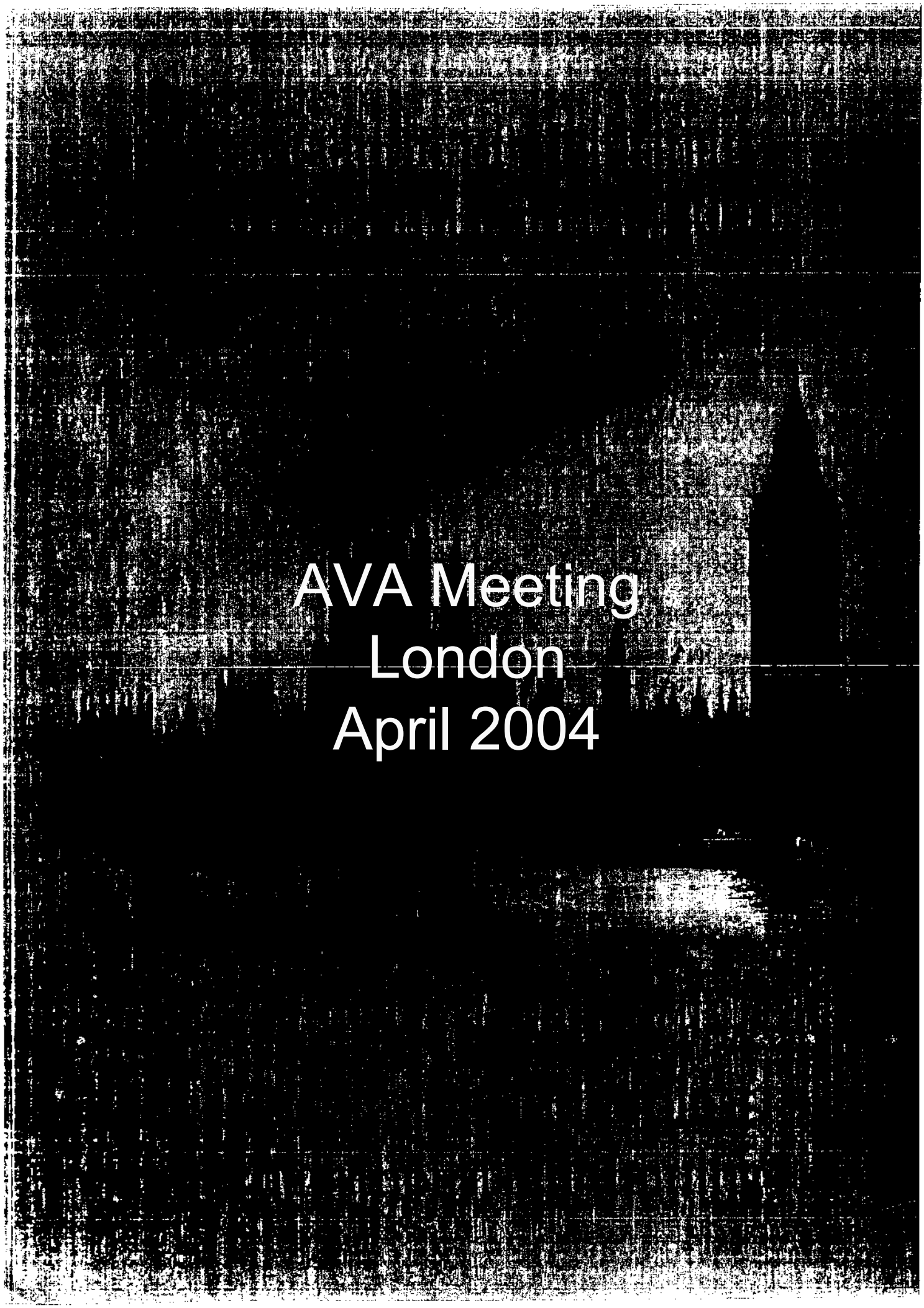

AVA Meeting
London
April 2004

Saturday 17th April. (09:00 - 17:00)

Trainee Anaesthetists Course: Lecture Theatre Brunei Gallery.

08:30 - 09:00 Registration

Time	Presenter	Topic	
09:00 - 10:00	Claire Bryant	Kinetics	6
10:00 - 11:00	Yves Moens	Capnograph	7
11:00 - 11:30	***Coffee/Tea Break***		
11:30 - 12:30	Sarah Watts	Non-Human Primate Anaesthesia	14
12:30 - 13:30	***Lunch Break***		
13:30 - 14:30	Hatim Alibhai	Central Venous Pressure	21
14:30 – 15:30	Belinda Farnfield	Statistics	25
15:30 - 16:00	***Coffee/Tea Break***		
16:00 - 17:00	Eddie Clutton	How to write a paper	28

PHARMACOKINETICS FOR ANAESTHETISTS

Clare Bryant

At first site pharmacokinetics appears mathematical, dry, dull and boring, however the basic principles underlying this subject are critical to understanding how anaesthetic drugs behave and explains how the rational design of dosing regimes is achieved in the normal and diseased patient. Mathematically this is difficult in people let alone the vast range of species that veterinary anaesthetists have to deal with. In this lecture I will cover basic principles and definitions to clarify the terminology of pharmacokinetics and then discuss how this applies to anaesthetic drugs. The following topics will be covered

1. Basic pharmacokinetics
2. Kinetics of injection and inhalation anaesthetics
3. Compartmental models
4. Context sensitive half times

Further reading:

Peck, T.E., Hill, S.A. and Williams, M. "Pharmacology for anaesthesia and intensive care." 2nd Edition Published by Greenwich Medical Media.

NON-HUMAN PRIMATE ANAESTHESIA

Sarah Watts

Introduction

Classification

The order Primata is extremely diverse containing species that range in size from a 100g to 300kg. There are 3 suborders of primates, Prosimii, Tarsoidea and Anthropoidea. Prosimii include species such as lemurs. Anthropoidae consists of 2 infra-orders, Platyrrhini (New World monkeys e.g. marmosets) and Catarrhini (Old World monkeys e.g. macaques, apes and Man). Many species are highly adapted for living in particular habitats.

Comparative Anatomy

Muscles. The largest muscle mass is the quadriceps and should be used for intramuscular injections.

Subcutis. The skin is fairly closely adhered to the underlying tissues so only small volumes of injectate can be given by the subcuticular route, between the shoulder blades or over the rib cage.

Blood vessels. The cephalic vein runs down the dorsal aspect of the forearm. The femoral vein and artery are very superficial (except in fat animals) on the medial aspect of the upper thigh. There is another superficial artery on the dorso-medial surface of the distal tibia. The saphenous vein lies superficially on the plantar aspect of the lower hind limb above the calcaneus.

Anaesthesia

Considerations

A number of factors must be considered when choosing an appropriate anaesthetic regimen. The species involved, the animals size and its housing (a dart gun may be required) need assessing. In addition, the duration and depth of anaesthesia wanted, the equipment available and the expertise of personnel requires consideration.

Pre-anaesthetic preparation

Health. Non-human primates carry a number of zoonoses, for example, Herpes B virus, Tuberculosis and Hepatitis A, so as such need to be handled with care especially if the health status of the animals is not known. For a detailed list of diseases consult the following reference, Lab Animals 1999 33 Suppl. S1:3-S1:18. Conversely there are a number of diseases that Man carries that are harmful to primates, for example, Flu, Tuberculosis, Herpes Simplex (marmosets) and measles, mumps and rubella and so precautions need to be taken to not compromise the health of the primates.

Behaviour. The normal defence response in primates is to bite and even small primates such as marmosets can inflict a nasty injury, so care needs to be taken when handling these animals. This can make obtaining a detailed pre-anaesthetic examination difficult unless the animal is used to being handled. Handling often will induce a marked stress response in primates if they are unaccustomed to it so parameters like, for example heart rate, may be considerably different from the norm. Obtaining an accurate weight for larger primates can also be difficult, this has implications not only for health assessment but also for determining drug doses. Small primates though usually can be caught by hand and placed in a weigh box. It should be noted however, that primates are highly intelligent and they can be trained, with positive

reinforcement techniques, to co-operate with husbandry/handling procedures avoiding the stress of restraint. For example, they can be trained to enter weigh boxes or to accept intramuscular injections or blood sampling.

Starvation. It is advisable to starve primates for up to 12 hours prior to anaesthesia. However, personal experience has indicated that the incidence of vomiting in anaesthetised marmosets and rhesus macaques is negligible. I also personally believe that consideration of the size and metabolic rate of the animals should be made before an animal is starved.

Sedation/induction

The ideal agent should be
- Fast acting
- Wide safety margin
- Injectable in small volumes via i/m route
- Minimal side-effects

Ketamine
- Pros
  - Onset of action < 5 minutes
  - Wide safety margin and top up doses easily given if initial dose is not enough
  - Reliable sedation and loss of pain reflex
  - Small volumes – 0.1-0.4ml/kg (10mg/ml)
  - Duration of action ~ 20 minutes
  - Minimal effect on cardiovascular and respiratory system
- Cons
  - Poor muscle relaxation
  - Increased salivation

Alpha-2-adrenoceptor agonists
- Pros
  - When used in combination with ketamine it produces good surgical anaesthesia with muscle relaxation and analgesia
  - Reversible – administer the same volume of atipamezole as medetomidine. Personal experience indicates that it is not as effective in marmosets
- Cons
  - Produces very unreliable sedation when used on its own even at high doses – animals very easily aroused – dangerous
  - Usual cardiovascular and respiratory effects

Benzodiazepines
- Pros
  - Minimal effects on cardiovascular and respiratory system
  - Useful adjunct to ketamine and steroid anaesthesia
  - Reversible
- Cons
  - Not reliable on their own as sedatives for large primates

Steroids – alphaxalone/alphadolone
- Pros
  - Heavy sedation < 5 minutes
  - Wide safety margin
  - Top up doses can be given
  - Good for use in neonates
- Cons

Relatively large volumes to be given by i/m route

Barbiturates

Pros

Rapid induction

Duration of action dependant on the agent – thiopentone ~5-10 minutes c.f. pentobarbitone 30-60 minutes

Cons

Can not be given i/m, so would usually require sedation with another agent first

Propofol

Pros

Rapid induction

Rapid recovery

Cons

Intravenous route only

Maintenance

Certain anaesthetic protocols may provide anaesthesia for the required length of time. For example, ketamine plus diazepam or medetomidine will give 30-40 minutes of surgical anaesthesia. Below is a selection of agents that can provide anaesthesia for longer than 30 minutes.

Injectable agents

Steroids – alphaxalone/alphadolone

Top up doses of 5mg/kg i/v can be used

Continuous infusion at a rate of 0.2-0.4mg/kg/minute can be used

Propofol

An infusion of 0.5mg/kg/minute can be used

Inhalation agents

Any of the commonly used agents, for example halothane or isoflurane, can be administered to primates. A facemask can be used in small primates, but ideally endotracheal intubation should be performed. This can be done in small primates such as marmosets as well as the larger primates. The larynx should be sprayed with local anaesthetic to eliminate laryngeal reflexes. Nitrous oxide can be used in addition to oxygen.

Local anaesthesia

Local anaesthetic techniques can be used successfully in primates, however, it is unlikely that such techniques can be used alone without sedation/general anaesthesia.

Local anaesthetic cream can be applied to superficial blood vessels for vasodilation prior to catheter placement.

Infiltration techniques can be used to provide analgesia to sites of trauma prior to repair.

Epidural/spinal techniques could be used, but be mindful that primates will want to climb on recovery from anaesthesia so loss of limb function may be stressful to them. Lumbar puncture is likely to result in spinal anaesthesia and epidural anaesthesia is more likely at sacro-coccygeal junction.

Neuromuscular blocking agents

Primates have been used for the experimental evaluation of NMBs (J Pharmacol Methods 1984 12 (1) 1-27), but their use clinically is limited.

It should be noted that ketamine will potentiate the action of non-depolarising NMBs and so if used together the dose rate of NMBs will need to be reduced. (Anesth Analg 1989 68(1) 5-8).

Monitoring

Temperature

Prevent losses – wrap in bubble wrap, or heat retaining blanket
Provide heat – heat pads, water blankets, etc
Provide heat in recovery – infra-red lamps

Cardiovascular system

Heart rate and rhythm - ECG
Pulse oximetry – works well even in small primates
Blood pressure – non-invasive, not suitable for small primates. Invasive - can use coccygeal artery in small primates, but some pressure transducers may not detect the pressures, so systems available for rodents would be more suitable.

Respiration

Rate
Capnometry – care in small primates with low tidal volumes, mainstream analysers will increase the dead space and side-stream analysers may underestimate $ETCO_2$ due to dilution from anaesthetic gases.

Depth

As with any species, familiarity will increase the perception of depth of unconsciousness

Pedal withdrawal reflex – once this is lost surgical anaesthesia is achieved
Eye reflexes – if ketamine is used then palpebral reflex will be brisk
Physiological parameters – as with other species these can be unreliable indicators

Recovery

Provide heat
Reduce cage height - natural instinct is to climb

Analgesia

Pain

Signs of pain in primates are quoted as follows, but there are likely to be species differences:-

Vocalisation/screaming
Unkempt appearance
Reduced fluid/food intake
Isolation from group or increased attention from group
Grimacing

Opioids

All the commonly encountered opioids can be administered to primates. Buprenorphine will provide analgesia for the longest duration (~6-12 hours). The sedative effect of opioids may increase recovery times, which may cause problems in some situations. Fentanyl patches could be used (25μg/hr <10kg - 100μg/hr >30kg) but a primate jacket would have to be worn to prevent their removal.

NSAIDs

NSAIDs can be administered to primates but there is little experimental/clinical data on effective dose rates and duration of action. I assume a duration of action of 24hrs and have used carprofen, meloxicam and tepoxalin. Oral administration is problematical as most primates can detect substances in food however well disguised in fruit or flavoured drinks.

Clinical data

	Marmoset	**Rhesus**	**Baboon**
HR	210-250	100-200	100-200
RR	36-44	40	30
BP mean mmHg	70-100	100	100
Temperature	38.5	38	38
RBC ($x10^6/mm^3$)	6	5	5
PCV (%)	45	35	35-40
Hb (g/dl)	16	12	12
WBC ($x10^3/mm^3$)	8	10	8
Urea (mg/dl)	<50	<40	
Creatinine (mg/dl)	1	2	1

Dose rates

Drug	Dose	Route	Duration
Carprofen	4mgkg^{-1}	i/v, s/c	~24hrs
Meloxicam		Oral	~24 hrs
Tepoxalin	10mgkg^{-1}	Oral	~24 hrs
Buprenorphine	0.005-0.01mgkg^{-1}	i/m, i/v	6-12 hrs
Morphine	1-2 mgkg^{-1}	s/c, i/m	4 hrs
Pethidine	2-4 mgkg^{-1}	i/m, i/v	2-4 hrs
Alphaxalone/ Alphadolone	12-13 mgkg^{-1}	i/m	10-20
Diazepam	1mgkg^{-1}	i/m	
Ketamine	Up to 40mgkg^{-1}*	i/m	20 min
Diazepam + Alphaxalone/ Alphadolone	0.5-1mgkg^{-1} + 10-12mgkg^{-1}	i/m	40 min
Diazepam + Ketamine	0.5-1mg/kg + 15mg/kg	i/m	30-40 min
Medetomidine + Ketamine	25-50μgkg^{-1} + 10mg/kg	i/m	30-40 min

Thiopentone	15-20mgkg^{-1}	i/v	5-10 min
Propofol	7.5-12.5mgkg^{-1}	i/v	5-10 min
Alphaxalone/ Alphadolone infusion	0.2-0.4mg/kg/min	i/v	
Propofol	0.5mg/kg/min	i/v	

* Smaller primates with high metabolic rates usually require proportionately higher does of ketamine

Further Reading:

General primate references

UFAW Handbook – ISBN 0-582-40911-X
Handbook of Laboratory Animal Management and Welfare – ISBN 0-632-05052-7
PrimateLit http://www.primate.wisc.edu/pin/

Anaesthesia

Laboratory Animal Anaesthesia ISBN 0-12-200361 3
Lab Animals 1983 17 196-197
Lab Animals 1999 33 24-29
http://www.med.stanford.edu/school/Comparative Medicine/SOP/Program/anesthetics-primates.html

CENTRAL VENOUS PRESSURE

Hatim I K Alibhai

Central venous pressure (CVP) is the measure of hydrostatic pressure within the thoracic vena cava. This value allows the veterinarian to assess how well blood is returning to the heart and also the ability of the heart to receive and pump blood. In a normal animal with no vascular obstruction CVP can be reflective of right atrial pressure and provides information concerning the adequacy of venous blood volume. Low cardiac out as a result of hypovolaemia may lead to a low CVP and a high CVP accompanied by low cardiac output may indicative of heart failure. CVP measurements also provide evidence of a volume overload in a patient receiving fluid therapy, recurrent pericardial effusion, or right-sided heart failure. CVP may be similar to pulmonary arterial wedge pressure, but are never considered a substitute for the measurement of pulmonary arterial wedge pressure. Pulmonary arterial wedge pressure measurements are considered more accurate in evaluating a patient for left-sided congestive heart failure.

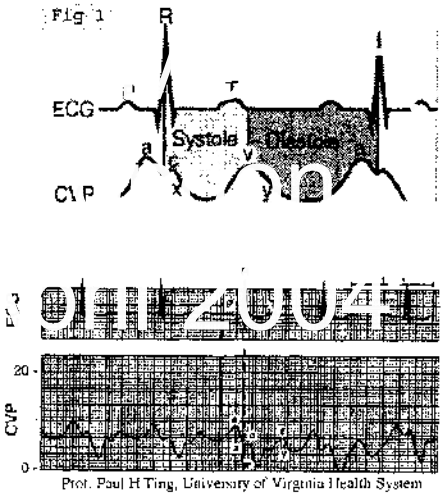
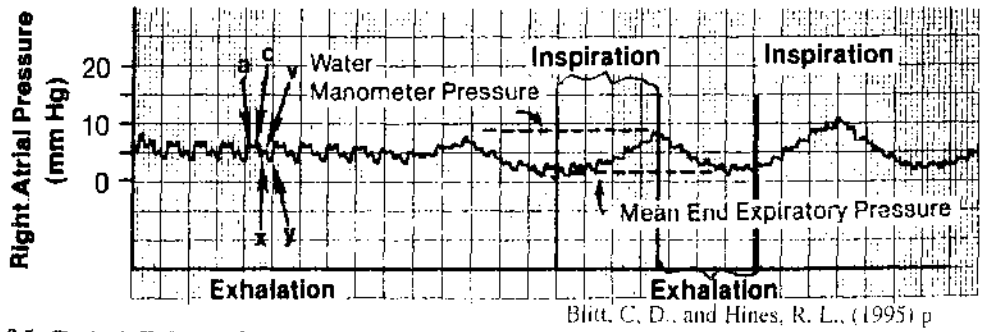


Fig. 1. a = atrial contraction, c = bulge of the tricuspid valve during systole, v = rapid atrial filling with tricuspid valve closed, x = reduction of atrial pressure during ejection and y = rapid ventricular filling phase.

When measured continuously, the CVP waveform can be evaluated for characteristic changes reflective of various parts of the cardiac cycle. Cardiac and blood volume abnormalities affect the CVP waveform in predictable fashions depending on location and type of the problem.

Respiratory effects



Blitt, C. D., and Hines, R. L., (1995) p

Fig. 9-5. Typical CVP waveform of a patient receiving controlled mechanical ventilation. a-, c-, v-waves and x-, y-descents are indicated (see text). The lowest pressure measured by a water manometer is often the highest pressure seen during the respiratory cycle, whereas the desired pressure is that at the end of exhalation.

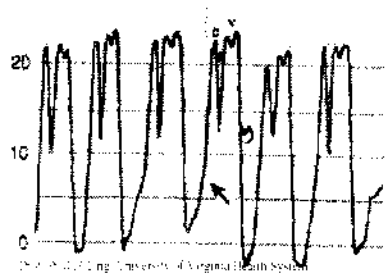
During spontaneous ventilation, a decrease in pleural and pericardial pressures occurs during inspiration - these are pressures that are transmitted to the right atrium. This causes a decrease in the measured CVP (but transmural pressure may actually INCREASE). Mechanical ventilation causes the opposite effect during an forced inspiratory breath. Pleural and pericardial pressures are almost equal to atmospheric pressure at end-expiration. This is true with both spontaneous and mechanical ventilation. This point in time provides the best estimate for transmural pressure and cardiac preload.

Bradycardia

Prof. Paul H Ting, University of Virginia Health System

Bradycardia causes each wave to become more distinct. Clearer separation of x and x'. "h" wave may become evident - plateau wave in mid- or late diastole. The "h" wave has very little clinical significance

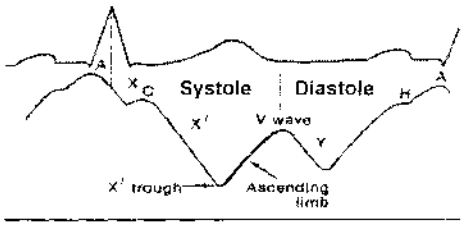
Tricuspid Regurgitation



The right atrium gains volume during systole - so the "c" and "v" wave is much higher. The right atrium "sees" right ventricular pressures and the pressure curve becomes "ventricularised"

Other examples

Waveform	Cardiac Condition
Absent a wave	Atrial fibrillation, sinus tachycardia
Flutter waves	Atrial flutter
Prominent a waves	First-degree atrioventricular block
Large a waves	Tricuspid stenosis, right atrial myxoma, pulmonary hypertension, pulmonic stenosis
Cannon a waves	Atrioventricular dissociation, ventricular tachycardia
Absent x descent	Tricuspid regurgitation
Prominent x descent	Conditions causing enlarged a waves
Large cv waves	Tricuspid regurgitation, constrictive pericarditis
Slow y descent	Tricuspid stenosis, right atrial myxoma
Rapid y descent	Constrictive pericarditis, severe right heart failure, tricuspid regurgitation, atrial septal defect
Absent y descent	Cardiac tamponade



JAMA (1996) 275: 630-634.

Clinical Techniques for Measurement of Central Venous Pressure

Things to think consider..

It CVP is a waveform and not a straight line, where does the number come from?
At what point on the curve do I measure CVP?
Why don't I just use the number that the monitor gives me? NOTE: Machines just average the measurement.
What about respiration ventilation? NOTE: Measure at the end of expiration.
There are three parts of the waveform that are systolic events (c, x, v)
There are two parts of the waveform that are diastolic events (a, y)
The ECG is used as a reference to properly identify the parts of the waveform
The terms systole and diastole refer to VENTRICULAR events only
The CVP wave represents changes in pressure, not changes in volume
Mnemonic for the CVP wave

- "a" wave due to atrial contraction
- "c" wave due to tricuspid closure and ventricular contraction
- "v" wave due to venous filling of atrium

CVP in dogs and cats has been reported to be 0 to 10 cm of water. Values in millilitres of mercury can be converted to centimetres of water by multiplying by a factor of 1.36. Values of CVP of less then 0 cm of water may indicate hypovolaemia, and values greater than 15 cm of water may suggest volume overload. Always observe trends in individual patients.

CVP may be estimated or directly measured. Estimates of CVP may be made by direct examination of the neck veins for distension. This is a relatively inaccurate method. Only tells you if the CVP is increased. Hard to get a specific number (gross observation, not direct measurement). Hard to trend over time.

CVP can also be measured using either a water manometer or a pressure transducer which requires a placement of a central venous catheter. The central venous catheter

can be placed via the jugular vein, the femoral vein, or the saphenous vein. The tip of the catheter should be at the level of the junction of the right atrium (for the jugular catheter) or caudal vena cava (when the hind limb vessel is used) (de Laforcade and Rozanski 2001).

The patient should be placed in sternal or lateral recumbency. A reference point that correlates with the right atrium is determined. This is the "0" reference point. The catheter is then connected to the water manometer or electronic device by non-distensible extension set. The extension set is then connected to a water manometer or transducer kept at the level of the right atrium. These techniques allows for the CVP pressure to be observed and recorded (de Laforcade and Rozanski 2001).

Further Reading:

Blitt, C, D., and Hines, R. L., (1995) Monitoring in Anaesthesia and Critical Care. (3rd Ed) Churchill Livingstone, London.

Daly, C. M., Swalec-Tobias, K., Tobias, A. H., et al., (2002) Cardiopulmonary Effects of Intrathoracic Insufflation in Dogs. J Am Hosp Assoc. 38(6): 515-520.

de Laforcade, A. M., and Rozanski, E. A. (2001) Vet Clin North Am Small Anim Pract. 31(6): 1163-1174.

Gookin, J. L. and Atkins, C. E., (1999) Evaluation of the Effect of Pleural Effusion on Central Venous Pressure in Cats. J Vet Intern Med. 13(6): 561-563.

Hall, L. W., and Nigam, J. M., (1975) Papers and articles measurement of a central venous pressure measurement in horses. Vet Rec. 97(4): 66-69.

Ikeda, S. and Schweiss, J. F (1985) Maximum Infusion Rates and CVP Accuracy During High-Flow Delivery Through Multilumen Catheters. Crit Care Med. 13(7): 586-588.

McKelvey, D. and Hollingshead, K. W. (2000) Veterinary Anaesthesia and Analgesia. Mosby, London.

Oakley, R. E., Olivier, B., Eyster, G.E., et al., (1997) Experimental Evaluation of Central Venous Pressure Monitoring in the Dog. J Am Anim Hosp Assoc. 33(1): 77-82.

Sykes, M. K., Vickers, M. D., and Hull, C. J. (1991) Measurement and Monitoring in Anaesthesia and Intensive Care (3rd Ed) Blackwell Scientific Publications, London.

STATISTICS

Belinda A Farnfield

Outline

Some knowledge of statistics is essential for all anaesthetists:

to interpret data - your own and published data

ECVA candidates: "sufficient knowledge of statistics to analyse results and interpret published work", "approach problems in an analytic and scientific way"

RCVS Diploma: "techniques of biological measurement used in clinical and experimental animals and interpretation of results including statistics"

Introduction

Samples and populations

A typical research project will involve collection of data from a small sample of animals. The data from this sample are then used to draw conclusions about a large group of animals: the population.

Types of data

Numerical

Continuous: any value possible E.g. arterial blood pressure.

Discrete: only certain values are possible e.g. litter size.

Categorical

Descriptive data e.g. coat colour.

Ranks and scores.

Data may be shown graphically as a frequency distribution. If continuous numerical data are collected from a large number individuals, the frequency distribution histogram often has a symmetrical bell-shape, following (i.e. similar to) the Normal or Gaussian distribution.

68% values lie within 1 SD of the mean
95% " " 2 SD of the mean

A guide to summarising data

If the data follow a Normal distribution	Tables: mean with standard deviation Graphs that use the mean, eg show mean with error bars for one standard deviation above and below The standard deviation tells you how close the individual data points are to the sample mean ie how the data are scattered.
If data do not follow a Normal distribution	Tables: median with interquartile range Graphs that use the median, eg box-and-whisker plots

Using data to estimate

Data are collected from a small sample. From the data, you wish to draw conclusions about a population. E.g. if you want to use the sample mean as an estimate of the true population mean, it is important to know how good the estimate is. There are two basic ways to do this:

Calculate the standard error of the mean: tells you how close the sample mean is to the population mean it is estimating.

Calculate a confidence interval: gives you a range within which you are likely to find the population mean.

Using data to test hypotheses

To investigate whether drug X affects heart rate during anaesthesia:

Null hypothesis would be "administration of drug X during anaesthesia has no effect on heart rate."

If the null hypothesis is true, all variations in heart rate after administration of drug X are due to chance or random variation alone. If false, variations in heart rate after administration of drug X are due to chance/random variation **and** a genuine drug effect.

Two groups of anaesthetised animals. Group 1 receives drug X. Group 2 receives saline control. Heart rate measured in both groups 10 minutes after administration of drug X or saline. Mean heart rate calculated for Group 1 and Group 2.

Statistical test used to examine the difference between means.

Output is $p = 0.04$.

p is a probability. p = 0.04 means that if drug X has no effect on heart rate, 4% of experiments will result in the observed difference between the means. Usual to reject the null hypothesis when less than 5% of experiments would result in the observed results. So for this example can state that there is a significant difference between the means and the null hypothesis is rejected. Can conclude that drug X has a significant effect on heart rate during anaesthesia.

A guide to statistical tests

In order to	With data following a Normal distribution (parametric)	With data that do not follow a Normal distribution (non-parametric) eg scores
Compare two groups		
unpaired	unpaired t-test	Mann-Whitney test
paired / matched	paired t-test	Wilcoxon test
Compare three or more groups		
No matching	Analysis of variance (ANOVA)	Kruskal-Wallis test
Matching	Repeated measures ANOVA	Friedman test

Resources

Reading list for RCVS Certificate and Diploma in Anaesthesia contains a useful book list. Available from RCVS website (http://www.rcvs.org.uk/vet_surgeons/education)

Further reading:

Greenhalgh, T. (1997). Statistics for the non-statistician. In *How to read a paper*, pp. 69-86. London, UK: BMJ Publishing Group.

Motulsky, H. (1995). Intuitive Biostatistics. New York: Oxford University Press.

Festing, M. F. W., Overend, P., Gaines Das, R., Cortina Borja, M. and Berdoy, M. (2002). The Design of Animal Experiments. London, UK: The Royal Society of Medicine Press Ltd on behalf of Laboratory Animals Ltd.

Stats for Vet + Animal Science - Aviva Petrie + Paul Webb

www.graphpad.com

How to Write a Scientific Paper
(not design a scientific study)

R. E. Clutton

Introduction

Acquiring the skills required to be able to write scientific papers or manuscripts should, to a large extent, be self-taught; in getting to the stage where he or she needs to write a paper, a post-graduate author should have read enough to glean what is involved. However, this is not always the case, a situation made worse by supervisors who abrogate their responsibilities.

Function

The function of a paper is to make new important information available, as rapidly as possible, to people who can best deal with the information, for the purposes of

a) bettering the lot of animals (or human beings)[1]
b) preventing research being repeated
c) to optimise allocation of research funding.

(Unfortunately, writing papers has become something less than this:

a) a measure of academic productivity: "the currency of academia" (along with other measures like teaching assessments etc.). The love production of papers, due to preoccupation with their production, not their content, has led to devaluation in this currency: many papers are pointless and dull.
b) to meet board examination criteria, i.e. to demonstrate that clinicians can do research
c) writing papers is intimately involved with experimental design (not the subject of this work).

To meet this end, a scientific paper should allow the reader to:

a) assess the observations made
b) repeat the experiment if necessary
c) determine if the data support the conclusions

Before writing anything, the author should ask five questions:

1) What am I trying to say ?
2) Is it worth saying ?
3) What is the right format for this (paper, or brief communication ?)
4) What is the audience for the message?
5) What is the right journal for publication, i.e who needs to read and benefit from the work? (GPs [Veterinary Record] versus anaesthetists [VAA]). The choice of Journal is influenced by impact factors.

Once it has been decided which Journal to submit to, the document must be written in the precise and specific format required by that journal. Most, except "Nature" have similar formats. In writing the paper, the "Guidelines for authors" must be read and followed during all stages of writing, i.e. before starting the first draft, during writing and on the perceived conclusion. Guidelines to audiences may exist is short (per issue) and extended (annual) forms. Full details are available on the Journal's web-site.

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[1] The importance of information should be an important submission to acceptance determinant, not the submission date, i.e., unimportant information can wait.

Appropriate formatting is important: ignoring the guidelines will immediately alienate Editors, and in the case of poor papers lead to immediate rejection.

The Paper

Despite the author's efforts and conviction that their paper is important, few people will read the whole article. Most will read the title, a few will read the summary or abstract, and some might skip to the conclusion.

Title

The title & summary are important for "catching the eye" and for indexing purposes.

The editor's immediate reaction to a paper, i.e. to read it and begin processing immediately, or to leave it until time is less pressing depends largely on the title.

Many Journal readers will just scan the contents page looking for key words; a good title in conjunction with key words is required to "snare" such scanners.

A bad title will mean a potentially interested reader misses the work

A title should not be a précis of the work.
It must be concise and informative, i.e. should say what the paper is about
It should be alluring
It can be a statement of fact; or posed as a question

Authorship list

There are increasing editorial pressures on controlling this aspect of papers. In some areas, it has become a Christmas card list, with the same connotations.

All authors must have made significant contributions to a) design, b) execution; c) analysis and d) writing up of the paper. Consequently, all authors must be prepared to share responsibility for what was done and what has been written.

English speakers in the list should be responsible for the standard of English of foreign papers.

"Gift authorships" are highly inappropriate.

Acknowledgements

Whilst acknowledgements are normally written last; they often appear first on the manuscript.
Technical staff and others should be acknowledged, and not given authorship if their contribution was part of their daily duties.
Always acknowledge fund providers; to identify conflict of interest as much as anything else
Always give the reason for acknowledgement
Don't gush!

Abstract

After the title, this is often the only other part of the paper which is ever read (usually the electronic form)
So for authors out to make their reputation, it must be the most polished part of the paper. It will be what many people come to know your work by - alone.

It must entirely reflect the main paper in terms of methodology and conclusions.

It should be short, intelligible, interesting and informative

It must stand alone

The word count must be adhered to.

The "structure" of structured abstracts must be adhered to

In addition.....

The authors should provide a running title (the editor will help with this)

Provide key words for indexing purposes (the editor may over-ride). These appear as medical subject headings (MeSH) in Index Medicus (or alternatively, the Veterinary Bulletin).

Introduction.

The introduction has three objectives. It must indicate to the reader:

1) why the work was done
2) why it is important
3) why it is an improvement over pervious work

.....and in a brief and arresting way.

The first sentence should be bold in order to captivate the reader. This can be done in one of two ways;

1) by explaining that the paper solves a problem the reader will have, or is likely to encounter; or
2) by explaining in no uncertain terms why the work is a major contribution to the scientific literature,

If it is a repeated study, it must be emphasised why the current manuscript is better.

It is of paramount importance that the reader has absolutely no doubt what specific question(s) is (are) being asked. To this extent, the introduction follows the project design: i.e.,

A question is asked
All relevant information is gathered, in all languages, published or otherwise
The weakest information is discarded
The remainder is synthesised (the introduction must be brief, and not become a literature review)
A conclusion related to the question is drawn.
If the question is not answered, then a study is designed explaining how the question will be answered.

Reporting this process provides the introduction.

Within this process the reader must be convinced that the study was justified. This can be done in one of several ways:

a) The question being asked is really important (explain why this is so), or
b) although previous workers also thought the question was important, they haven't solved the problem properly i.e., describe (rather than attack) the limitations of previous work.

If course a) is taken, there must be strong evidence showing that the work has not been done before This might include meeting experts in the field, Pub Med reviews, or a review of recent proceedings \ reviews. It is insufficient to say "Despite an exhaustive search, nothing was found". Consider "Despite a Medline search using 15 different key phrases, an examination of recent review articles (cite) personal

contact with 2 world experts etc, we found nothing to indicate that this has been done before. It is mainly the editor, and the older worker in the field who will need convincing of the originality of the work.

When attempting to convince the reader of what is already known, do not provide a literature review or unnecessary lists of inappropriate citations, i.e. textbooks; rather cite 3 - 4 recent references from different well-recognised / regarded groups in different countries).

In convincing the reader of the importance of the work, don't be patronising, don't state the obvious, and don't attempt to baffle the reader.

The introduction can be done before the study starts but usually isn't!

Material & Methods

Basically, "How was the work done?" Describe in sequence

a) how the study was designed
b) how the study was performed
c) how the data were analysed.

The methods are easily written concisely and can be done as the work is in progress. However, it is often best to do it before you start (and have it checked). If the methods are wrong; the paper may be rejected. It is this part which will be most critically dissected by reviewers to ascertain if the study was done correctly and to determine if the conclusions can be made as soundly as they are made.

The statistical analysis should be decided upon as an *a priori* step, to avoid bias in the findings. They should be non-parametric to begin with, becoming parametric if the results prove to be parametrically distributed. Statisticians should be consulted from the outset.

As a rule, "M&M" should be sufficiently detailed to allow a competent worker to repeat the whole experiment.

A statement from the ethical committee or Home Office PIL number must be provided in this section.

Study design

Provide a clearly stated hypothesis.
Information on this is best done using phrases like matched-pairs, parallel controlled prospective etc.
The purpose is to describe and to defend, if necessary, the experimental design.

Study conduct

Always incorporate the following:

Subject recruitment and selection, and exclusion.
Do not give biographic data at this stage; these are results.
Subject sources, laboratory acclimatization, diet, photoperiod etc. but only if pertinent
Report how randomisation was performed
Give accurate details of materials and methods in a chronological sequence
When talking about "blinded observers" explain how "ignorance "was achieved

When established techniques are used; cite earlier work, e.g. echocardiography. If these techniques have been modified then they must be detailed.

The apparatus used must be described in sufficient detail that the reader is confident of the accuracy of results. Is the apparatus appropriate, sensitive enough (detect low measures), accurate (same results as a gold standard), and reproducible (gives same value on successive readings).

The methods used to standardize, calibrate, assess linearity and frequency response of the device may require description.

However, not all details are necessary, e.g. IV catheters for induction of blood pressure measurement.

For complex study designs a flow diagram may be used

Data analysis

Provide a p value to disprove the null hypothesis
Give an estimate of the B error, i.e. the likelihood of a false negative
Give the exact statistical tests chosen *a priori*

Results

This section describes what was found using text, tables and illustrations to lead the reader through (principally) the major expected results (the answer to the principal question) less important unexpected results and then the unexpected. The text tells the story, the tables summarizes the evidence, the figures emphasize the highlights. Give the size of the effect and its significance of a and b).
The reader should not be fobbed of with: "the results are presented in tables 1 – 10".

Section 1 of the results should describe the subjects and groups (this should not be in materials and methods) in sufficient detail that the reader can determine if: a) the groups are sufficiently similar to be compared and b) the subjects of the study are sufficiently similar to those encountered in the reader's practice to establish relevance to the reader. If group differences exist then the cause, and the effect of the differences on the drawn conclusions must be discussed later.

Section 2. Present results, start with text, but lead through tables and figures. Tables are the "meat" of the data and justify the statistics. Figures should be used to emphasise important points. The tables and figures must be "stand alone", i.e the legend must say enough without reader having to go back to text. These will include statements like "Cardiopulmonary variables in 12 halothane – anaesthetized dogs undergoing cardiopulmonary bypass".

In describing the results, give as much information in as few words as possible. This will mean:

N
Measure of central tendencies (means or medians)
Measure of dispersion (SEM or Confidence limits of the mean or SD
Range of results

If data is not normal, either transform, or give the median, its CI and the quartiles

If a complex analysis is used and applied, the PI should make an attempt to understand it, but if this is not possible, a statistician should write this section and be consulted *a priori* before further work, with the prospect of co-authorship.

Tables

The first table offered will normally describe general characteristics of the subjects. The second and subsequent will give details of the results. Not all data points are required. Some points on tables:

The western eye moves from left to right, not top to bottom, so changes should go from L to R in a row.
Variables will be listed in column 1.

Ensure the values in the tables mirror the stats, e.g. don't use mean +/- SD if the stats were non-parametric.
Do not use too many significant irrelevant figures
Ensure there is a stand alone title
Do not over-use grid lines, i.e. don't put lines where they are not needed.
Ensure units of measurements are included
Always define ± (SE or SD)
Always indicate n
Always indicate significant changes
Check journal format

Figures and Illustrations

A different issue; and a different talk ?

Discussion

The discussion section should answer the reader's question "What do the findings mean?" and "How do they compare with other peoples results?".

Discussions tend to be too long (they should not be more than 1/3 the total length of introduction, materials, results and discussion).

This is the section most often regarded as being most difficult to write. The following format may help.

a) Summarise major findings; encapsulate this in two sentences without statistics, i.e., in plain English. In this section, do not over-repeat data given in the results section.

b) Compare results with previous work (this tend to be overdone, often in the guise of a literature review) and explain inconsistencies with the current and previous work. Do not examine every paper ever written, just the most pertinent to the present study (usually those in the introduction). Do not cite work that only supports the current findings (good reviewers will pounce on this).

c) Discuss problems and limitations with the methods in the current study, i.e. what the study failed to do (maybe in hindsight). Do this particularly if there is discrepancies in part b. Discuss group differences and their effects on the conclusions.

d) Discuss the clinical and scientific implications of the work

e) Suggest further work

f) Provide a conclusion

References

Format appropriately.
Don't use inappropriate text-book references; use those who performed the work.
List only relevant citations
An exhaustive citation list indicates insecurity and lack of familiarity with literature.

General

Know what you're saying and who you want to read it
Have introduction drawn up first and do not waiver from goals
Have M& M written beforehand or as the study is conducted

Have document checked periodically as you proceed
At the end, repeat the literature review to ensure nothing has been published since the study began.

It is most important that the paper is written in a way that allows its message to be fully understood by the target audience. However, the author's commitment to an intelligent lay readership should not be forgotten. To this end, it must not contain professional "slang", or jargon. This is often difficult given that it is the spoken language of the work place, e.g. "the animal was pre-medicated with....," or "a GGE mixture was dripped to effect", or "the observer was blinded" (which gets a prize for the daftest thing ever said).

Formatting

Check Guidelines for authors.
Every new section on a new page
Paginate
Tables come after references with their own legends (which must describe all)
Figures come separately, with their legends on a separate sheet

Bibliography

Hall GM, Smith R, Drummond GB, Norman J, Spence AR, & Lilleyman JS. In: Hall GM. How to write a paper. 2nd edition. London: BMJ, 1998