was most often induced with propofol in dogs and cats (Table 2). The next most commonly used agents were thiopentone in dogs and ketamine combinations, thiopentone and Saffan in cats. Maintenance of anaesthesia was primarily undertaken with isoflurane in both dogs and cats, with 96% of clinics routinely using isoflurane for maintenance of anaesthesia, and 21% routinely using halothane. Eight centres (7% of centres)

CEPSAF Update

routinely used sevoflurane in dogs and cats. Nitrous oxide was infrequently used in dogs and cats (27% of clinics). Dogs were routinely intubated at all centres and cats at all but one centre.

Rabbits were primarily anaesthetised with medetomidine and ketamine combinations with some centres using Hypnorm (fentanyl and fluanisone)(Table 3). Most centres used one combination exclusively, whilst 14 clinics (12%) used both combinations regularly. Isoflurane was regularly used for maintenance by 89% of centres, halothane by 6% and sevoflurane by 5%. Sixty centres (51%) indicated they regularly intubated rabbits.

Risks of Anaesthetic-Related Death

Approximately 100,000 anaesthetics were recorded in dogs, 80,000 in cats and 10,000 in rabbits. The risk of anaesthetic-related death was approximately 0.17% in dogs and 0.24% in cats (1 in 601 dogs, 1 in 419 cats, Table 1). The risks in other species were much higher and some are reported here (Table 1). In healthy patients the risks were 0.05%, 0.11% and 0.73% in dogs, cats and rabbits (1 in 1849, 1 in 895 and 1 in 137 respectively, Table 2). Sick patients (ASA grade 3-5) were at a substantially higher risk of anaesthetic-related death than healthy patients, with over 1% of all severely ill dogs and cats and 7% of sick rabbits dying within 48 hours of anaesthesia (Table 2).

Table 1 Anaesthetic-related risk of death in small animals (Brodbelt 2006)

Species	Number at Risk	Number of Anaesthetic-Related:			Risk of Anaesthetic related death / euthanasia (95% Confidence Interval)
		Deaths	Euthanased	Total Fatalities	
Dog	98,036	154	9	163	0.17% (0.14 – 0.19%)
Cat	79,178	179	10	189	0.24% (0.20 – 0.27%)
Rabbit	8,209	111	3	114	1.39% (1.14 – 1.64%)
Guinea Pig	1,288	48	1	49	3.80% (2.76 – 4.85%)
Hamsters	246	9	0	9	3.66% (1.69 – 6.83%)
Chinchilla	334	11	0	11	3.29% (1.38 – 5.21%)
Rat	398	7	1	8	2.01% (0.87 – 3.92%)

Table 2 Risk of anaesthetic-related death in healthy and sick patients (Brodbelt 2006)

Species	Health status*	Deaths**	Estimated number of Anaesthetics per stratum	Risk of Anaesthetic related death	95% Confidence Interval
Dog	Healthy ASA 1-2	49	90,618	0.05 %	0.04 – 0.07 %
	Sick ASA 3-5	99	7,418	1.33 %	1.07 – 1.60 %
Cat	Healthy ASA 1-2	81	72,473	0.11 %	0.09 – 0.14 %
	Sick ASA 3-5	94	6,705	1.40 %	1.12 – 1.68 %
Rabbit	Healthy ASA 1-2	56	7,652	0.73 %	0.54 – 0.93 %
	Sick ASA 3-5	41	557	7.37%	5.20 – 9.54 %

*ASA 1-2: no/mild disease, ASA 3-5: severe disease. ** Only deaths where a questionnaire was returned were included.

The majority of anesthetic-related deaths occurred postoperatively, and of the postoperative deaths nearly half occurred within 3 hours of termination of the procedure (Table 3).

CEPSAF Update

Table 3 Timing of death in Dogs, Cats and Rabbits (Brodbelt 2006)

Timing of Death	Dogs	Cats	Rabbits	*Only deaths where a Case-Control questionnaire was returned were included here. **Postoperative deaths were additionally categorised by time after anaesthesia.
After Premedication	1 (1%)	2 (1%)	0	
Induction of anaesthesia	9 (6%)	14 (8%)	6 (6%)	
Maintenance of anaesthesia	68 (46%)	53 (30%)	29 (30%)	
Postoperative death**	70 (47%)	106 (61%)	62 (64%)	
0-3 hours postoperative	31 (44%)	66 (62%)	26 (42%)	
3-6 hours postoperative	11 (16%)	9 (8%)	7 (11%)	
6-12 hours postoperative	12 (17%)	7 (7%)	13 (21%)	
12-24 hours postoperative	13 (19%)	12 (11%)	9 (15%)	
24-48 hours postoperative	3 (4%)	10 (10%)	3 (5%)	
Unknown time	0	2 (2%)	4 (6%)	
Total*	148 (100%)	175 (100%)	97 (100%)	

Conclusions

The results of this study represent a marked reduction since the last UK study with an approximate halving of the risk in healthy dogs and cats from 1 in 870 dogs and 1 in 552 cats (Clarke and Hall 1990) to 1 in 1,849 dogs and 1 in 895 cats. However, in comparison to man where a comparable risk of anaesthetic-related death is approximately 1 in 2,000 – 5,000, the risks of death remain high. Cats were at a substantially greater risk than dogs and other small animal species were at an even greater risk.

In particular, greater attention to poor health status patients could reduce mortality and closer monitoring of patients in the early postoperative period could also reduce risk. 'Exotic' small animals were at substantially greater risk than dogs and cats and their management should be targeted for improvement.

In summary, serious anaesthetic complications are an increasingly rare event in small animal practice. However in comparison to human anaesthesia we still have room for improvement. A knowledge of these complications should form a platform on which to improve the anaesthesia of small animals in practice.

Acknowledgements

The authors would like to acknowledge the hard work of all the practices that took part in CEPSAF, the AVA, BSAVA and BVHA who endorsed CEPSAF and Pfizer Animal Health that funded the work.

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Some good news

**Chaired by
Dr Kathy Clarke**

**Speakers
Dr Polly Taylor
Prof Jennie Hunter**

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A feline ABC: Analgesia, Buprenorphine, Cat

Polly M. Taylor MA, VetMB, PhD, DVA, DipECVA, MRCA, MRCVS

Taylor Monroe, Ely, Cambridgeshire, UK

Graduated from Cambridge in 1976 and worked in general practice for three years. Then worked in anaesthesia at the Cambridge University Veterinary School, obtaining the RCVS DVA in 1980. Became chief of anaesthesia at the Animal Health Trust, Newmarket in 1983 and gained her PhD (Cambridge University) in 1987 for her thesis concerning equine anaesthesia. In 1994 she became University Lecturer in anaesthesia at the Cambridge University Veterinary School where she was responsible for running the clinical anaesthetic service, teaching undergraduates and post graduates in anaesthesia and for the anaesthesia research program. She became a Diplomate of the European College of Veterinary Anaesthesia in 1995 and was founding President of the College. Awarded the 1997 UK Equestrian Outstanding Scientific Achievement Award and BSAVA Simon Award in 2001. Became Reader in Anaesthesia at the University of Cambridge in 2000. She now works as a freelance consultant in anaesthesia, with work ranging from clinical anaesthetic services and teaching to drug registration and research. Current research interests continue in anaesthesia and analgesia. Has studied pain and analgesia in cats since the 1980s and a number of papers on opioids and NSAIDs in cats have been published. Has published numerous papers on anaesthesia and analgesia and is a contributor to Flecknell's "Pain Management in Animals". Also a partner in "Musical Chairs", making handmade, hardwood furniture. Interests include riding (eventing) sailing, skiing, music and gardening.

A Feline ABC: Analgesia, Buprenorphine, Cat

Cats are the most popular pet in many countries, and the majority of these are neutered, hence millions of cats undergo surgery at least once in their lifetime. However, their perioperative pain is under treated and they receive less analgesic treatment than the dog for similar surgery (Dohoo & Dohoo 1996, Watson et al 1996, Lascelles et al 1999, Joubert 2001, Williams et al 2005). Recently the need for analgesia in cats has become better acknowledged, and many clinical and research studies have been undertaken to address the deficiency. These have been recently reviewed (Robertson & Taylor 2004, Taylor & Robertson 2004).

Morphine is generally regarded as the "gold standard" analgesic. Myths about morphine-induced mania in cats have prevented wide use of morphine in this species, in spite of clear demonstration that, at clinical doses in cats with a painful condition, morphine is both effective and does not cause mania (Robertson & Taylor 2004). Some of morphine's analgesic effect is due to production of morphine metabolites. Taylor et al (2001) demonstrated that cats have limited ability to produce these metabolites which could reduce the analgesic efficacy in this species. Alternative opioids may result in better analgesia than morphine in cats.

Buprenorphine is a partial mu (Op3) agonist opioid that was originally developed in the 1970s for treatment of drug addicts as well as for analgesia (Mello & Mendelson 1995). It was first investigated in veterinary patients in the 1980s (Taylor & Houlton 1984) in a study of post operative analgesia in dogs. Buprenorphine has since become the most popular opioid used in small animal practice in the UK (Lascelles et al 1999) and is also widely used in the rest of Europe, Australia and South Africa (Watson et al 1996, Joubert 2001). It currently holds market authorisation for dogs in the UK as Vetergesic (Alstoe Animal Health) and is commonly used in the cat via the "cascade" (The Veterinary Medicines Regulations 2005).

Laboratory studies have demonstrated that buprenorphine is long acting and rarely causes vomiting or dysphoria in cats. (Robertson et al 2003, Robertson et al 2005a). Generally, cats become sedated, appearing happy and euphoric. After intramuscular injection (0.01 mg/kg) buprenorphine increased thermal thresholds for considerably longer than morphine, pethidine and particularly butorphanol; it was also extremely effective for 6 hours after mucosal absorption via the buccal route (0.02 mg/kg) (Robertson et al 2003, 2005a).

A number of studies have evaluated buprenorphine for clinical management of pain in cats. Buprenorphine has produced effective analgesia in a range of clinical conditions, although there are few placebo-controlled studies. Three early investigations showed that buprenorphine produced better analgesia than morphine (Stanway et al 2002), oxymorphone (Dobbins et al 2002) and pethidine (Slingsby & Waterman-Pearson 1998). More recent studies have demonstrated that buprenorphine, although providing analgesia, did not perform as well as meloxicam or carprofen (Gassel et al 2005, Mollenhoff et al 2005). Curcio et al (2006) found that a bupivacaine local block did not further enhance buprenorphine analgesia for post onychectomy pain.

Recent studies draw particular attention to the importance of the route of administration and the dose of buprenorphine in producing profound analgesia. The studies reporting better pain relief after NSAID treatment both used either 0.01 mg/kg, the subcutaneous (SC) route, or both (Gassel et al 2005, Mollenhoff et al 2005). Steagall et al (2005) reported smaller increases in thermal threshold after SC buprenorphine compared with those reported by Robertson et al (2005a) after IV and buccal dosing. A buprenorphine patch maintained similar plasma concentrations to those reported after IV and buccal dosing, without the initial peak; however, thermal threshold did not increase (Murrell et al 2006). This result was considered likely to arise from the hysteresis between plasma and effector site concentration. Presumably, adequate effector site concentration was not reached as there was never a sufficient concentration gradient to drive the drug to the effector site as would occur, for instance, after IV administration. The SC route is presumably intermediary between transdermal and IV in achieving a sufficient concentration gradient, resulting in a lesser degree of analgesia than IV. Hysteresis with buprenorphine is in marked contrast with fentanyl, demonstrating the need to understand all

A feline ABC: Analgesia, Buprenorphine, Cat

aspects of an analgesic's pharmacokinetics and pharmacodynamics in order to develop the most effective treatment regimen (Robertson et al 2005a, 2005b).

The dose of buprenorphine has commonly been restricted as a result of early studies demonstrating a "bell shaped" concentration curve, where higher doses led to a reduced analgesic effect (Cowan et al 1977). However, there is good evidence, at least in dogs, that doses which may reduce the effect are much higher than those used under clinical conditions, and that doses higher than 0.01 mg/kg provide more analgesia, not less (Slingsby et al 2006). Further investigation into the analgesic effects of doses above 0.01-0.02 mg/kg are warranted.

An analgesic given preoperatively for post operative analgesia may affect the course of anaesthesia. Opioids commonly reduce volatile anaesthetic requirements and are usually beneficial in reducing the required dose of sedatives and injectable anaesthetics. They may however, exacerbate anaesthetic induced cardiopulmonary depression. Buprenorphine has been widely used for premedication in cats and is generally regarded as a suitable opioid for this purpose. Akkerdaas et al (2001) considered buprenorphine and acepromazine to be better than midazolam/ketamine or medetomidine prior to IV induction and isoflurane maintenance as cardiopulmonary characteristics were acceptable. Ilkiw et al (2002) reported that buprenorphine reduced isoflurane MAC, although this was less than after butorphanol or high doses of morphine.

Buprenorphine has many characteristics making it suitable for routine perioperative analgesia in cats, and there is considerable anecdotal evidence that it is widely used in this way. Recently, a multicentre prospective clinical trial was conducted under ATC No. 00117/2004 comparing the post operative analgesia produced by buprenorphine and butorphanol in order to provide data to extend the current Vetergesic® Market Authorized indications to cats. Comparison was made with butorphanol as this was the only non schedule 2 opioid analgesic with UK Market Authorisation for use as an analgesic in cats.

Materials and Methods

One hundred and fifty three cats admitted for surgery at seven veterinary practices in the UK were studied. They were randomly allocated to receive either buprenorphine (Vetergesic; Alstoe Animal Health) (0.01-0.02 mg/kg IM) or butorphanol (Torbugesic; Fort Dodge Animal Health) (0.4 mg/kg IM) approximately 60 minutes prior to induction of anaesthesia. Acepromazine was also given as premedication, but no other analgesics. Anaesthesia was induced with propofol, Saffan® or thiopentone and maintained with isoflurane or halothane in oxygen, with or without nitrous oxide. Routine physiological monitoring took place during anaesthesia and in the immediate post operative period. After anaesthesia and surgery was completed the cats were assessed by an individual who did not know which opioid had been administered. A four point simple descriptive scale (SDS) was used to assess the degree of pain and sedation at 1,2,4,8 and 20-24 hours after the end of anaesthesia. Pain scoring was as follows: score 0 indicated no pain and score 3 was maximum pain for the surgery. Sedation was scored similarly: score 0 indicated no sedation and score 3 an unrousable cat. During the assessment period, repeat administration of the same dose of the same analgesic was given if required, followed by rescue analgesia with carprofen if the repeat dosing did not alleviate the pain. Pain and sedation data were compared using non parametric contingency tables and the Chi squared test. Numerical data describing the cats were compared using t tests or ANOVA as appropriate.

Results

There were no differences between the groups in respect of age, sex, body weight, breed and type and duration of surgery. Most cats were domestic short haired undergoing neutering, but dental surgery, excision of superficial neoplastic masses, thyroidectomy and orthopaedic surgery were also included. Surgery lasted an average of around 20 minutes. Approximately 90 minutes elapsed between administration of the test drug and the end of anaesthesia (time 0).

The mean dose of buprenorphine was 0.013 mg/kg, but doses ranged between 0.008 and 0.021 mg/kg. 18 cats received more than 0.018 mg/kg. The mean dose of butorphanol was 0.4 mg/kg, although doses ranged between 0.31-0.57 mg/kg. Most cats received propofol and isoflurane, but Saffan, thiopentone and halothane were also used in both groups. There were no differences between the groups in the dose or identity of the anaesthetics used.

During anaesthesia, heart and respiratory rates remained within a normal range for anaesthetised cats. There were no reports of apnoea or bradycardia, and there were no significant differences between the groups. After surgery, all values remained within normal limits for cats, and no life threatening cardiovascular or respiratory events occurred. During this period, heart rate was higher in the buprenorphine group than in the butorphanol group at 2 hours and respiratory rate was lower at 1 and 2 hours. However, none of these values was abnormal. Indirect blood pressure monitoring and pulse oximetry was carried out in around 60 cats. Oxygen haemoglobin saturation (SpO₂) was generally above 95%; only one cat in the buprenorphine group had a transient reading below 90% (89%) when breathing air. Mean arterial blood pressure (MABP) ranged between 50 and 160 mmHg. There were no significant differences between the groups in either SpO₂ or MABP.

In both groups more cats fell into the lower pain score groups than according to random distribution, suggesting that both drugs produced some pain relief. There was no significant difference between the groups preoperatively. At all post surgical time points there were more buprenorphine cats with pain score 0 and more butorphanol cats with pain score 3 (Table 1). The difference between the groups was significant at 2 hours and 24 hours after surgery but not at 1, 4 or 8 hours. Hence, buprenorphine produced analgesia at least as good as butorphanol overall, and produced better analgesia at 2 hours and 24 hours. Further analgesia was required in 15% of the cats: 11 cats in the buprenorphine group and 12 in the butorphanol group ($P > 0.05$). Repeat analgesia was required 6.4 ± 6.3 (1-24) hours after surgery in the buprenorphine group and 5.6 ± 5.3 (1-14) hours after surgery in the butorphanol group ($P > 0.05$). The original dose of buprenorphine given to cats which required further analgesia was 13 ± 4 (9-19) $\mu\text{g/kg}$. The time at which further analgesia was required was not related to the original dose given. Rescue analgesia was required in only two cats, both in the butorphanol group, at 2 and 24 hours after surgery.

A feline ABC: Analgesia, Buprenorphine, Cat

Discussion

Cats were drawn from the regular owned pet population admitted to general veterinary practice clinics for surgery. The cats recruited were highly representative of the normal pet cat population in that the majority were young domestic short haired cats undergoing neutering. However, a wide age range was included, as were some pedigree animals and a variety of other common types of surgery in a small subgroup for both treatments.

Anaesthetic and perioperative management was according to each practice's normal protocol. A good selection of anaesthetic related products commonly used in feline practice were represented.

Buprenorphine clearly provided effective analgesia in the post operative period. Although no untreated control group was used, the fact that more cats than random received the low pain scores suggests both drugs provided some analgesia. Buprenorphine always produced more pain free cats (score 0) and less maximum pain scores (score 3) than butorphanol, indicating that it performed as an analgesic better than a product which already has Market Authorisation for this purpose. The significant difference at 24 hours shows that buprenorphine also provided analgesia of considerably longer duration than butorphanol.

The dose of buprenorphine ranged up to 0.021 mg/kg. A number of studies have investigated the analgesic effect of this opioid in cats (Slingsby & Waterman Pearson 1998, Stanway et al 2002, Dobbins et al 2002, Gassel et al 2005, Mollenhoff et al 2005, Curcio et al 2006) and there is some suggestion that doses greater than 0.01 mg/kg provide better analgesia than lower doses. The data presented here indicate that the higher doses are effective without causing unwanted side effects. Three cats receiving doses marginally below 0.01 mg/kg had pain scores of 0 or 1 at most time points, although one had a score of 2 at one time point. This suggests that even low doses provide some analgesia.

Physiological data collected during anaesthesia and in the recovery period indicate that buprenorphine was safely used for premedication before general anaesthesia with a range of different anaesthetic agents. Heart and respiratory rates, MABP and SpO₂ were well within the normal range for cats undergoing anaesthesia and surgery, and there were never any moments where adequate cardiovascular and respiratory function were in question. Only one cat, which was breathing air, had an oxygen haemoglobin saturation reading of 89%. This was transient, and is only marginally below the accepted safe minimum of 90%. Anaesthesia will always cause some respiratory depression, and the decrease in respiratory rate seen in both groups was not unusual. There were minor but statistically significant differences between the two groups in both heart and respiratory rates post operatively. Two hours after surgery, heart rate was slightly higher with buprenorphine and respiratory rate was lower. However, all values were well within the normal range and no significant biological effect can be attributed to this statistical difference. All the cardiorespiratory data indicate that buprenorphine at up to 0.021 mg/kg can be used for premedication in cats in order to provide post operative analgesia.

All cats recovered normally from anaesthesia, and there was no difference between the groups in the waning of sedation. By 4 hours after surgery, only one cat in the butorphanol group was still moderately sedated, and around 80% were fully conscious. Buprenorphine, even at the higher doses, did not appear to prolong recovery in comparison with butorphanol.

No attempt was made to assess the degree of sedation provided before anaesthesia. However, a number of comments were made on the record sheets remarking on the good quality of sedation afforded by both opioids in combination with acepromazine. Two cats became aggressive after butorphanol, leading to a difficult induction. This may be related to its known dysphoric effect (Lascelles & Robertson 2004), which was never seen with buprenorphine.

Conclusions

Buprenorphine, at 0.01-0.02 mg/kg body weight given before analgesia, produced analgesia at least as good as butorphanol. As with any analgesic, some animals required additional analgesia, but this was not unexpected. It is well recognised that some animals respond less well to analgesics than others, and there are always some patients that experience more pain than others in any analgesic trial. Buprenorphine produced complete analgesia that lasted at least 24 hours in over 80% of animals where butorphanol produced this effect in only 63%. Buprenorphine proved to be as safe as other commonly used premedicants in that its use was not associated with any adverse effects during anaesthesia with a range of commonly used agents. It was notable that there were no adverse effects of any consequence, and all cats were discharged after successful completion of surgery. Buprenorphine at 0.01-0.02 mg/kg body weight can be considered suitable for preoperative administration to cats in order to provide effective and safe post operative analgesia for a wide range of surgical procedures in general veterinary practice. If additional analgesia is required, the dosage may be repeated in 1-2 hours without compromising the patient, even when buprenorphine doses above 0.015 mg/kg have been given.

Acknowledgements

Alstoe Animal Health who funded the trial. The veterinarians and nurses in the veterinary practices who collected the data.

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Table 1. Post operative analgesia

Group	Vetergesic n=83 percentage of group	Torbugesic n= 70 percentage of group
Pre		
Score 0	95	93
Score 1	4	6
Score 2	0	1
Score 3	1	0
1 hr post		
Score 0	49	41
Score 1	25	34
Score 2	22	16
Score 3	4	9
2hr post *		
Score 0	51	43
Score 1	29	37
Score 2	17	12
Score 3	3	8
4hr post		
Score 0	57	54
Score 1	27	28
Score 2	13	13
Score 3	3	5
8hr post		
Score 0	66	61
Score 1	25	27
Score 2	5	5
Score 3	4	7
24 hr post *		
Score 0	82	63
Score 1	11	23
Score 2	4	3
Score 3	4	11

*Significant difference between groups

A feline ABC: Analgesia, Buprenorphine, Cat

A feline ABC: Analgesia, Buprenorphine, Cat

A novel approach to reversal

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Professor Hunter graduated with commendation from the University of St. Andrews in 1971 and then embarked upon her career in anaesthesia. She soon gained her Fellowship of The Royal College of Anaesthetists, and went on to complete a PhD entitled 'Pharmacodynamics and pharmacokinetics of neuromuscular blocking drugs in health and disease.' Professor Hunter is a world-renowned expert in this field, and has been honoured with many prestigious awards including the Gold Medal of The Royal College of Anaesthetists in 2004, and the Featherstone Award of the Association of Anaesthetists of Great Britain and Ireland in 2005. Amongst her many honorary appointments, she was Editor-in-Chief of the British Journal of Anaesthesia from 1997-2005, and now chairs the Board of the BJA. She is extremely active in the world of anaesthesia and has recently become Chairman of the Scientific Programme Committee of the European Society of Anaesthesiology. Professor Hunter has worked and taught in the Royal Liverpool University Hospital since it opened in 1978, and was awarded a Personal Chair at the University of Liverpool in 2000.

A novel approach to reversal

Although the vast majority of anaesthetists use anticholinesterases in their daily practice, they recognise the limitations of these drugs. The most important is that recovery from block needs to be established before these drugs are given; reappearance of the second twitch of the train-of-four (TOF) response is often recommended¹. Other (lesser) disadvantages, some of which are related to the muscarinic effect of these drugs, include: nausea and vomiting; bronchoconstriction; abdominal cramps; bradycardia; and a prolonged effect in the presence of renal dysfunction.

An ideal antagonist to a neuromuscular blocking drug would work at *any* time after *any* dose of muscle relaxant is administered to *any* patient (even one who is acidotic or has sub-clinical myopathy). No side-effects, including allergy, would be encountered. Will such a perfect reversal agent ever exist? Probably not, but it would be ideal if any new one was so predictable that it removed the need for neuromuscular monitoring. Such versatility is probably, in pharmacological terms, unrealistic.

The novel concept of using a ring-shaped cyclodextrin to engulf a neuromuscular blocking drug is fascinating.² Cyclodextrins are cyclic oligosaccharides which are recognised to encapsulate lipophilic molecules such as steroids. They are water soluble and well tolerated biologically. Org 25969 consists of eight such sugar molecules in a ring, the outside of which is hydrophilic, and the inside, hydrophobic. The size and shape of the ring is designed to produce a cavity into which a neuromuscular blocking drug such as rocuronium will tightly fit. Org 25969 is capable of forming a binary host – guest complex of high affinity with rocuronium, for two of its externally charged side-chains react with the quaternary nitrogen groups of the muscle relaxant. It is able to encapsulate all four steroidal rings of rocuronium within its lipophilic cavity. This *encapsulation* or *chelation* reverses the effect of rocuronium, by preventing its access to the nicotinic receptor and promoting its dissociation from it. Reversal of rocuronium is more efficacious with Org 25969 than with neostigmine; Org 25969 reverses profound block at three times the rate of the anticholinesterase. The complex is filtered by the glomerulus and excreted in the urine. As Org 25969 has no direct cholinergic effect, there is no need to administer an antimuscarinic drug with it.

Bom and colleagues (2001) demonstrated 90% recovery from profound (90%) block within three minutes after Org 25969 1 mg kg⁻¹ had been given to three animal species (guinea pig, cat, monkey), albeit with a marked variability of effect (SEM = 1.3 min).³ Similar findings were reported by Gijsenberg et al in 29 human volunteers, with doses of Org 25969 up to 8 mg kg⁻¹, and no signs of recurarisation after 90 min.⁴ There were no serious adverse events in the human studies except for paraesthesiae in the conscious subjects, which is also described when small doses of neuromuscular blocking drugs are given to awake volunteers. No marked cardiovascular changes were noted. In animal studies, antagonism by Org 25969 has not been found to be dependent on renal perfusion and not modified by acid-base changes.

Thus, at this early stage in its development, Org 25969 would seem to produce rapid reversal of profound neuromuscular block produced by rocuronium without significant side-effects. It is unfortunate, but predictable, that this specific cyclodextrin does not appear to antagonise other neuromuscular blocking drugs. Most clinical anaesthetists would undoubtedly prefer to use the same antagonist throughout their practice. It is also too early to be certain about lack of side-effects; these are often not confirmed with a new drug until several thousand exposures have occurred. Nevertheless, Org 25969 is a most exciting approach to antagonism of neuromuscular block, which heralds a new development in anaesthetic pharmacology. Initial results of its use in several animal species, including man, to reverse rocuronium are encouraging.

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A novel approach to reversal

A novel approach to reversal

A miscellany

**Chaired by
Nicki Grint**

- 4.00pm** **J Paterson, N Caulkett, M Woodbury, M Cattet**
Saskatchewan, Canada
“Comparative physiological effects during carfentanil-xylazine anaesthesia in North American elk (*Cervus elaphus*) supplemented with naso-pharyngeal medical air or oxygen insufflation”
- 4.15pm** **L Hughes**
Dublin, Ireland
“Propofol and fentanyl infusions in mixed breed dogs undergoing surgery”
- 4.30pm** **D Pang, J Allaire, Y Rondenay, S Cuvelliez, E Troncy**
Montreal, Canada
“Suitability of lingual venous blood to determine the acid-base and blood gas status of dogs under anaesthesia”

Abstracts – A miscellany

Comparative physiological effects during carfentanil-xylazine anaesthesia in North American elk (*Cervus elaphus*) supplemented with naso-pharyngeal medical air or oxygen insufflation.

J.M. Paterson, N.A. Caulkett, M.R. Woodbury, and M.R.L. Cattet

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This study compares specific cardiopulmonary effects and the overall quality of anesthesia during carfentanil-xylazine anaesthesia in hypoxemic vs. normoxemic elk.

Eight female habituated elk were studied with a randomized crossover design. Each elk's nasopharynx was insufflated with oxygen (OXY) or medical air (AIR) at 10L min⁻¹ throughout anaesthesia. Baseline data were collected before intramuscular (IM) injection of carfentanil (10µg kg⁻¹) and xylazine (0.2mg kg⁻¹). Arterial blood gases, direct arterial pressure, heart rate, respiratory rate, and somatic reflexes were assessed at 3 minute intervals for 30 minutes. Naltrexone (1mg kg⁻¹) and tolazoline (2mg kg⁻¹) were administered IM at 30 minutes. Induction and recovery times were analyzed with a paired t-test. Physiological responses over time and between treatments were compared with one and two-way ANOVA and a Bonferroni's post hoc test. Incidence of rigidity and movement at different levels of PaO₂ were compared with a Chi-square test. Significance was set at P < 0.05.

Induction and recovery were both significantly shorter in OXY, (208 ± 39 sec) and (333 ± 63) respectively, vs. AIR, (306 ± 84) and (532 ± 201). Elk in OXY had significantly higher PaO₂ and PaCO₂, and significantly lower pH and heart rate compared to AIR. Maximum PaCO₂ was 89 (± 5) in OXY, and 64 (± 4) mmHg in AIR. Minimum PaO₂ was 75 (± 30) in OXY, and 28 (± 6) mmHg in AIR. There was a trend (P = 0.08) towards decreased respiratory rate in OXY. Frequency of rigidity and movement increased at PaO₂ < 70 mmHg.

Animals nasally insufflated with air experienced slower inductions and recoveries, severe hypoxemia (PaO₂ < 35 mmHg), and increases in heart rate, muscle rigidity, and movement. Nasal insufflation of oxygen prevented hypoxemia and improved both cardiovascular stability and the quality of anesthesia but induced greater hypoventilation and respiratory acidosis.

Acknowledgements: Major sources of funding for this project were provided by the Western College of Veterinary Medicine Research Fund, and the Saskatchewan Canada Agrifood Innovation Fund Specialized Livestock Research Trust.

Abstracts – A miscellany

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Abstracts – A miscellany

Propofol and fentanyl infusions in mixed breed dogs undergoing surgery.

J.M.L. Hughes

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The use of propofol and opioid infusions has proved satisfactory for surgical anaesthesia in humans. Propofol and fentanyl have previously been used together for anaesthesia of ventilated greyhounds that were not undergoing surgical procedures¹.

Ten healthy mixed breed dogs (mean weight 30 ± 8.6 kg) undergoing elective surgery were premedicated with intramuscular (IM) acepromazine (0.04 ± 0.01 mg kg⁻¹). Anaesthesia was induced with intravenous (IV) propofol (4.0 ± 1.1 mg kg⁻¹). Propofol infusion was administered at 0.4 mg kg⁻¹ min⁻¹ for 20 min and then reduced to 0.3 mg kg⁻¹ min⁻¹. When mean arterial blood pressure (ABP) decreased below 70 mmHg in four dogs, infusion rates were reduced further to 0.2 - 0.25 mg kg⁻¹ min⁻¹. Five minutes after anaesthesia induction, fentanyl was administered IV (2.03 ± 0.13 µg kg⁻¹) followed by an infusion at 0.5 µg kg⁻¹ min⁻¹. Atropine was administered IV (40 ± 0.9 µg kg⁻¹) immediately following fentanyl injection. The trachea of all dogs was intubated with a cuffed endotracheal tube: the lungs were ventilated (with 100% oxygen) to normocapnia throughout anaesthesia (end-tidal carbon dioxide 4.9 ± 0.31 kPa). Recordings of heart rate, ABP and depth of anaesthesia were made every 5 min. The presence of palpebral reflex, increase in jaw tone, swallowing and limb movement were recorded every 5 min until extubation. Propofol and fentanyl infusions were discontinued at the conclusion of surgery; mean infusion time was 117 ± 45 min. Recovery times and characteristics were noted.

Over the anaesthetic period mean heart rate was 99 ± 30.6 beats per minute. Mean ABP recorded was: systolic 102 ± 16.8 , diastolic 56 ± 13 and mean 75 ± 14 mm Hg. After discontinuation of the infusions, mean time to spontaneous ventilation, extubation and head lift were 26 ± 9.6 min, 35 ± 18.7 min and 88 ± 123 min respectively. All but one dog recovered smoothly.

Propofol and fentanyl infusions provided satisfactory conditions for surgery. All dogs required positive pressure ventilation to maintain normocarbida. Some modifications of infusion rates are required to improve the long recovery times recorded in this study.

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Acknowledgements. Schering Plough for supplies of propofol.

Abstracts – A miscellany

This image shows a single sheet of white paper with horizontal green ruling lines. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.

Abstracts – A miscellany

Suitability of lingual venous blood to determine the acid-base and blood gas status of dogs under anesthesia.

DSJ Pang, J Allaire, Y Rondenay, SG Cuvelliez, E Troncy

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In previous studies,^{1,2} a linear correlation has been found between lingual (LBG) and arterial (ABG) blood gases in dogs anaesthetised for surgery. The goal of this prospective, clinical study was to quantify this relationship.

Twenty-three dogs, of mixed breeds and ages scheduled for surgery and classified as ASA I/II were included in this study. Simultaneous samples were taken from the dorsal pedal artery (via catheter), and from a lingual vein, generating paired data. Two paired samples were collected from each dog. Samples were taken with a mean arterial pressure between 60 to 100 mm Hg, oesophageal temperature of $37.0 \pm 1^\circ\text{C}$ and end-tidal carbon dioxide between 4.7 to 6.0 kPa. Sampling was performed anaerobically using a heparinised syringe and samples analysed within 5 minutes of collection using a calibrated blood gas analyzer. Sample processing utilised a standardised technique and the order of analysis was randomized. All sampling was performed by two experienced anaesthesia technicians. A modified Bland and Altman method was used to examine data.

The pH of LBG overestimated (positive bias) ABG by 0.004, with limits of agreement (95% confidence interval) of (-0.022, 0.031). The PCO_2 of LBG overestimated ABG by 0.075 kPa, with limits of agreement of (-0.55, 0.70) kPa. The PO_2 of LBG underestimated ABG by 11.17 kPa, with limits of agreement of (-25.25, 2.91) kPa. The standard BE of LBG overestimated ABG by 0.7 mmol L^{-1} , with limits of agreement of (-1.9, 3.4) mmol L^{-1} . The range (median) of ABG PO_2 sampled was 53.5 – 75.8 (66.8) kPa.

The pH, PCO_2 and SBE of LBG samples provide clinically acceptable substitutes of ABG samples in the patient population studied. The wider limits of agreement for PO_2 render it less reliable as a substitute for ABG.

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Acknowledgement: Financial support for this study was provided by the Fonds du centenaire (University of Montreal).

This study was carried out according to animal utilisation protocols approved by the animal care committee of the University of Montreal, which operates under the auspices of the Canadian Council on Animal Care.

Abstracts – A miscellany

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Some more good news

Some more good news

**Chaired by
Miss Alex Dugdale**

**Speaker
Dr Kirby Pasloske**

Sponsor



Neurosteroids in veterinary Anaesthesia

Kirby Pasloske DVM DVSc Dipl.ACVC

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Dr. Kirby Pasloske (paz law ski) joined Jurox Pty. Ltd. in July of 2003 as Research Program Manager-Pharmaceuticals. Since joining Jurox, Kirby has spent the majority of his time working with the injectable anaesthetic, Alfaxan®-CD RTU, completing the studies and documentation required for its registration in the UK, Europe, South Africa and North America.

Dr. Pasloske is a 1991 graduate of the Western College of Veterinary Medicine, Saskatoon, Saskatchewan, Canada. From 1991-1994 Dr. Pasloske was in private veterinary practice in Vancouver, British Columbia, Canada. The years 1994-1997 were spent completing a residency and Doctorate in Veterinary Sciences (DVSc) at the Ontario Veterinary College (Guelph, Ontario, Canada) in the discipline of Clinical Pharmacology. Dr. Pasloske's thesis was on the pharmacokinetics and pharmacodynamics of the NSAID, ketorolac tromethamine (Toradol®) in the dog.

In 1997, Dr. Pasloske was hired by Merck and Co., Inc. in Sommersfield, NJ, USA to act as a Research Veterinarian in Drug Discovery where he performed studies on drug proof of concept for efficacy, safety and pharmacokinetics/pharmacodynamics principles in multiple veterinary species.

In 2000 Dr. Pasloske accepted a position with Elanco Animal Health in Greenfield, IN, USA to become a Senior Scientist in Pharmacology and eventually the Group Leader for Drug Evaluation and Pharmacology. Over the three years he spent at Elanco Dr. Pasloske managed multiple Discovery and Development programs in many therapeutic areas looking at drug safety, pharmacokinetics and pharmacodynamics.

Dr. Pasloske has been a Diplomate of the American College of Veterinary Clinical Pharmacology since 1999. He is an active member of the American Academy of Veterinary Pharmacology and Therapeutics. Dr. Pasloske has published and presented on NSAIDs, antimicrobials and centrally acting agents.

Neurosteroids in Veterinary Anaesthesia

The anaesthetic properties of steroids have been known now for 65 years. In the early 1940s, Hans Selye reported reversible unconsciousness in rats given intraperitoneal injections of large quantities of steroid hormones [1]. The steroid, pregnanedione, was the most potent of those steroids tested [2]. In 1955 P'An et al reported their observations on a close structural relative of pregnanedione called hydroxydione [3]. Hydroxydione had a wide margin of safety and was more potent than thiopentone. However, hydroxydione was limited in that it produced a delayed anaesthetic induction (i.e. ~ 2-3 minutes) and had to be solubilised at an alkaline pH causing venous thrombosis. Further work on structure activity relationship of the pregnane steroid nucleus by Robertson and Wynn Williams [4], Cocker et al [5] and Atkinson et al showed that manipulation of the 3 and or 21 carbon position altered neurosteroid potency. Eventually, the compound 3 α -hydroxy-5 α -pregnane-11,20-dione (alfaxalone) was discovered by the Glaxo UK pharmacology department. Similar to the barbiturates, benzodiazepines and propofol, alfaxalone works by modulation of the neuronal cell membrane chloride ion transport, induced by binding to GABA_A cell surface receptors [6]. Alfaxalone was later combined with alfadolone (21-acetoxy-3 α -hydroxy-5 α -pregnane-11,20-dione), Cremophor EL (B.A.S.F.) and sodium chloride to yield formulation CT1341. Child et al [7] performed a battery of pharmacological tests on CT1341 in laboratory animals and found it offered significant advantages over the other injectable anaesthetics in that it had a higher margin of safety, it was non irritant to tissues including veins, it was compatible with the adjuvant and pre-anaesthetic drugs, it did not accumulate and it produced a pleasant anaesthetic experience for the patient. In the early 1970s, CT1341 was introduced as an intravenous (IV) anaesthetic induction agent for humans (Althesin®) and as an IV and intramuscular anaesthetic (Saffan®) for cats and monkeys. Saffan® was not licensed in dogs because it was known that the genus Canis exhibited an over zealous histaminergic response to polyoxyethylated emulsifying agents like Cremophor EL [8]. Both products, Althesin® and Saffan®, were rapidly adopted by clinicians in both fields of medicine, however, it soon became obvious that the CT1341 formulation caused an unacceptable number of serious "anaphylactoid" type of reactions in people [9, 10]; so much so that the drug was withdrawn from the market in the early 1980s. In cats, Saffan® can cause anaphylactoid type reactions as well, but more common are local histaminergic reactions including unilateral or bilateral flushing and oedema of the paws and pinnae (product drug insert). In an effort to remove the side effects observed with drug carriers such as Cremophor EL, groups like Brewster et al [11, 12] found that alfaxalone and other drugs could be solubilised in safe carriers like 2-hydroxypropyl cyclodextrins (2-HPCD). In 2000, Jurox Pty. Ltd. began marketing the first ready-to-use (RTU), water soluble formulation of alfaxalone, using 2-HPCD, in Australia and New Zealand. Since its registration, Jurox Pty. Ltd. has continued to perform numerous studies elucidating the safety, tolerance, pharmacokinetics, pharmacodynamics, and clinical utility of Alfaxan®-CD RTU in both dogs and cats [13-21]. Jurox Pty. Ltd. has also produced alfaxalone liver metabolism data in the dog and cat, substantiating earlier findings that it is progressively eliminated by the liver so that recovery from anaesthesia does rely simply on redistribution [22]. These studies have both demonstrated and confirmed the known anaesthetic attributes of the alfaxalone neurosteroid and in addition, confirmed that the formulation is devoid of the anaphylactic and histaminergic activity of its predecessor.

Neurosteroids in veterinary Anaesthesia

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Neurosteroids in veterinary Anaesthesia

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Poster presentations

**During morning and afternoon
coffee and tea breaks**

Tuesday 4th April

Session 1 10.30 – 11.00am

Chaired by Mark Senior

**A Enderle, O Levionnois, U Schatzmann
Wahlstedt, Germany**

“Comparison between isoflurane alone and its combination with ketamine and lidocaine constant rate infusions for general anaesthesia in horses”

**C Hackenbroich, J Pabst, I Prella, D Prüße, M Fehr
Hannover, Germany**

“Total intravenous anaesthesia with propofol in rhesus macaques (*Macaca mulatta*) during magnetic resonance imaging”

Session 2 3.30pm-4.00pm

Chaired by Nicki Grint

**A Dugdale, S Taylor, P Turner, I Young
Liverpool, UK**

“Applications of miniature mass spectrometry in equine anaesthetic monitoring”

POSTER SESSIONS

Comparison between isoflurane alone and its combination with ketamine and lidocaine constant rate infusions for general anaesthesia in horses.

A. Enderle, O.L. Levionnois, U.Schatzmann.
Pferdeklinik Wahlstedt, Wahlstedt, Germany.

We hypothesised that ketamine and lidocaine infusions reduce the isoflurane requirements, thereby limiting cardiovascular depression and enhancing immobility during surgical stimulation.

Forty horses (ASA I-III) scheduled for surgical procedures were randomly allocated to receive isoflurane anaesthesia alone (ISO) or with ketamine and lidocaine (LKI). Animals were premedicated with romifidine ($80 \mu\text{g kg}^{-1}$) intravenously (IV) and anaesthetised with diazepam (0.1 mg kg^{-1} , IV) and ketamine (3 mg kg^{-1} , IV). The isoflurane end-tidal concentration was set at 1.3% and further individually adjusted by an anaesthetist (unaware of treatments) to maintain light surgical anaesthesia. LKI received additionally lidocaine (1.5 mg kg^{-1} ; $40 \mu\text{g kg}^{-1}\text{min}^{-1}$) and ketamine ($60 \mu\text{g kg}^{-1}\text{min}^{-1}$) IV. Standard clinical cardiovascular and respiratory parameters were monitored. All horses' lungs were mechanically ventilated to maintain end tidal CO_2 at 5.3 kPa. Mean arterial pressure (MAP) was maintained over 70 mm Hg with dobutamine infused as necessary. Thiopental ($0.5\text{-}1.5 \text{ mg kg}^{-1}$) was given if the horses moved. Recovery quality was scored from 1 to 5 (very good to very poor). Differences between ISO and LKI were analysed with a two-sample t test for parametric data or a Fischer's exact test for proportions ($p < 0.05$ for significance). Results are mean $\pm$ SD.

Sex, age and breed of the horses, types of surgical procedure, duration of anaesthesia and recovery, body position, PaO_2 , PaCO_2 , pH, MAP and recovery scores were not significantly different between the two groups. Heart rate was lower ($p = 0.001$) for LKI (29 ± 4) than for ISO (34 ± 6). End-tidal concentrations of isoflurane (ISO: $1.57\% \pm 0.22$; LKI: $0.97\% \pm 0.33$), number of horses requiring thiopental (ISO: 10; LKI: 2) and use of dobutamine (horses; $\mu\text{g kg}^{-1}\text{min}^{-1}$; ISO: $8; 0.26 \pm 0.09$; LKI: $3; 0.18 \pm 0.06$) were significantly lower in LKI compared to ISO ($p < 0.001$).

These results support the use of this protocol to improve immobility and cardiovascular stability during isoflurane anaesthesia in ventilated horses.

POSTER SESSIONS

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POSTER SESSIONS

Total intravenous anaesthesia with propofol in rhesus macaques (*Macaca mulatta*) during magnetic resonance imaging

Ch. Hackenbroich, J. Pabst, I. Prella, D. Prüße, M. Fehr; Small Animal Clinic, University of Veterinary Medicine Hanover, Foundation, Bischofsholer Damm 15, 30173 Hannover, Germany

The aim was to investigate the use of a total intravenous anaesthesia with propofol in spontaneous breathing rhesus macaques during magnetic resonance imaging (MRI).

Six male rhesus macaques received atropine 0.01 mg kg^{-1} followed by ketamine 15 mg kg^{-1} intramuscularly. Following sedation, a catheter was placed into the saphenous vein. Propofol was given to effect to allow endotracheal intubation (20-30 minutes after ketamine) after topical application of lidocaine to the vocal cords.

Then propofol was administered at a dosage of $10 \text{ to } 15 \text{ mg kg}^{-1} \text{ h}^{-1}$ intravenously to maintain anaesthesia. The infusion rate was based on a preliminary trial. The animals were breathing room air during the course of anaesthesia. Heart rate, respiratory rate, oxygen saturation and end tidal CO_2 were monitored continuously and recorded every fifth minute for about 45 minutes. Data were compared by one way analysis of variance with repeated measurements or the Friedman-test.

Anaesthetic induction was smooth. Heart rate showed a slight decrease from an initial 134 ± 21 (mean $\pm$ SD) to 122 ± 17 beats min^{-1} after 45 minutes ($p > 0.05$). Respiration rate varied during the observation time between 25 ± 5 and 30 ± 7 breaths min^{-1} ($p > 0.05$). Oxygen saturation increased from initial 96.5 (92-100 [range]) to 98 (96-100) towards the end of anaesthesia ($p > 0.05$). The end tidal CO_2 varied between 5.85 (3.5-6.4) to 6.33 (4.0-7.6) kPa during anaesthesia ($p > 0.05$). Complete recovery from anaesthesia occurred within 28 ± 5 minutes of the ending of the propofol infusion. Excitations were not observed during recovery of anaesthesia.

The maintenance of anaesthesia with a continuous infusion of propofol $10 \text{ to } 15 \text{ mg kg}^{-1} \text{ h}^{-1}$ was a reliable method in rhesus macaques during MRI. The values of respiration rate were slightly below the physiological range ($32 \text{ to } 50$ breaths min^{-1})¹, but no negative clinical effect could be observed. The values of heart rate, oxygen saturation and end tidal CO_2 were within the physiological range.

1. www.info.med.yale.edu/yarc/vcs/normativ.htm

POSTER SESSIONS

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POSTER SESSIONS

Applications of miniature mass spectrometry in equine anaesthetic monitoring

A.Dugdale¹, S.Taylor², P. Turner² and I. Young¹

¹School of Veterinary Science, ²Department of Electrical Engineering and Electronics, University of Liverpool, Liverpool, Merseyside, L69 3BX.

Mass spectrometry is a powerful analytical technique previously under-utilised for clinical purposes due to excessive size and weight of the equipment. Current instruments including vacuum systems weigh upwards of 20-25kg; it is essential to reduce this for field portability to extend the range of environments where mass spectrometry can be employed.

This study establishes the advantages of employing commercially available mass spectrometers to monitor the volatile agents halothane, isoflurane and sevoflurane during anaesthesia. It has been shown that the presence of methane gas in exhaled breath can lead to inaccurate measurements of the concentration of halothane and isoflurane during equine anaesthesia when monitored with machines employing IR wavelengths c.3-4 μ m^{1,2}.

A Pfeiffer Vacuum quadrupole mass spectrometer was used in a preliminary study of 20 equine anaesthetics. Gas samples were drawn (at ~20ml min⁻¹) into the mass spectrometer via a capillary tube connected to a needled inserted into the endotracheal tube near the horse's incisor arcade. When measuring low molecular weight residual gases such as methane, the low resolution operation of the instrument resulted in peak overlap of masses 15 and 16, corresponding to oxygen and methane. During low resolution monitoring when F_IO₂ > 80%, false positive readings were obtained for methane. Operating at a higher resolution and consequently higher power is not always feasible with larger instruments as the power requirements are dependent on size of the analyzer.

Mass spectrometry can produce overlapping peaks in the low mass region, but typically the volatile anaesthetic agents have unique molecular ion peaks at higher isolated masses. All three volatile agents were shown to be measurable using this technique and yielded an array of fragmentation peaks from which calibration can be achieved. Monitoring and calibration of other respired gases (oxygen and carbon dioxide) is also considered, although the sampling time was too slow to allow complete discrimination between breaths. The problems associated with water vapour condensing in the sampling capillary, and varying the sampling time will be discussed.

This work has been funded by the MRC.

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POSTER SESSIONS

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Poster presentations

**During morning and afternoon
coffee and tea breaks**

Wednesday 5th April

Session 3 10.30am- 11.00am

Chaired by Briony Alderson

**T Bosmans, I Polis, L Duchateau, T de Bruin, G Verhoeven, F Gasthuys
Ghent, Belgium**

“A comparison of tepoxalin-buprenorphine and buprenorphine for post-operative analgesia in dogs: a clinical study”

**K Kamm, M Mosing, U Auer, Y Moens
Vienna, Austria**

“Gastric tonometry during anaesthesia for elective surgery in the dog”

Session 4 3.30pm-4.00pm

Chaired by Mark Senior

**N Grint, B Alderson, A Dugdale
Liverpool, UK**

“Clinical comparison of medetomidine-buprenorphine and acepromazine –buprenorphine followed by anaesthesia with propofol and isoflurane in dogs”

POSTER SESSIONS

A comparison of tepoxalin-buprenorphine combination and buprenorphine for post-operative analgesia in dogs: a clinical study.

T. Bosmans¹; I. Polis¹; L. Duchateau²; T. de Bruin³; G. Verhoeven³; F. Gasthuys⁴, ¹Department of Small Animal Medicine and Clinical Biology, ²Department of Physiology and Biometrics, ³Department of Medical Imaging of Domestic Animals, ⁴Department of Surgery and Anesthesiology of Domestic Animals, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium.

Pre-emptive analgesia is well accepted in current anesthesia protocols¹. This study compares the analgesic effects of a tepoxalin–buprenorphine combination to buprenorphine alone in the 24h peri-operative period.

Twenty dogs (11 breeds) undergoing cranial cruciate ligament repair, with a mean mass of 29.89 kg $\pm$ 15.46 ($\pm$ SD) and a mean age of 7.1 years $\pm$ 3.18 ($\pm$ SD) were included in this blinded clinical study, with client consent obtained. They were randomly assigned to 2 groups: group A, receiving a placebo per os (PO) before premedication and buprenorphine 10 μ g kg⁻¹ intravenously (IV), starting from the end of surgery, given every 6 hours until 24 hours post-operative and group B, receiving tepoxalin (10 mg kg⁻¹PO) prior to premedication and buprenorphine cfr. group A. Premedication consisted of acepromazine (0.01 mg kg⁻¹IV) and methadone (0.1 mg kg⁻¹IV). Anesthesia was induced with propofol (4-6 mg kg⁻¹ to effect) and maintained with isoflurane in oxygen. An investigator (unaware of treatments) allocated pain scores at the time of endotracheal extubation and at 1, 2, 6, 12 and 24 hours post-operative, using a visual analogue scale (VAS) and a multifactorial pain scale (MFPS). The VAS-scores were analysed by a mixed model with dog as random effect, treatment as categorical fixed effect and time and treatment by time interaction as continuous fixed effects (significance level=5%). MFPS-scores were summed over the entire period and analysed by a T-test (significance level=5%).

VAS-scores decreased significantly over time ($p < 0.0001$). The decrease in the two groups were not significantly different from each other ($p = 0.059$), with a linear decrease of -0.687 (SE=0.16) in group A, compared to a decrease in group B of -1.12 (SE=0.16). No significant differences were found when comparing MFPS-scores ($p = 0.43$).

In the present study, no statistical evidence could be found for the superiority of tepoxalin-buprenorphine over buprenorphine alone.

1. Lascelles B.D.X., Cripps P.J., Jones A. et al. (1998). Efficacy and kinetics of carprofen, administered preoperatively or postoperatively, for the prevention of pain in dogs undergoing ovariohysterectomy. Vet. Surg., 27; 568-582.

This work was supported by Schering-Plough Animal Health.

POSTER SESSIONS

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POSTER SESSIONS

Gastric tonometry during anaesthesia for elective surgery in the dog

K. Kamm, M. Mosing, U. Auer, Y. Moens

Clinic of Anaesthesiology and perioperative Intensive Care, University of Veterinary Medicine, Veterinärplatz 1, A-1210, Austria

Gastric balloon tonometry is used in human medicine to measure gastric mucosal PCO_2 (P_iCO_2) and pH (pHi), which give an indication of gastric mucosal perfusion. This study evaluates the feasibility to monitor these indices during clinical anaesthesia in dogs undergoing various elective surgical procedures.

Twenty five dogs scheduled for elective surgery and categorised as ASA I and II were premedicated with methadone (0.1 mg kg^{-1}) intravenously (IV). Anaesthesia was induced with propofol ($6\text{--}7 \text{ mg kg}^{-1}$) IV and maintained with isoflurane in oxygen in combination with fentanyl continuous rate infusion ($10 \mu\text{g kg}^{-1} \text{ h}^{-1}$). After induction a balloon-tipped air-filled tonometer was introduced orally into the stomach. The tonometer was connected to the measuring unit (Tonocarp®) and baseline measurements were taken (T_0). Immediately following reading of baseline measurements ten dogs were randomly assigned to receive an IV bolus of medetomidine ($5 \mu\text{g kg}^{-1}$) (group M), the remaining 15 dogs were considered as controls (group C). After baseline measurement tonometric parameters were collected every 10 minutes during one hour (T_{10} - T_{20} - T_{30} - T_{40} - T_{50} - T_{60}). Simultaneously an arterial blood sample was collected for measurement of PaCO_2 and pHa. For statistical analysis ANOVA with repeated measurement was used to compare time points within groups and a paired t-test if significance was detected. For comparison between groups an unpaired t-test was performed. Data are presented as mean $\pm$ SD.

Table1

			P_iCO_2		PaCO_2		pHi	pHa
Group C	T_0	Mean $\pm$ SD	5.86 $\pm$ 1.06	kPa	5.86 $\pm$ 0.80	kPa	7.25 $\pm$ 0.07	7.25 $\pm$ 0.05
	T_{60}	Mean $\pm$ SD	7.06 $\pm$ 0.80	kPa	6.13 $\pm$ 0.80	kPa	7.16 $\pm$ 0.06	7.22 $\pm$ 0.05
Group M	T_0	Mean $\pm$ SD	6.00 $\pm$ 1.06	kPa	5.73 $\pm$ 0.93	kPa	7.25 $\pm$ 0.08	7.28 $\pm$ 0.04
	T_{60}	Mean $\pm$ SD	8.00 $\pm$ 1.60	kPa	6.80 $\pm$ 1.47	kPa	7.17 $\pm$ 0.06	7.24 $\pm$ 0.06

The P_iCO_2 and PaCO_2 increased significantly ($p < 0.05$) in both groups, whereas the pHi and pHa decreased over time (Table1). No significant differences were found between groups.

Gastric tonometry is feasible during clinical anaesthesia. The increase in P_iCO_2 and decrease in pHi suggests a decrease of gastric perfusion over time. No significant influence of medetomidine administration on the measured tonometric parameters could be demonstrated.

POSTER SESSIONS

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POSTER SESSIONS

Clinical comparison of medetomidine-buprenorphine and acepromazine-buprenorphine followed by anaesthesia with propofol and isoflurane in dogs.

N.J. Grint, B. Alderson, A.H.A. Dugdale

The University of Liverpool, Small Animal Referral Hospital, Crown St, Liverpool, L7 7EX.

The cardiovascular effects of 2 doses of medetomidine / buprenorphine intramuscularly compared to acepromazine / buprenorphine intramuscularly as a premedicant agent prior to propofol/isoflurane anaesthesia were studied in a prospective, randomised, blinded clinical trial.

Forty eight dogs (19 female, 29 male) of mixed breed, age 3.57 ± 3.30 yrs and weight 23.55 ± 12.29 kg, ASA I or II were anaesthetised for procedures of a mild to moderate stimulus. Baseline heart rate (HR) and respiratory rate (RR) were measured. Premedication was with buprenorphine 0.02 mg kg^{-1} in combination with: medetomidine 5 ug kg^{-1} (Group M5); medetomidine 10 ug kg^{-1} (Group M10); or acepromazine 0.03 mg kg^{-1} (Group A) all drugs were administered intramuscularly. After 15 minutes (Group M5 and M10) and 30 minutes (Group A), HR and RR were recorded. Anaesthesia was induced with propofol and maintained with isoflurane in 100% oxygen via a non-rebreathing system. HR, RR, haemoglobin oxygen saturation ($\text{SpO}_2\%$) and non invasive blood pressure were measured every 5 minutes throughout anaesthesia. Normally distributed data were compared using a one-way ANOVA, results are presented as mean $\pm$ SD. Non-normally distributed data were compared using Kruskal-Wallis test, results are presented as median (total range). Significance was taken as $p < 0.05$.

HRs were lower and average mean and diastolic blood pressures (mmHg) were higher in the medetomidine groups than the ACP group and all blood pressures (systolic, diastolic and mean BP) in the M10 group were higher than the M5 group (see table 1). Mean $\text{SpO}_2\%$ remained above 96% in all groups. Isoflurane concentrations and the degree of surgical stimulation were similar across the groups.

	Group A	Group M5	Group M10
Average HR (bpm)	85.76 (± 13.92) ¹	73.27 (± 22.91) ¹	74.21 (± 18.21) ¹
Average SpO_2 (%)	96.8 (95.2-98.7)	97.1 (92-99)	96.4 (90.0-97.5)
Average Systolic BP (mmHg)	108.42 (± 16.33) ¹	107.49 (± 13.07) ¹	133.93 (± 23.99) ¹
Average Mean BP (mmHg)	76.88 (± 13.67) ¹	79.44 (± 15.63) ¹	84.00 (± 20.82) ¹
Average Diastolic BP (mmHg)	53.25 (± 12.23) ¹	64.23 (± 16.28) ¹	65.14 (± 21.20) ¹

All results presented as mean ($\pm$ SD) or median (total range) from pooled data.

¹ = statistically significant results

These premedicant combinations were appropriate for this group of animals, with medetomidine resulting in higher mean arterial blood pressure compared to acepromazine.

Acknowledgements: Pfizer Animal Health for their support with this project.

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