THE EFFECTS OF FOUR DIFFERENT INDUCTION TECHNIQUES ON ANAESTHETIC MAINTENANCE AND RECOVERY IN HORSES

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ABSTRACT

Anaesthetic recoveries have been the target of little research, and the information available on the effect of anaesthetic induction agents on recovery lacks detail and specificity. The aim of this study was to compare the anaesthetic recovery periods after 4 different induction procedures:
(1) acetylpromazine, glycerol guaiacolate, thiopentone; (2) xylazine, glycerol guaiacolate, thiopentone; (3) xylazine, ketamine; (4) acetylpromazine, glycerol guaiacolate, ketamine, which were followed by 1 hour of halothane in oxygen anaesthesia . Ten horses each received all 4 techniques with at least 1 week between successive anaesthetics. The 10 results for each induction technique were grouped, means determined, and statistical analysis performed on these group means.

Strikingly, the use of thiopentone, when compared to ketamine combinations, resulted in consistently poorer recoveries. The possibility that this may be due to the persistence of subanaesthetic barbiturate levels during the recovery period is discussed. In man, residual barbiturate levels have been shown to increase the awareness of pain, and it is possible that a similar effect may be present in horses, detrimentally affecting their anaesthetic recoveries. The role of ketamine in the consistently better recoveries is unclear. It is hypothesised that it may be due to residual ketamine levels in plasma exerting a stimulatory effect on areas of the central nervous system.

Interestingly, the use of acetylpromazine as a premedicant before both thiopentone and ketamine combinations, prolongs recovery and significantly increases 3 hour post anaesthetic creatinine phosphokinase (CPK) levels. No statistical relationship was found between longer recumbency times and elevated CPK levels, and it is postulated that the CPK rise may have been indirectly caused by acetylpromazine lowering the packed cell volume, and therefore muscle tissue oxygen supply.

The difference in pharmacokinetics of the individual drugs used apparently influenced the smoothness and the rate of recovery observed. It cannot be

assumed therefore, that horses experiencing longer or shorter anaesthetic periods would show similar recovery atttributes to those found in this study.

It was concluded that, after 1 hour of anaesthetic maintenance using halothane in oxygen mixtures, there is a better chance of horses having a coordinate recovery if ketamine combinations are used as induction agents; and a more rapid recovery if xylazine/ketamine is used to induce anaesthesia.

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CHAPTER 1

INTRODUCTION

In no animal is the challenge of a safe and successful anaesthetic as great as in the horse. It is the large size and frequently fractious temperament in this animal that render anaesthesia difficult. Its size dictates that anaesthetic procedures should be rapid, smooth and accomplished with a minimum of excitement and restraint to avoid injury to anaesthetic personnel or the horse. The temperament of the horse necessitates the use of sedatives to smooth induction and recovery from anaesthesia. Aside from these obvious physical difficulties, horses pose two major physiological problems during anaesthesia and recovery. One is the development of a large pulmonary shunt and a ventilation to perfusion mismatch whilst recumbent and anaesthetised, that may lead to arterial hypoxaemia even with high inspired oxygen concentrations (Hall, 1971; McDonnell *et al*, 1979; Nyman *et al*, 1988 and 1990). The other is the occurrence, in some horses, of a post anaesthetic myopathy. This myopathy has been linked to hypotension and poor muscle perfusion (Richey *et al*, 1990), and, as a consequence, may impede the horse's attempt to rise after anaesthesia. In extreme cases, euthanasia of the horse may be necessary on humane grounds (Trim and Mason, 1973; White, 1982). A great deal of research has been carried out to establish the causes and remedies of these problems.

To minimise anaesthetic complications in horses, fast and smooth anaesthetic recoveries are required. The rapidity of recoveries is important because firstly, it reduces the length of time in which horses have poor ventilation/perfusion ratios (Hall, 1971; Hedestierna *et al*, 1987) and secondly, because it reduces the potential for post anaesthetic myopathy to occur (Grandy *et al*, 1987). The smoothness of recovery is also important because well coordinated movements result in less self trauma and less disruption to surgical wounds. However, in no aspect of anaesthesia does the equine anaesthetist have less control than the recovery. Therefore equine anaesthetists have examined the effect of different anaesthetic induction and maintenance agents on the quality and duration of recovery. The search for

an ideal drug combination, that provides a smooth induction and quiet, short recovery, as well as minimally affecting the horse physiologically, continues. The aim of this experiment was to compare the recovery from anaesthesia induced by a variety of induction techniques, and maintained for one hour using halothane in oxygen mixtures.

The information available on anaesthetic recovery in horses, aside from the syndrome of post anaesthetic myopathy, is scant. A brief review of pertinent factors which may influence recovery from anaesthesia is presented under the following headings -

(i) EQUINE POST ANAESTHETIC COMPLICATIONS
  (a) Death
  (b) Fracture
  (c) Myopathy

(ii) ANAESTHETIC RECOVERY

(iii) ANAESTHETIC AGENTS USED IN THE HORSE

(i) EQUINE POST ANAESTHETIC COMPLICATIONS

(a) Death

Anaesthesia, and its associated complications, are a major cause of morbidity and mortality in equine surgery (Hall and Clarke, 1983). Death following anaesthesia and surgery in non-seriously ill patients has been estimated to be 1.5% of operations (Tevick, 1983). These deaths may occur on induction, during maintenance, or at recovery. Most are seemingly related to the pharmacological effects of the drugs used on the horse's cardiovascular, pulmonary or central nervous systems. However, some of these deaths may be the result of euthanasia of horses suffering from severe myopathy following surgery, or for self injuries that occur during excited and incoordinate recoveries.

Records at the Massey Veterinary Hospital, where the anaesthesia/surgery mortality in recent years has been between 1 and 1.5%, show that approximately one quarter of the associated deaths are due to sudden cardiac arrest. A further quarter occur in poor anaesthetic risk patients which have varying degrees of cardiopulmonary collapse on admission to surgery. The remaining half are euthanased following surgery for a variety of reasons including fracture and severe postanaesthetic myopathy.

(b) Fracture

The most common complication necessitating euthanasia following anaesthesia in horses is long bone fracture. These usually occur in the hindlimbs and involve the femur, tibia, or metatarsus. They appear to result from uncoordinated attempts by the horses to regain a standing position.

The incidence of fractures during recovery is highest following orthopaedic surgery. This may be for several reasons including:

(i) the presence of undetected fractures in the limb at the time of surgery
(ii) the longer than average time taken to perform some orthopaedic procedures leading to an increase in the possibility of post anaesthetic myopathy occurring
(iii) an increased difficulty in coordinating limb movements when casting or bandaging material have been used
(iv) the painful nature of some orthopaedic procedures leading to painful and stressful recoveries.

(c) Myopathy

Probably the most common complications occurring during, and immediately after, anaesthetic recovery in horses are lameness and muscle damage. These are alarming peculiarities of prolonged equine anaesthesia. In fact, according to some surgeons (B.E.Goulden, personal communication), surgical procedures of increasing complexity necessitating longer surgical times, are being hindered from development because of these troublesome difficulties. These problems, and their association with prolonged anaesthesia, have been

recognised by veterinary surgeons since the turn of the century (White, 1982), and have been loosely classified under the heading post anaesthetic myopathy.

The lameness following anaesthesia may be neurologic or muscular in origin. The former is almost invariably associated with radial nerve damage and is rare (Trim and Mason, 1973). The lameness due to muscular damage may involve a variety of muscles in all, or one, limb. Most commonly the muscles contacting the table or floor surface are the ones that demonstrate some form of inflammation and muscle dysfunction (Trim and Mason, 1973; Klein, 1978; Grandy *et al*, 1987). On clinical inspection, the affected muscles feel hard on palpation and may have a superficial plaque-like swelling. When the triceps muscles are involved, the affected limb has a characteristic dropped elbow but extensor function is still present so weight may be taken on the leg. Hindlimb extensor muscle damage results in an inability to extend the digit and knuckling of the fetlock. Horses may also show rigidity prior to standing, generalised muscle weakness, muscle fasciculations on standing, and pass brown discoloured urine (myoglobinuria). Systemic signs of pain such as sweating, treading, increased respiratory and heart rates, or violent behaviour may be seen (Klein, 1978; Dodman *et al*, 1988).

The cause of this myopathy appears to be multifactorial. Duration of recumbency and hypotension are the two factors consistently implicated in its occurrence (Grandy *et al*, 1987; Richey *et al*, 1990). A decrease in muscle perfusion with ensuing local hypoxia, energy starvation, and other metabolic alterations are thought to occur (Richey *et al*, 1990). Serum biochemical analysis reveals that muscle enzymes CPK and GOT increase significantly following anaesthesia in horses that show clinical signs of this anomaly (Trim and Mason, 1973).

(ii) ANAESTHETIC RECOVERY

Anaesthetic recoveries have been monitored and recorded since the first use of barbiturates in the 1950s. Henderson and Brooksby (1950), recorded a 20-30 minute recovery period in horses after an anaesthetic induction using 3 grams of thiopentone sodium. They found it necessary to maintain some form

of restraint on the horse for twenty minutes during early recovery to control movement and that there was still "undesirable struggling" in the attempt to attain a standing position. The use of promazine as a premedicant by Jones et al (1960), increased the duration of recovery after an anaesthetic dose of thiopentone, and although recoveries were no longer violent, some were still visually disturbing. Since Jones' work in 1960 the use of premedicants to smooth induction of, and recovery from, anaesthesia, has become accepted practice. Littlejohn (1970), presented a study on the behaviour of six horses recovering from thiopentone, halothane/oxygen anaesthesia of undefined duration. He described the anaesthetic recovery in three stages: deep sleep in lateral recumbency (27 minutes); locomotor activity in lateral recumbency (23 minutes); sternal recumbency (15 minutes). Five of the six horses rose from sternal recumbency with one effort, while one of the horses required three efforts. This simple study highlighted the paucity of information available at the time on horses recovering from anaesthesia, and the apparent degree of individual variation.

Since the 1970s, with the introduction of a number of new anaesthetic drugs, research interest has largely focused on the biochemical and physiological changes occurring with anaesthetic drug use. Limited reference has been made to the quality of recovery. It was the introduction of the use of ketamine hydrochloride and the emergence of new inhalant anaesthetic gases in the late 1970s that alerted the veterinary profession to the concept that equine anaesthetic recoveries did not have to be variable, uncoordinated and at times dangerous. Ellis et al (1977), and Muir et al (1977), investigated the use of xylazine/ketamine combinations in horses as a short term surgical anaesthetic combination and mentioned that recoveries were rapid and smooth. Hall and Taylor (1981), studied the use of xylazine/ketamine when followed by halothane/oxygen maintenance of anaesthesia for an average of ninety minutes. The recoveries were again classified as smooth and fast, but not quite as good as those following xylazine/ketamine alone.

Apart from the work of Littlejohn in 1970, the only other study to specifically examine anaesthetic recovery was that of Auer et al (1978). Theirs was a comparative analysis of the effect of isoflurane, methoxyflurane, enflurane

and halothane on anaesthetic recoveries in horses. They found significant differences in recoveries, both in speed and smoothness. The best recoveries followed isoflurane use. The recovery from enflurane was more rapid, but was associated with periods of excitement. The differences in recoveries were linked to ventilatory clearance of the gases and, it was speculated that residual pharmacological effects of enflurane were responsible for the poor quality of recoveries following its use.

Other information available in the literature is not detailed and comparisons between recovery data collected by different researchers is not possible. The most common parameter used to evaluate recovery has been time from drug injection, or cessation of gas administration, to attainment of a standing position (Henderson and Brooksby, 1950; Jones *et al*, 1960; Heath and Gabel, 1967; McCashin and Gabel, 1975; Wintzer *et al*, 1975; Muir *et al*, 1977; Muir *et al*, 1978; Muir *et al*, 1979b; Brouwer *et al*, 198O). Others extended the concept of time measurement to include : time to first movement, time to swallow, time to attain sternal recumbency (Jennings, 1966; Heath and Gabel, 1970; Schatzmann, 1974; Schatzmann *et al*, 1978; Auer *et al*, 1978: Hall and Taylor, 1981; Taylor and Hall, 1985). The quality of recovery has been more difficult to assess and, until the creation of a grading system by Taylor and Hall (1985), comments on recovery quality were sparse, vague and often misleading. This grading system is numerical, 0-4 representing recoveries that are poor to excellent. The criteria included in assessing recoveries includes : number of attempts to stand, degree of incoordination, presence or absence of muscle fasciculations on standing,and degree of ataxia once walking. This grading system has been used many times by Taylor (Taylor and Hall, 1985; Taylor, 1986, 1989 and 1990).

(iii) ANAESTHETIC AGENTS USED IN THE HORSE

Obviously no drug when used in the horse is ideal in every respect. To overcome this deficiency, combinations of drugs are commonly used. This allows the amount of each drug component of the combination to be lowered, thus minimising side effects. The search for an ideal drug or drug combination continues.

The intravenous drugs which have gained most popularity in the horse worldwide have included, either singly or in combination: succinylcholine, chloral hydrate, thiamylal, thiopentone and glycerol guaiacolate. Often these drugs are preceded by tranquilisers or sedatives to produce smoother induction and recovery from anaesthesia, to intensify analgesia, and to decrease the amount of induction drug needed. The sedatives which are commonly used are promazine, acetylpromazine, xylazine, detomidine and proprionylpromazine/methadone combinations.

In New Zealand, the most commonly used premedicant and induction agents are acetylpromazine, xylazine, glycerol guaiacolate, thiopentone and ketamine. These drugs are used in the present study. In order to understand their possible effects on anaesthetic recovery some knowledge of their pharmacology and pharmacokinetics is required. For this reason, a brief synopsis of their relevant actions is presented below.

Acetylpromazine.

Acetylpromazine is a phenothiazine derivative, its chemical name being 2-acetyl-10-(3-dimethylaminopropyl) phenothiazine. It is a yellow, odourless crystalline powder.

The principal activity of phenothiazines is the blockade of dopamine, a catecholamine neurotransmitter, principally found in the basal ganglia. The result is sedation and a reduction in spontaneous motor activity (Booth and McDonald, 1988). At higher doses, extrapyramidal symptoms (rigidity, muscle tremor) may be seen (Booth and McDonald, 1988). In the horse, the recommended preanaesthetic dose ranges from 0.02-0.05 mg/kg (Booth and McDonald, 1988). Sedation is apparent within minutes of an intravenous dose, effective clinical sedation is seen for 2 hours and a tranquillising effect may persist as long as 24 hours (McKenzie and Snow, 1977; Booth and McDonald, 1988).

Phenothiazines have an adrenergic blocking activity. This effect on the vascular system coupled with a direct action on myocardial and vascular smooth muscle results, in the horse, in lowered systemic arterial pressure,

peripheral vasodilation and a compensatory tachycardia (Kerr *et al*, 1972a; Muir *et al*, 1979a; Parry *et al*, 1982). The drop in arterial blood pressure is greater after intravenous doses and is dose dependent. The systolic blood pressure after 0.025 mg/kg remains significantly below controls for more than 6 hours after intramuscular injection (Parry *et al*, 1982). Acetylpromazine has another important effect on the cardiovascular system. It causes a significant drop in packed cell volume. This fall in the percentage of circulating red blood cells is dose dependent (Ballard *et al*, 1982).

Acetylpromazine decreases respiratory rate, but a compensatory increase in tidal volume leaves respiratory minute volume unaltered. There is no significant effect on PaO_2, $PaCO_2$ and arterial pH (Popovic *et al*, 1972; Muir and Hamlin, 1975; Muir *et al*, 1979a).

The extensive distribution of acetylpromazine results in a very slow elimination,the half life being 185 minutes (Ballard *et al*, 1982). It is metabolised in the liver and excreted in the urine (Booth and McDonald, 1988).

The major limitations of phenothiazines are their uncertainty of action,the limited degree of sedation that is not enhanced by increasing the dose, and the interval between injection and peak effect (up to 15 minutes after intravenous injection and 1 hour after intramuscular injection) (Carey and Sandford, 1963; Mackenzie and Snow, 1977). Side effects include: occasional excitement, the ability to be aroused easily when challenged, and priapism (Pearson and Weaver, 1978; Taylor, 1985).

Xylazine

Chemically, xylazine is 2 (2,6,-dimethylphenylamino)-4H-5,6,dihydro-1,3,-thiazine hydrochloride. It is related to clonidine, a drug used to control arterial hypertension in humans. Pharmacologically xylazine is classified as a sedative, analgesic and muscle relaxant (Booth and McDonald, 1988). Its sedation is caused by stimulation of α_2 adrenergic receptors. It also has potent α_1 adrenergic effects and so elicits both peripheral and central adrenergic activity (Booth and MacDonald, 1988).

Both the degree and duration of sedation are dose related. Maximal sedation is seen at 1.1 mg/kg iv and 3mg/kg im, and lasts approximately 40 minutes (Clarke and Hall, 1969; Tronicke and Vocke, 1970; Hoffman, 1974; Taylor, 1985). Although sedation is marked, stimulation of a sedated horse can result in instant awareness and protective responses (Muir *et al*, 1979a).

The adrenergic pressor reactions result in an initial rise then a prolonged fall in arterial blood pressure. A decrease in cardiac contractility drops cardiac output by up to 35% (Garner *et al*, 1971a; Kilde *et al*, 1975; Muir *et al*, 1977; Muir *et al*, 1979a; Brouwer *et al*, 1980). Bradycardia and 2nd degree atrioventricular heart block occur and are controlled by prior administration of atropine. The significance of the 2nd degree heart block is not clear (Hoffman, 1974) as it can occur in up to 16% of normal horses and in these instances is not considered pathologic because it disappears spontaneously (Smetzer *et al*, 1969).
Effects on respiratory rate and arterial blood gas tensions are not significant (Garner *et al*, 1971b; Kerr *et al*, 1972b; McCashin and Gabel, 1975; Muir *et al*, 1979a; Rietmeyer *et al*, 1986). Effective visceral analgesia may last up to 90 minutes after high doses (Booth and McDonald, 1988).

Xylazine undergoes rapid metabolism with a short systemic half life of 50 minutes (Garcia-Villar *et al*, 1981).

Disadvantages of xylazine include ataxia at high doses, the retention of the ability to respond to stimuli, and the associated profound bradycardia (Booth and McDonald, 1988).

Glycerol guaiacolate.
Chemically glycerol guaiacolate is 3-(0-methoxyphenoxy)-1,2-propanediol. It is a centrally acting skeletal muscle relaxant that selectively blocks nerve impulse transmission at the internuncial level of the spinal cord, brainstem and subcortical areas of the brain (Davis and Wolff, 1970). It produces relaxation of the skeletal muscles but the diaphragm continues to function normally. It also acts as a sedative and has some analgesic effects (Gycha, 1953; Schebitz and Tronicke, 1964; Gertsen and Tillosten, 1968; Schatzmann,

1974). Glycerol guaiacolate potentiates the depressant effects of other sedatives and anaesthetic drugs (Mostert, 1963; Roberts, 1968; Funk, 1970).

A dose of 160 mg/kg produces recumbency with minimal effects on cardiovascular and respiratory function. Only a slight decrease in systemic arterial pressure is noted (Frtisch, 1965; Tavernor, 1970; Jackson and Lundvall, 1970; Davis and Wolff;1970).

The major disadvantages of its use is its tendency to cause haemolysis restricting concentrations less than 15% and necessitating the use of large volumes (Davis and Wolff, 1970; Schatzmann, 1974; Grandy and McDonnell, 1980). It also has the potential to cause thrombophlebitis (Dickson *et al*, 1990).

Glycerol guaiacolate is metabolised in the liver and removed through urinary excretion. Its elimination half life shows some variation with sex, males having a significantly longer plasma half life than females (Davis and Wolff, 1970).

Thiopentone sodium

Thiopentone is a sulphur containing derivative of barbituric acid. Barbiturates work by depressing cellular activity throughout the central nervous system, how they exactly do so is unclear but it appears to involve inhibition of the release of a variety of neurotransmitters (Booth and MacDonald, 1988). CNS depression produced by barbiturates is dose dependent and varies from mild sedation to anaesthesia (Booth and McDonald, 1988).

Rapid intravenous injection of thiopentone affects the vasomotor centre causing a transitory fall in arterial pressure, an increase in heart rate, and a fall in cardiac output(Booth and MacDonald, 1988). The combination of thiopentone with premedicants and halothane results in more severe and sustained cardiovascular depression (Taylor, 1989 and 1990).

Thiopentone slows respiratory rate and frequently causes periods of irregular respiration or apnoea. The result is an elevation of $PaCO_2$ and a concomitant drop in arterial pH (Booth and MacDonald, 1988; Taylor, 1990).

Disadvantages of its use include its respiratory depression, the increased incidence of cardiac arrhythmias when used with halothane, and its thrombogenicity (Booth and MacDonald, 1988).

Thiopentone, as all barbiturates, undergoes rapid redistribution from plasma to adipose tissues following intravenous injection. This redistribution is responsible for the short duration of clinical effect of the injected dose. Thiopentone is only slowly metabolised by the liver and its metabolites are excreted in the urine (Price *et al*, 1957; Brandon and Baggot, 1981; Booth and MacDonald, 1988).

Ketamine

Ketamine is a phencyclidine and chemically is designated as 2-(o-chlorophenyl)-2-(methylamino)-cyclohexanone hydrochloride. A specific braincell receptor for ketamine has not been identified but it is thought to bind with a receptor common with other phencyclidines (Booth and MacDonald, 1988). Ketamine is classified as a dissociative anaesthetic that produces a cataleptic state of light surgical anaesthesia and analgesia (Booth and MacDonald, 1988).

Ketamine causes an increase in cardiac output, mean aortic pressure, pulmonary arterial pressure, central venous pressure and heart rate (Wilson *et al*, 1965; Folts *et al*, 1975; Chen and Ensor, 1979; Kilde, 1975). However it also increases myocardial work and oxygen consumption (Folts *et al*, 1975; Diaz *et al*, 1976).

Ventilatory responses are not depressed and laryngeal and pharyngeal reflexes remain intact (Booth and MacDonald, 1988).

Disadvantages in the horse include excitement and incoordination when used as the sole anaesthetic agent; abrupt recoveries, and nystagmus during anaesthesia (Fuentes *et al*, 1973; Taylor and Hall, 1985).

Ketamine is rapidly distributed to all body tissues and is biotransformed in the liver. The elimination half life in the horse is 42 minutes (Kaka *et al*, 1979).

Halothane

Chemically halothane is a multihalogenated ethane, and is a clear, colourless liquid.

Halothane is capable of depressing all functions of the CNS at all levels or gradations until coma or death is produced (Booth and MacDonald, 1988). Induction of anaesthesia is rapid as are recoveries (Booth and MacDonald, 1988).

Cardiopulmonary depression in the horse is proportional to the level or depth of anaesthesia (Steffey and Howland, 1978). Halothane decreases cardiac output, stroke volume, left ventricular work, systemic arterial blood pressure and central venous pressure (Fourcade *et al*, 1972; Steffey *et al*, 1974). There is an increase in $PaCO_2$ and a concomitant drop in pH (Eger *et al*, 1970; Steffey and Howland, 1978, 1979 and 1980). The effects of other anaesthetic drugs, such as barbiturates, are additive to the cardiopulmonary depressant effects of halothane (Booth and MacDonald, 1988).

Disadvantages of halothane include its cardiac arrhythmogenic potential and the rare occurrence of malignant hyperthermia (Manley *et al*, 1983; Bednarski *et al*, 1985; Booth and MacDonald, 1988).

Recovery from halothane is primarily due to clearance by ventilation. Some metabolism of halothane does occur in the liver,but its effect on recovery times is minimal (Stoeling and Eger, 1969; Booth and MacDonald, 1988).

CHAPTER 2

MATERIALS AND METHODS

Ten thoroughbred horses were used in this study; 9 were females and 1 a gelded male. They ranged in age between 2 and 10 years and varied in weight between 364-500 kilograms (Table 1). Each horse was clinically examined prior to inclusion in the study. Blood samples were taken from each and assessed for the following: haemoglobin concentration, packed cell volume, red blood cell, white blood cell and differential white cell counts, total protein, fibrinogen, blood urea nitrogen, serum glutamic oxalacetic transaminase (GOT), creatinine phosphokinase (CPK), albumin, and α, β and γ globulins.

Table 1 Age and weight range of horses

HORSE	AGE (YRS)	WEIGHT RANGE OVER STUDY (KG)
1	4	475-483
2	3	424-430
3	2	364-374
4	5	452-470
5	4	445-454
6	10	494-500
7	5	450-461
8	4	460-464
9	8	450-470
10	4	472-476

The horses were kept on pasture during the experiment, except for a period of 2 to 4 hours prior to being anaesthetised. During this time they were confined to a concrete yard and starved but had free access to water.

1. ANAESTHESIA

(i) Induction Groups

Four different anaesthetic procedures were administered to each horse. The anaesthetic technique differed essentially in the induction agents used, and the different induction techniques were labelled 1 to 4

accordingly. At least one week was left between successive anaesthetics and the anaesthetic agents were chosen randomly.

The anaesthetic groups were as follows:

Group 1 Acetyl promazine premedication
Glycerol guaiacolate and thiopentone induction
Halothane/oxygen maintenance

Group 2 Xylazine premedication
Glycerol guaiacolate and thiopentone induction
Halothane/oxygen maintenance

Group 3 Xylazine premedication
Ketamine induction
Halothane/oxygen maintenance

Group 4 Acetyl promazine premedication
Glycerol guaiacolate and ketamine induction
Halothane /oxygen maintenance

(ii) Induction Technique

After premedication, and prior to induction, all horses had an 8.3 cm 14 gauge over-the-needle type teflon catheter (Angiocath, Desert Medical Inc, Utah, USA) placed, after local anaesthesia of the skin, in the right jugular vein midway between the mandible and the thoracic inlet. All drugs used for induction of anaesthesia were administered via the catheter. Immediately prior to anaesthetic induction, venous blood was withdrawn through the catheter for serum analysis of CPK and GOT. All anaesthetic inductions were performed in a padded room. In groups 1, 2 and 4 the horses were manhandled during induction of anaesthesia by directing their fall against a wall. Group 3 horses were left to lie down by themselves after drug administration.

All horses were positioned in right lateral recumbency for the duration of the experiment.

(a) *Group 1*

Acetylpromazine (ACP, Techvet Lab Ltd, NZ) 0.06 mg/kg was given intramuscularly in the left side of the neck. Twenty minutes later, anaesthesia was induced as follows: approximately 50 mg/kg of 10% glycerol guaiacolate (Giafen, Parnell Lab NZ Ltd) was given through the catheter using a flutter valve and gravity flow till relaxation of the horse's hindquarters was seen. This was followed by an intravenous bolus of thiopentone sodium (Thiovet, Techvet Lab, NZ) at 5.6 mg/kg. Once the horse was recumbent a further 50mg/kg of glycerol guaiacolate was given prior to endotracheal intubation.

(b) *Group 2*

Xylazine (Rompun, Bayer NZ Ltd) at a dose of 0.2 mg/kg was given intravenously into the left jugular vein. Anaesthesia was induced as follows: approximately 50 mg/kg glycerol guaiacolate was administered intravenously using a flutter valve and gravity flow until relaxation of the horses's hindquarters was seen. This was followed by an intravenous bolus of thiopentone sodium (5.6 mg/kg).Once the horse was recumbent,a further 50 mg/kg glycerol guaiacolate was given prior to endotracheal intubation.

(c) *Group 3*

Xylazine (1.1 mg/kg) was given intravenously and maximum sedative effect was judged as the time when the head drooped and the horse showed mild ataxia. Once this level of sedation had been achieved 2.2 mg/kg ketamine (Ketavet 100, Delta Vet Lab Pty, NSW, Australia) was administered intravenously. When the horse was recumbent an endotracheal tube was inserted.

(d) *Group 4*

Acetyl promazine premedication was given (0.06 mg/kg) intramuscularly in the left side of the neck. Twenty minutes later anaesthesia was induced as follows: approximately 50 mg/kg glycerol guaiacolate was administered intravenously using a flutter valve and gravity flow till relaxation of the horse's hindquarters was seen. At this time an intravenous bolus of ketamine (1.7 mg/kg) was administered. Once the horse was recumbent a further 50 mg/kg glycerol guaiacolate was given intravenously prior to endotracheal intubation.

(iii) Maintenance Technique

All horses were intubated with a rubber 25mm diameter cuffed endotracheal tube and connected to a large animal vapouriser-out-of-circuit circle anaesthetic system with a precision vapouriser (Turner Circle System, Technident Industries, Petone NZ Ltd). The anaesthetic system had been preloaded with oxygen together with 4% halothane for groups 1, 2 and 4, and 6% halothane for group 3. Initial oxygen flow rates were 6 litres per minute for 10 minutes and then a maintenance flow rate of 4 l/min. A balanced electrolyte solution (Lactated Ringers, Travenol Lab, USA) was given through the intravenous catheter (2 l/hr) during the maintenance period of anaesthesia.

Anaesthesia was maintained at a light surgical level using halothane and oxygen mixtures. The level of light surgical anaesthesia was assessed clinically using the following parameters: a medial to ventral eyeball position, slight palpebral reflex, constricted pupil, moist eyeball with small degree of lacrimation, regular thoracic respiration, mild anal constriction on pinching (Guedel,1937; Campbell and Lawson,1958). An anaesthetic recording chart was filled out at five minute intervals (Appendix 1).

(iv) Measurements during Induction and Maintenance

(a) *Induction Time*

This was defined as the time, in seconds, taken from the administration of the last induction drug to the horse assuming a recumbent position.

(b) *Induction Grade*

The depth of anaesthesia at induction was assessed and graded as follows:

1. Medium surgical - characterised by a ventral to lateral eyeball position, mild palpebral reflex and a constricting pupil, thoracico-abdominal respiration, very slight anal constriction on pinching with forceps.
2. Light surgical - characterised by a medial to ventral eyeball position, a slight palpebral reflex, a constricting pupil, a moist eyeball, regular thoracic respiration and mild anal constriction on pinching.
3. Non surgical - characterised by a central to medial eyeball position, a strong palpebral reflex, a dilated pupil and vigorous nystagmus. Limb movements may or may not be present.

(c) *Heart Rate*

Heart rate per minute was recorded at 5 minute intervals by counting pulses of the mandibular artery over a 30 second period.

(d) *Respiratory rate*

Respirations per minute were counted at 5 minute intervals by watching anaesthetic bag movement over a 30 second period.

(e) *Blood pressure*

A 22 gauge steel butterfly catheter (Abbott, Ireland) was placed aseptically in the left facial artery or left lateral metatarsal artery, whichever proved the most accessible. The catheter was

connected by saline filled tubing to a pressure transducer (Gould Inc, California, USA) and pressure measurements in millimetres of mercury (mmHg) were recorded on a monitor (Kontron Neonate Monitor, Roche NZ Ltd). The point of the shoulder was used as an indicator of approximate left atrial position to provide a baseline point for blood pressure readings. Systolic, diastolic and mean blood pressure were recorded in mmHg at 10, 30 and 60 minutes from the start of halothane administration.

(f) *Blood gases.*

Arterial blood samples were taken anaerobically from the indwelling arterial catheter at 10, 30 and 60 minutes. The samples were read immediately using a blood-gas machine (ABL300, Radiometer, Copenhagen) making adjustments for rectal temperature. Arterial partial pressures of oxygen (PaO_2), carbon dioxide ($PaCO_2$) and pH were recorded in mmHg.

2. RECOVERY

After one hour, all horses were disconnected from the anaesthetic machine. The blood pressure was monitored and catheters removed. The horses were then rolled into left lateral recumbency and oxygen was supplied at a flow rate of 15 litres per minute via the endotracheal tube till it was removed when the horse swallowed. The horse was left to recover in a quiet, dark padded box and the recovery was observed. Two people observed all recoveries so that continuity of assessment could be maintained. Once the horse was standing and could move without ataxia, it was removed from the box and taken back to pasture.

(i) Measurements made on Recovery

(a) *Time to extubation in minutes.*

Voluntary swallowing movements made by the horse, determined the time the endotracheal tube was removed

(b) *Time to lifting head in minutes.*

(c) *Time to sternal recumbency in minutes.*

(d) *Time to standing in minutes.*

(e) *Number of attempts to stand.*

An attempt to stand was defined as a positive effort to lift the head and simultaneously placing weight on one or both forelimbs.

All times were expressed in minutes from the time of disconnection from the anaesthetic machine.

(f) *Recovery Grade.*

A grading system was devised, by modifying the one used by Taylor and Hall (1985).

0 Very poor	more than 3 attempts to stand rolling, excitement collapse of more than 2 limbs on standing
1 Poor	more than 2 attempts to stand considerable ataxia partial collapse of limbs on weight bearing
2 Fair	1 or 2 attempts to stand mild ataxia muscle fasciculations
3 Good	standing on first attempt muscle tremors knuckling on 1 leg
4 Excellent	standing on first attempt no muscle tremors or ataxia on standing

3. MUSCLE ENZYMES

A blood sample was taken prior to induction of anaesthesia for CPK and GOT measurement. A 3 hour post recovery sample was taken for CPK analysis to coincide with peak CPK levels that develop post trauma (Cardinet *et al*, 1967; Gerber, 1968) and a 24 hour post

recovery sample was taken for GOT analysis to coincide with its peak blood levels (Cardinet *et al*, 1967; Gerber, 1968).

CPK and GOT levels in serum were determined using MAS reagents (Worthington Analyser II, Diagnostic Systems Inc, USA).

STATISTICAL ANALYSIS

All data recorded were evaluated by applying an analysis of variance to detect any differences between group means. Any variance detected with a variance-ratio (F) test underwent analysis for least significant difference (LSD) comparison of means.

Regression testing with graphical plots was done on the following:

(a) Recovery grade and -
induction grade; mean arterial blood pressures at 10, 30, 60 minutes; time to extubation; time to lifting head; time to sternal recumbency; time to standing.

(b) CPK and -
mean arterial blood pressures at 10, 30, 60 minutes; time to extubation; time to lifting head; time to sternal recumbency; time to standing; number of attempts to stand; recovery grade.

(c) GOT and -
mean arterial blood pressures at 10, 30, 60 minutes; time to extubation; time to lifting head; time to sternal recumbency; time to standing; number of attempts to stand; recovery grade.

The analyses were made using the statistical package MINITAB (Minitab Inc, State College, PA 16801, USA).

To determine whether serial anaesthetic procedures on each horse affected the parameters measured, scattergraphs, containing the results from each of the 4 anaesthetic procedures used on each horse, were constructed. The pattern of scatter of the results was carefully assessed visually to detect if there was any grouping of the results related to the anaesthetic timing.

CHAPTER 3

RESULTS

All data collected was tabulated (Appendix 2). An example of the detailed tables of the analysis of variance with the F and LSD tests are presented in Appendix 3, and regression analysis with scatter graphs in Appendix 4. A summary of pertinent statistical results is presented below. The standard error calculations were determined using error mean square calculations. Thus, an acceptable level of difference between means is represented by the standard error, which, if exceeded, indicates a significant difference.

ANALYSIS OF VARIANCE

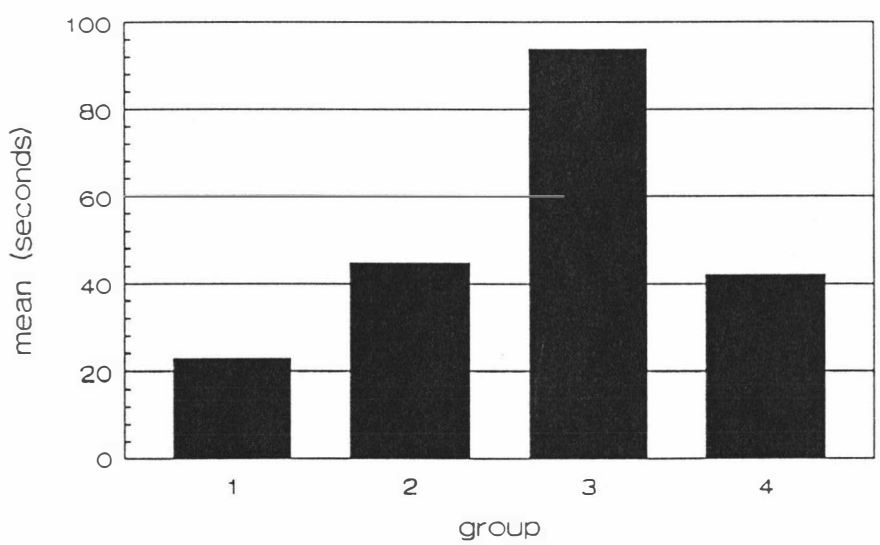
(1) Anaesthesia

(a) *Induction Time*

The horses in Group 3 had a significantly longer mean induction time than those of groups 1, 2 and 4.

GROUP	MEAN INDUCTION TIMES (SEC)
1	22.9
2	44.7
3	93.8
4	42.0
SE*	7.12

*standard error

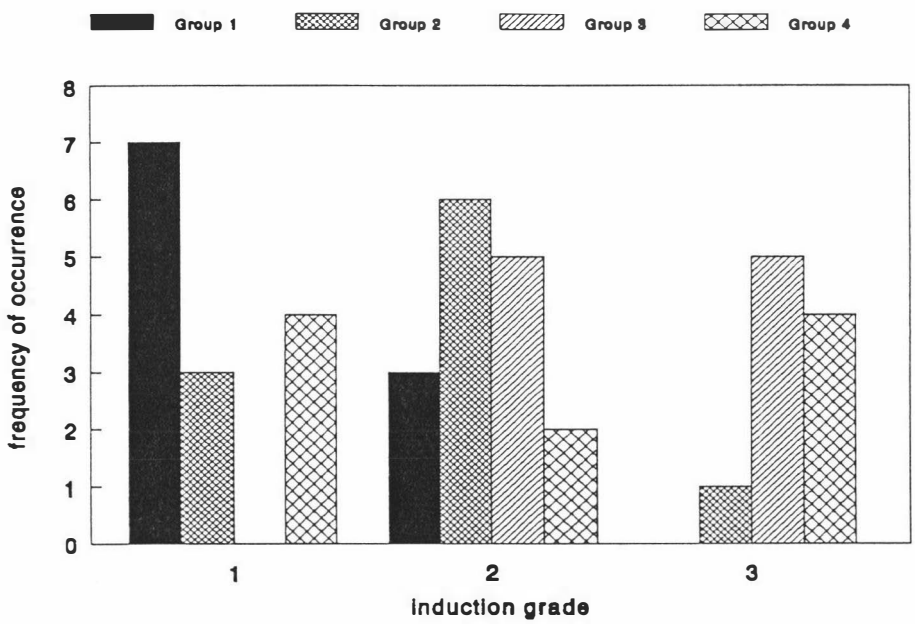


(b) *Induction Grade*

The level of anaesthesia immediately after induction was significantly lighter in group 3 compared to groups 1 and 2. It was also significantly deeper in group 1 compared to groups 3 and 4.

GROUP	MEAN INDUCTION GRADE
1	1.3
2	1.8
3	2.5
4	2.0
SE*	0.20

*standard error



1. medium surgical
2. light surgical
3. non-surgical

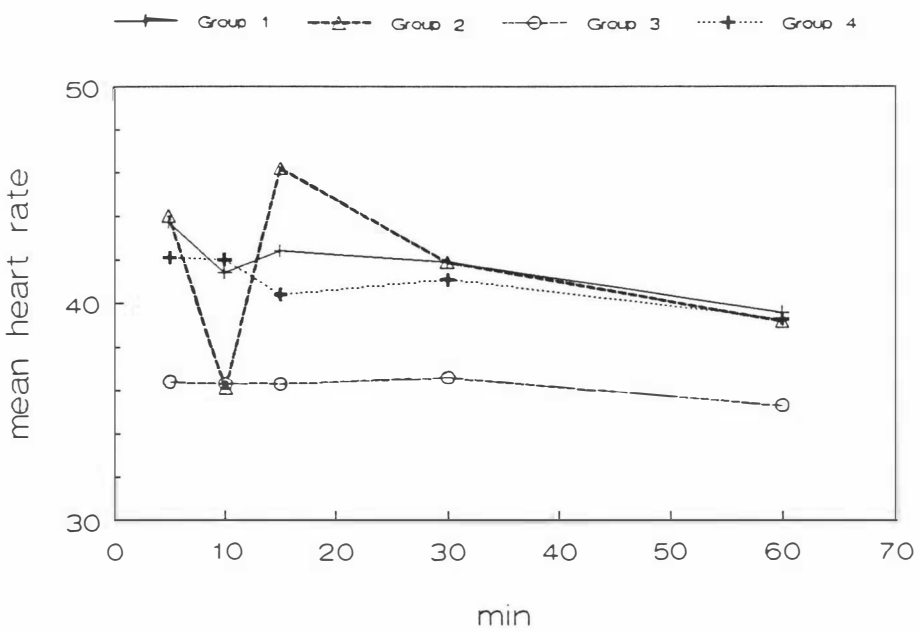
One horse from group 2 had a short excitement phase on induction.

(c) *Heart Rate*

The mean heart rate for group 3 horses was significantly lower than groups 1, 2 and 4 at 5, 10, 15 and 60 minutes.

GROUP	MEAN HEART RATE (MIN)				
	5	10	15	30	60
1	42.7	41.0	42.4	43.5	39.6
2	44.0	40.5	40.2	39.9	39.2
3	36.4	36.3	36.3	37.4	35.3
4	42.0	42.0	40.4	40.1	38.4
SE*	3.16	1.26	1.15	1.62	0.97

*standard error

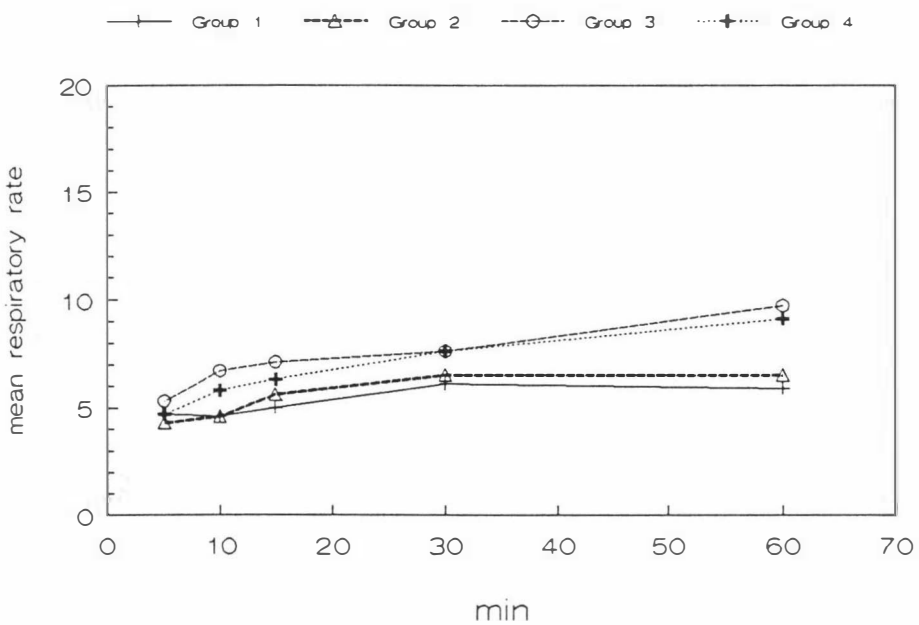


(d) *Respiratory Rate*

Mean respiratory rates increased from 5 to 60 minutes. At 10 minutes groups 1 and 2 respiratory rates were significantly lower than group 3. At 60 minutes groups 1 and 2 had significantly lower respiratory rates than groups 3 and 4.

GROUP	MEAN RESPIRATORY RATE (MIN)				
	5	10	15	30	60
1	4.7	4.6	5.0	6.1	5.9
2	4.3	4.6	5.6	6.5	6.5
3	5.3	6.7	7.1	7.6	9.7
4	4.7	5.8	6.3	7.6	9.1
SE*	0.68	0.48	0.54	0.57	0.67

*standard error



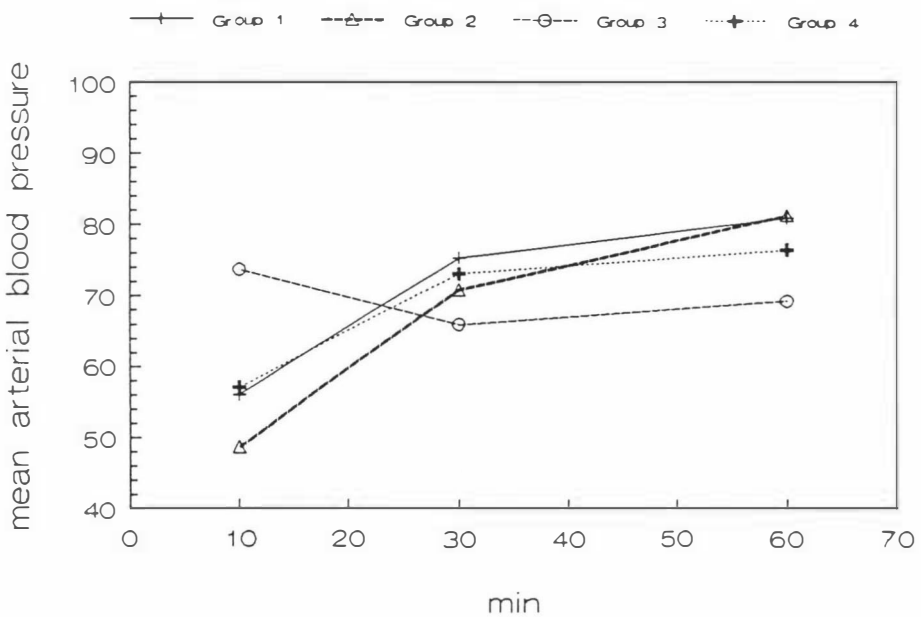
(e) *Blood Pressure*

After ten minutes of anaesthesia, horses from Group 3 had significantly higher mean blood pressure than those of Groups 1,2 and 4.

No significant differences were found in mean arterial blood pressure at 30 and 60 minutes.

GROUP	MEAN ARTERIAL BLOOD PRESSURE (MMHG)		
	10	30	60
1	55.9	75.3	80.8
2	48.6	70.8	81.2
3	73.7	65.9	69.2
4	57.0	73.1	76.4
SE*	3.16	4.39	4.05

*standard error



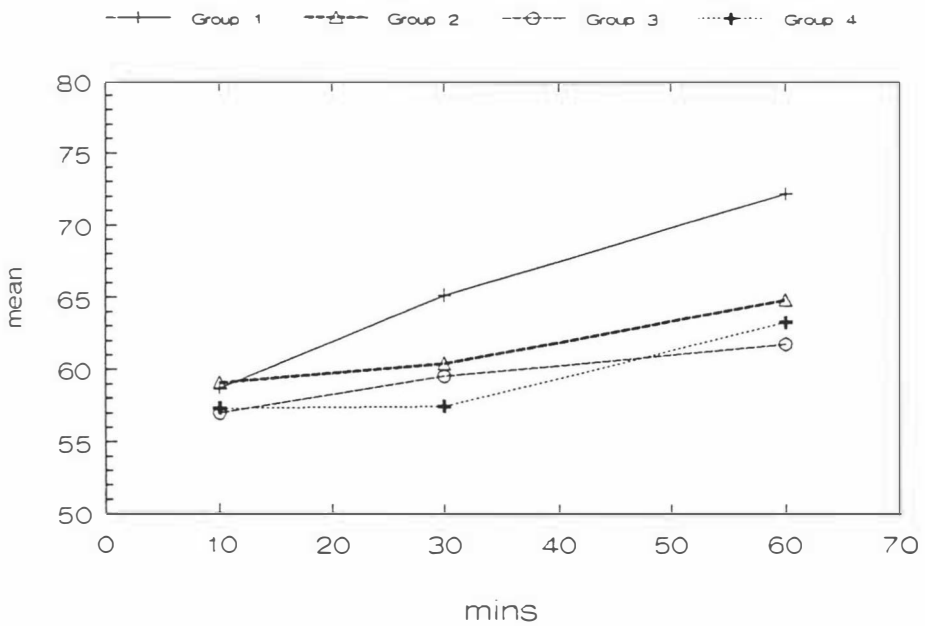
(f) *Blood gases*

(i) Arterial partial pressure of carbon dioxide ($PaCO_2$)

After 60 minutes, horses from Group 1 had significantly higher mean $PaCO_2$ levels than those of Groups 1, 2 and 4.

GROUP	MEAN $PACO_2$ (MMHG)		
	10	30	60
1	58.75	65.20	72.20
2	59.09	60.48	64.88
3	57.01	59.61	61.81
4	57.30	57.53	63.20
SE*	1.89	2.15	2.05

*standard error

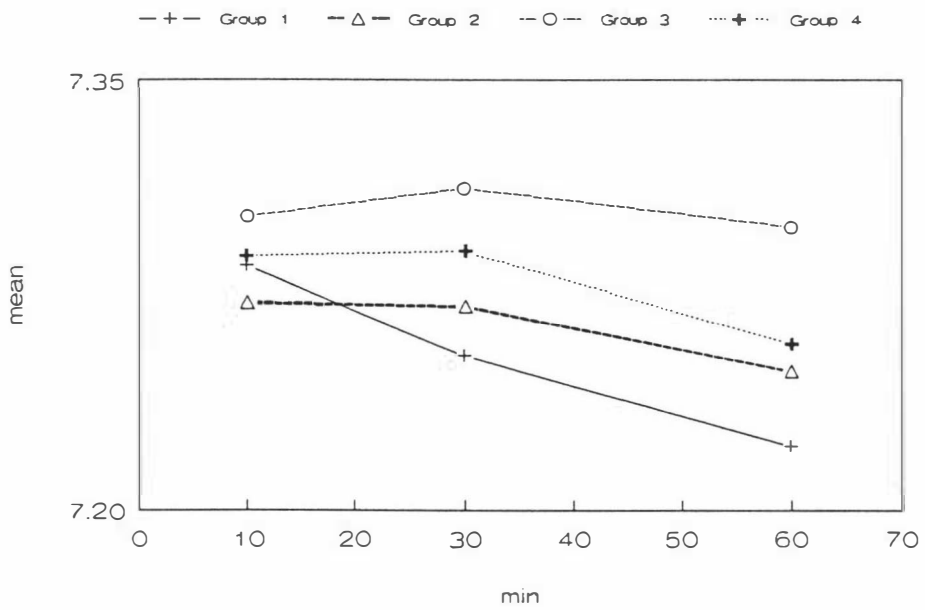


(ii) pH

Horses from groups 1 and 2 had a significantly lower mean pH than those of groups 3 and 4 at 30 minutes. After 60 minutes horses from group 3 had a significantly higher mean pH than the horses from other groups.

GROUP	MEAN pH		
	10	30	60
1	7.2820	7.2539	7.2223
2	7.2742	7.2712	7.2484
3	7.3027	7.3121	7.2985
4	7.2885	7.2903	7.2580
SE*	0.0100	0.0314	0.0110

*standard error

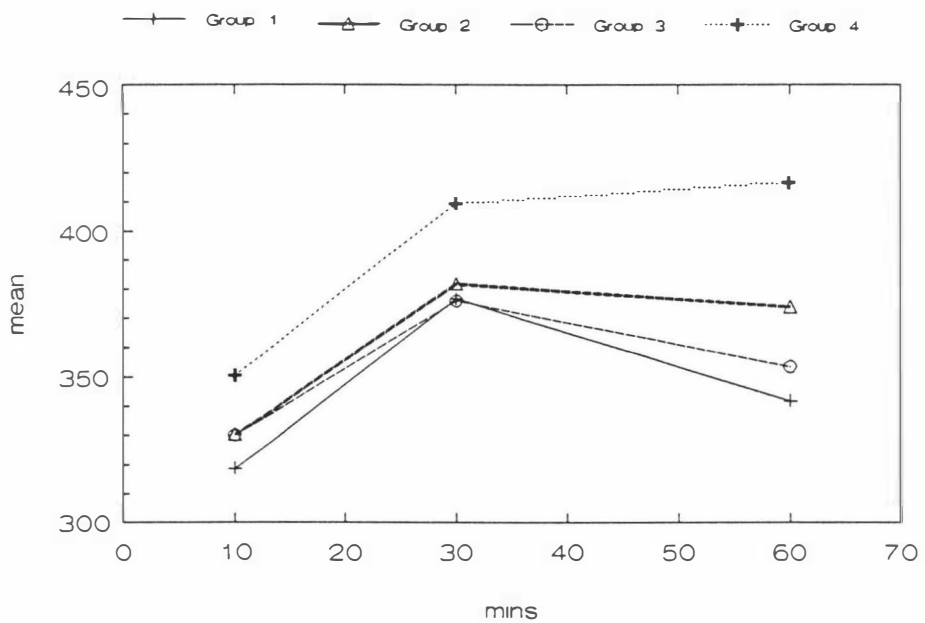


(iii) Arterial partial pressure of oxygen (PaO_2)

No significant differences between groups were found at 10,30 or 60 minutes.

GROUP	MEAN PaO_2		
	10	30	60
1	318.73	376.69	341.81
2	330.39	381.80	373.92
3	330.13	375.96	353.59
4	350.55	409.60	416.92
SE*	24.657	19.669	22.066

*standard error



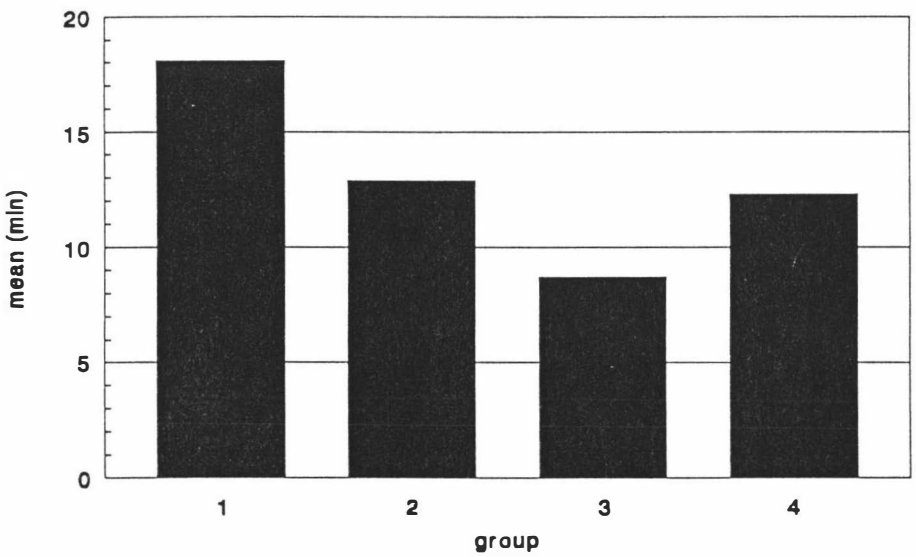
(2) RECOVERY

(a) *Extubation Time*

Horses from group 1 took a significantly longer mean extubation time than those of groups 2, 3 and 4.

GROUP	MEAN EXTUBATION TIME
1	18.075
2	12.865
3	8.700
4	12.275
SE*	1.854

*standard error

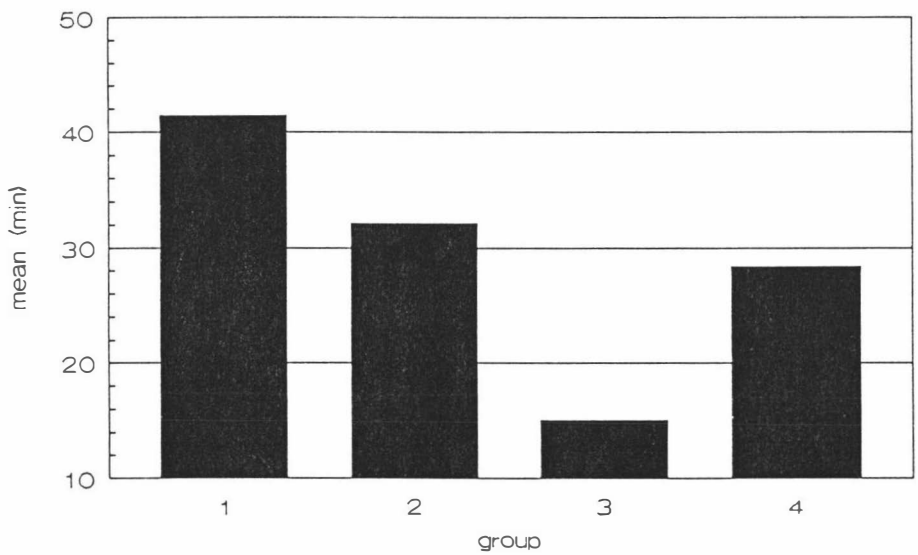


(b) *Time to Lifting Head*

Horses from group 3 had the significantly shorter mean time span from disconnection of anaesthesia to lifting the head.

GROUP	MEAN TIME TO LIFT HEAD
1	41.410
2	32.105
3	15.015
4	28.350
SE*	3.687

* standard error

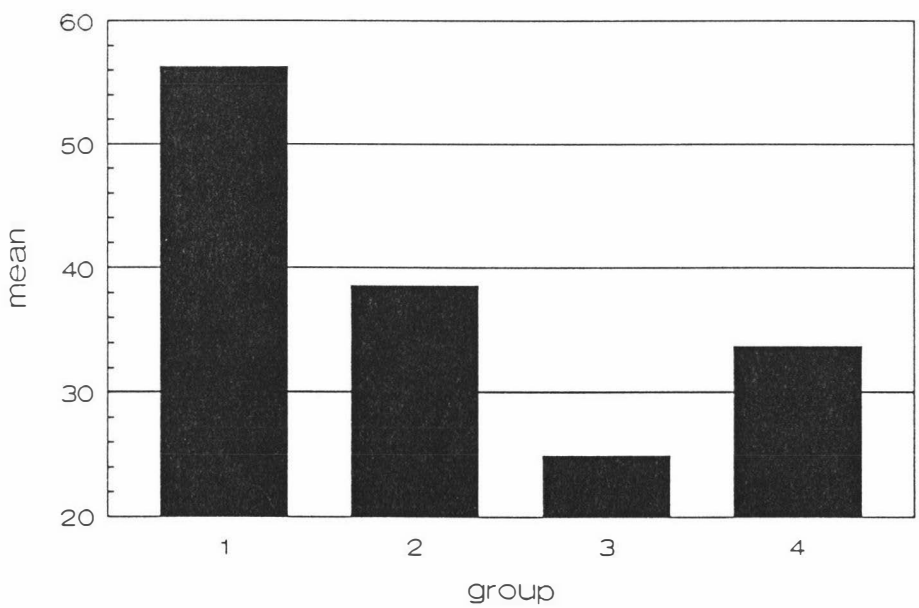


(c) *Time to Sternal Recumbency*

Horses from group 1 showed a significantly longer mean time to attain sternal recumbency than those horses in the other groups.

GROUP	MEAN TIME TO STERNAL RECUMBANCY
1	56.250
2	38.585
3	24.885
4	33.725
SE*	4.969

*standard error

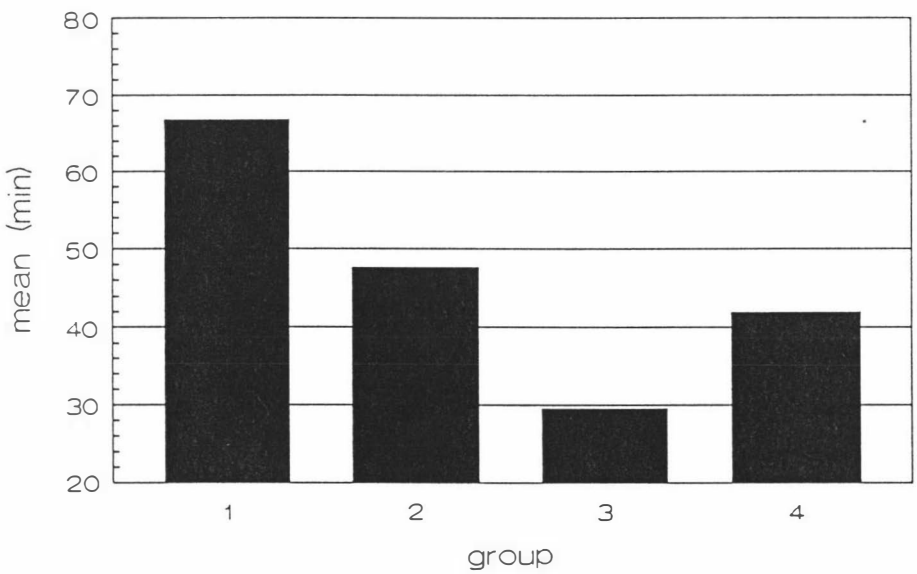


(d) *Time to Standing*

Horses from group 1 took a significantly longer mean time to attain a standing position than horses from the other groups. Horses from group 3 took a significantly shorter mean time to stand than horses from the other groups.

GROUP	MEAN TIME TO STANDING (MIN)
1	66.725
2	47.600
3	29.560
4	41.835
SE*	4.132

*standard error

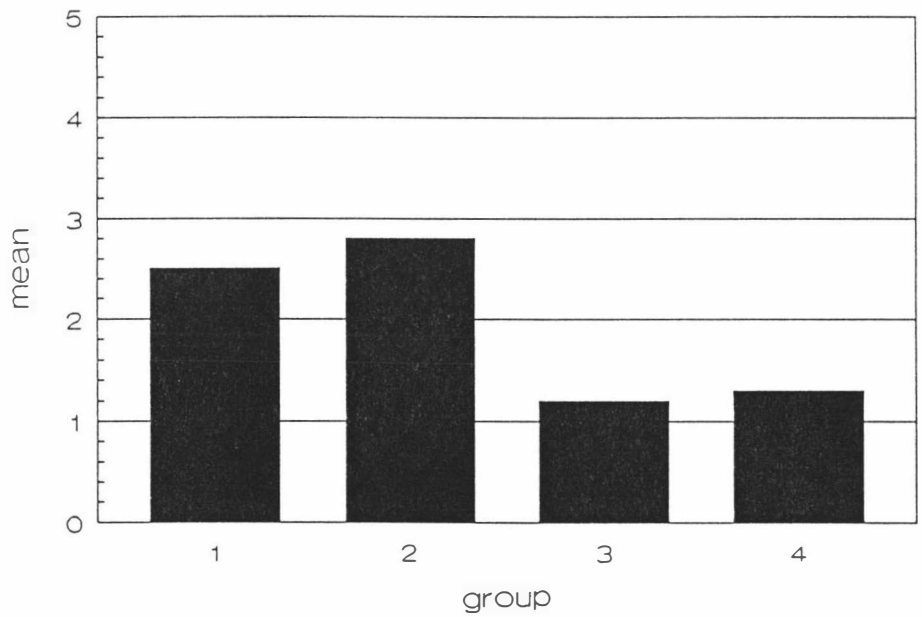


(e) *Number of Attempts to Stand*

Horses from groups 1 and 2 took a significantly greater mean number of attempts to stand than those from groups 3 and 4.

GROUP	MEAN NUMBER OF ATTEMPTS TO STAND (MIN)
1	2.5
2	2.8
3	1.2
4	1.3
SE*	0.27

*standard error

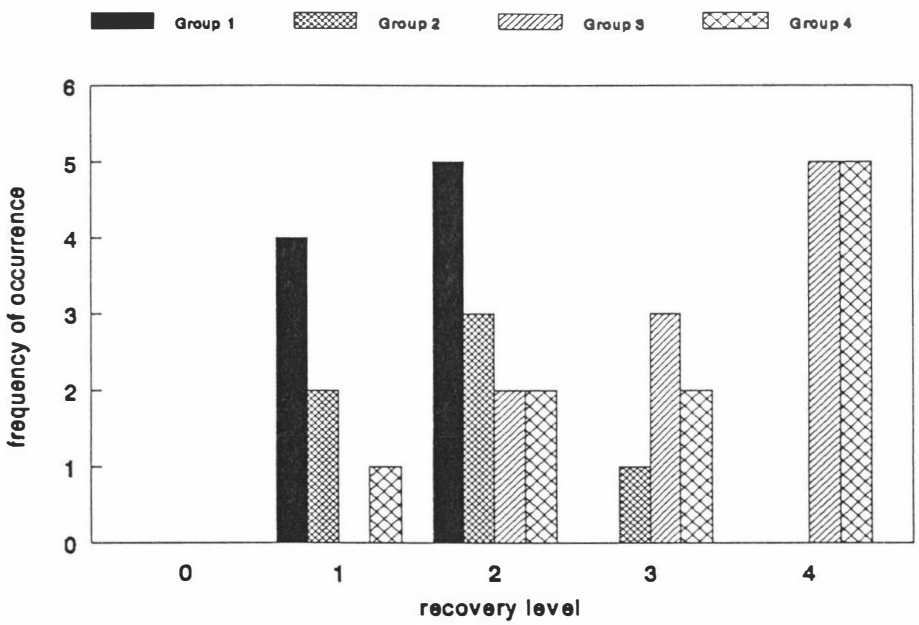


(f) *Recovery Grade*

The mean recovery grades of horses from groups 1 and 2 were significantly lower than those of groups 3 and 4, indicating poorer recoveries.

GROUP	MEAN RECOVERY GRADE
1	1.4
2	1.4
3	3.3
4	3.1
SE*	0.32

*standard error



0 = poor
1 = fair
2 = medium
3 = good
4 = excellent

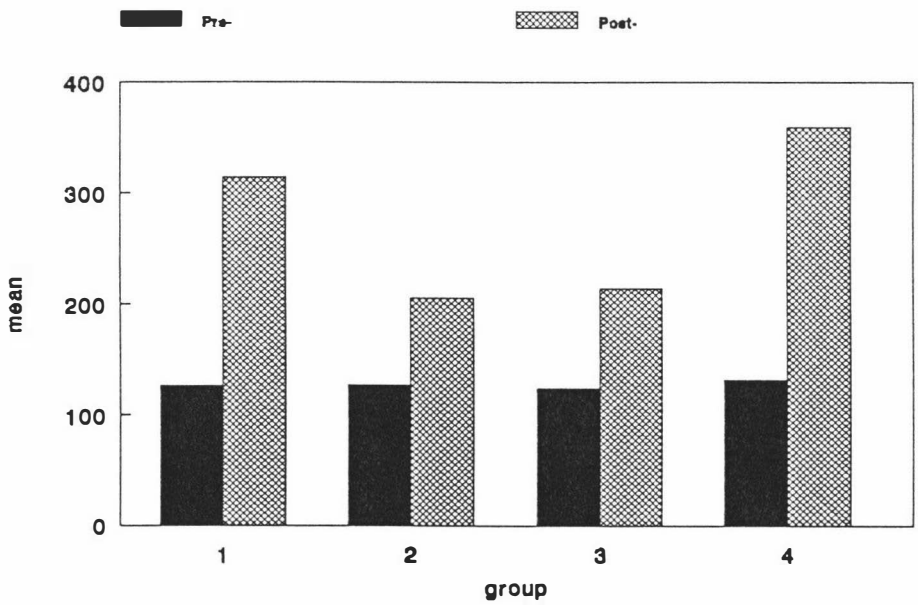
(3) MUSCLE ENZYMES

Horses from groups 1 and 4 showed significantly higher mean CPK levels at three hours post anaesthesia than those of groups 2 and 3. No significant difference between group means of GOT 24 hour post anaesthesia was demonstrated

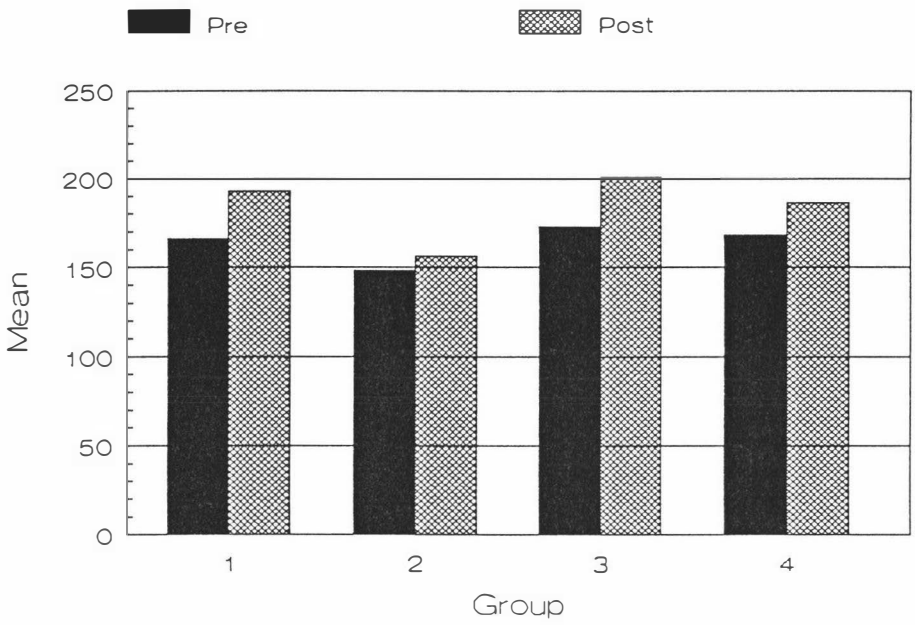
GROUP	CPK	GOT
1	188.1	26.6
2	81.2	13.7
3	90.4	28.9
4	228.0	19.1
SE*	23.14	5.08

*standard error

Pre and post anaesthesia serum CPK measurements



Pre- and post anaesthesia serum GOT measurements



REGRESSION ANALYSIS AND SCATTERGRAPHS

Regression analysis and scattergraphs showed no significant correlations between any of the parameters measured.

No temporal effect was found indicating that the last anaesthetic procedure given to each horse was not significantly different from the first one they received.

CHAPTER 4

DISCUSSION

Jennings (1966), described the requirements for good equine anaesthesia as: freedom from pain; freedom from fear in the animal; easy, rapid administration of anaesthetic; no struggling on induction, maintenance or recovery and a wide margin of drug safety. To these the following have been added more recently - adequate analgesia; excellent muscle relaxation; and minimal cardiopulmonary depression (Butera *et al*, 1978). It is unlikely that a single drug could meet all these requirements, so, over the years, the search for a perfect anaesthetic drug combination has continued.

The present study showed that under comparable conditions of anaesthetic maintenance, the induction drugs used had a considerable influence on the type and speed of recovery experienced by the horses. When xylazine and ketamine were used as the induction drug combination, the duration of recovery was short. In addition, the horses regained a standing position easily and had only slight ataxia when attempting to walk. In contrast, when thiopentone and glycerol guaiacolate were used in combination for induction, the recoveries were longer. Moreover the horses had considerable difficulty attaining a standing position, and were considerably ataxic when attempting to move.

The reasons for these differences will be discussed under the following headings -

1. ANAESTHESIA
   - (i) Induction
   - (ii) Maintenance

2. RECOVERY
   - (i) Recovery Quality
   - (ii) Recovery Length

3. MUSCLE ENZYMES

4. CRITICAL EVALUATION OF EXPERIMENT
   (i) Experimental design and limitations

   (ii) Clinical assessment of induction techniques

1. ANAESTHESIA

(i) Induction

Effective sedative premedication smooths the induction and maintenance of general anaesthesia, and ensures a quiet, uneventful recovery. A drug that is suitable for this purpose need not be particularly potent in its action but must persist to affect the recovery period.

Acetylpromazine and xylazine were chosen as premedicants in this study because they are the two most commonly used sedative agents in New Zealand at the present time and their actions on the cardiovascular and respiratory systems are well documented. Xylazine produced a heavier sedative effect than acetylpromazine at the doses used. This, however, had little effect on the initial depth of anaesthesia achieved. In fact, even after heavy xylazine sedation, the level of anaesthesia obtained after ketamine administration was lighter than that obtained with glycerol guaiacolate/ketamine (group 4) and glycerol guaiacolate/thiopentone inductions (groups 1 and 2). Why this occurred is not understood. As a result, following the induction of anaesthesia with xylazine/ketamine, higher doses of halothane were usually required to obtain a level of light surgical anaesthesia comparable to that experienced with the other groups.

One exception did occur. The excitement seen on induction of a horse receiving glycerol guaiacolate and thiopentone as induction agents, was presumably due to an inadequate barbiturate dose. High initial concentrations of halothane (8%) were required for ten minutes to appreciably deepen the anaesthetic plane. This type of unsatisfactory induction is known to occur with barbiturates and may be seen more often if

there is inadequate preanaesthetic sedation (Brouwer, 1985a) or if the horse is stimulated by loud noises prior to the administration of a barbiturate bolus (Booth and McDonald, 1988).

The extremely long induction time (over 90 seconds) associated with xylazine/ketamine combinations in the horse has been reported by previous authors (Ellis *et al*, 1977; Muir *et al*, 1977; Brouwer *et al*, 1980; Hall and Taylor, 1981; Taylor and Hall, 1985; Brouwer, 1985a and b). Why this drug combination takes twice as long to produce recumbency in the horse than any of the other combinations used, is not known. Nor have long induction times with intravenously administered ketamine been recorded in other species. When xylazine is used in high doses with other induction agents such as thiopentone, methohexitone or thiamylal in horses, induction times are not prolonged (Brouwer *et al*, 1980). Nor, as shown in the present study, are induction times increased when ketamine is used in combination with drugs other than xylazine (Muir *et al*, 1978; Muir *et al* 1979b). This significant increase in induction time which occurs when both of these drugs are used together appears to be unique to their combination.

The difference in ketamine doses used in the different groups in this study was intentional and followed recommendations by previous researchers (Muir *et al*, 1977; Muir *et al*, 1978; Muir *et al*, 1979b; Hall and Taylor, 1981). Why the doses differ is not known. It does not seem likely to be due to differing sedative effects prior to ketamine use. Xylazine premedication clinically provided heavier sedation than acetylpromazine and glycerol guaiacloate, therefore it would have seemed logical to use smaller doses of ketamine following xylazine administration. Experimental work needs to be done to determine if the dose of ketamine can be lowered to 1.7 mg/kg, or further, with xylazine combinations. If this were possible, it would offset the disadvantage of the high cost of ketamine and may decrease the central nervous excitatory effects associated with its use (Fuentes, 1978).

(ii) Maintenance

The initial maintenance procedures used in this experiment were designed to speed the equilibration of delivered and inspired anaesthetic gases. Two

factors oppose this rapid equilibration. One is the considerable amount of air present in the anaesthetic circuit. This large volume of air dilutes the concentration of inspired anaesthetic gases initially delivered. The second is that nitrogen is exhaled in the first few moments of a gaseous anaesthetic; this further dilutes inspired gases (Steffey and Howland, 1977). To minimise these problems, the anaesthetic machine was filled with a 4% halothane and oxygen mixture and oxygen flow rates of 6 l/min were used for the first 10 minutes of gaseous anaesthesia.

As previously mentioned,the xylazine/ketamine induction combination produced a lighter initial plane of anaesthesia than the other drug combinations. Furthermore, the duration of anaesthesia provided by this combination of drugs lasts only 20-25 minutes and is accompanied by an abrupt recovery (Hall and Taylor, 1981). To ensure that adequate surgical anaesthesia levels were attained quickly, and to effect an uneventful transition from induction to maintenance agent, the concentration of halothane prior to administration had to be increased to 6%, and kept at this level for at least 10 minutes following xylazine/ketamine use.

The principal reason for monitoring the heart rate during anaesthesia is to detect life threatening alterations in rate (either tachycardia or bradycardia) and rhythm. None of these were noted in the present study. A significantly lower mean heart rate however, was observed in horses which had a xylazine/ketamine induction. Previous authors (Steffey *et al*, 1985), had noted that when xylazine was given to already anaesthetised horses, the heart rate dropped for half an hour. In contrast, the mean heart rate of horses which had been induced with xylazine/ketamine in this study, remained significantly lower for the entire hour long anaesthetic period. This is presumably related to the longer duration of effect of the high dose of xylazine used (Clarke and Hall, 1969). Another feature of heart rate recordings in the present study was that no significant changes to these rates occurred, in any of the groups, throughout the hour long experiment. This observation confirms the experience of previous researchers (Eger *et al*, 1970; Steffey and Howland, 1978; Muir *et al*, 1979b; Steffey *et al*, 1987; Steffey *et al*, 1990a) that heart

rates do not change significantly over time,in man and horses, given halothane in oxygen.

Heart rate had very little significance as an indicator of cardiac function (Ganong, 1989), as it did not appear to influence blood pressure measurements. Moreover, heart rate is not an indicator of anaesthetic depth (Steffey and Howland, 1978), so the differing heart rates between groups in this study cannot be attributed to differences in anaesthetic level.

The low respiratory rates recorded after inductions using ultra short acting barbiturates are due to their respiratory depressant effects (Booth and McDonald, 1988) and are actually somewhat lower than the first two recordings indicate, as some horses developed apnoea and were ventilated manually 2-3 times a minute for up to 10 minutes. This apnoea, noted in some of the horses induced with glycerol guaiacolate and thiopentone combinations, according to information present in the literature (Jones *et al*, 1960; Tavernor and Lees, 1970; Muir *et al*, 1979b; Brouwer, 1985 a and b) is shorter in duration and lower in frequency than the apnoea incurred by the use of barbiturates alone. However, Schatzmann (1974), noted that as many as 30% of glycerol guaiacolate/thiopentone inductions result in apnoea. In this study the percentage was slightly lower, being 20%. The extent of respiratory depression in the first 10-15 minutes after thiobarbiturate use reflects the duration of clinical effect of these drugs. The persistence of statistically lower respiratory rates after thiopentone when compared to ketamine combinations, suggests that there is either a continuing depressant effect of residual barbiturate levels on the respiratory system, or, conversely, that there is an extended stimulatory effect of ketamine. It is not clear from this experiment which of these two drugs continues to affect respiratory rate, but none of the other drugs used appear to have been involved in its control.

The gradual increase in respiratory rate over time in all experimental groups under halothane anaesthesia has been noted before (Steffey *et al*, 1990a). A similar observation has been made in human anaesthesia, but the increase does not become significant till after three hours of constant halothane anaesthesia (Fourcade *et al*, 1972). The cause of this gradual increase is

unknown, but the present experiment has shown it does not result in improved $PaCO_2$ nor does it significantly affect PaO_2 levels (Appendix 1, Tables 6 and 8).

Systemic arterial pressure measurements permit the anaesthetist to monitor the adequacy of peripheral perfusion. Arterial pressure is the product of cardiac output and peripheral vascular resistance. Consequently factors that affect either of these two variables will also affect arterial pressure (Ganong, 1989). Differences of mean systemic arterial pressure were seen only at the 10 minute reading and correspond with the vasomotor, vasopressor and cardiac influence of induction drugs. Thereafter the readings are not statistically different, probably because halothane was the main determinant of arterial pressure after this time. The higher arterial pressure seen with xylazine/ketamine at 10 minutes is likely to be a result of the stimulatory effect of ketamine on the cardiovascular system (Folts *et al*, 1975; Booth and McDonald, 1988). Why the combination of ketamine with acetylpromazine and glycerol guaiacolate did not also result in a similar higher arterial pressure at this time is not clear. Acetylpromazine has a stronger hypotensive effect than xylazine due to it effect on total peripheral resistance (Muir *et al*, 1979a; Steffey *et al*, 1985), and this may have caused a greater drop in blood pressure, even in the presence of ketamine. The hypotension may also be the result of the lower dose of ketamine used (1.7 mg/kg) producing less of a cardiostimulatory effect, or of a combination of these two factors.

The low mean arterial pressures at 10 minutes with ultrashort acting barbiturate drug combinations are probably a result of the cardiovascular depressant effects of thiopentone and halothane combined. The drop in arterial pressure is less when thiopentone is used on its own than when halothane is administered once the horse is recumbent (Heath and Gabel, 1970; Tavernor and Lees, 1970; Taylor, 1989 and 1990). Anaesthetic induction for the anaesthetist is always a juggle between attaining adequate depth with induction drugs but not having the animal too deep on induction as precipitous falls in blood pressure can cause cardiac arrhythmias and death at this time. The recovery from the cardiac insult of injectable drugs is dependent on metabolism and redistribution of the drugs, whereas ventilation

rapidly changes anaesthetic gas level and therefore its drug effect (Eger, 1964). As a consequence, halothane is often used to supplement anaesthetic induction depth to attain the correct level for surgery. Caution must be used though as the results from this study indicate how precipitously the arterial blood pressure can fall.

Recordings of arterial blood pressure measurements under anaesthesia vary between authors. The levels obtained in this study correspond well with those obtained by researchers anaesthetizing experimental horses (Brouwer, 1985; Steffey *et al*, 1977a and b; Steffey and Howland, 1978; Steffey and Howland, 1980; Hodgson *et al*, 1986; Steffey *et al*, 1987; Steffey *et al*, 1990a). However, some authors (Heath and Gabel, 1970; McCashin and Gabel, 1975; Brouwer *et al*, 1980) have recorded higher arterial pressures in experimental horses than was found in this study. This variation could be related to a lighter plane of anaesthesia in these horses, as the depressant effects of halothane are dose dependent (Steffey and Howland, 1978). Additionally, with clinical anaesthetics, slightly higher arterial blood pressures are documented (Muir *et al*, 1979b; Hall and Taylor, 1981; Taylor and Hall, 1985). This could reflect the effect of surgical stimulation on arterial pressure (Eger *et al*, 1970; Steffey and Howland, 1978).

The tendency, as found in this study, for arterial blood pressure to slowly increase under halothane anaesthesia is well documented in the literature,both in man and horses (Eger *et al*, 1970; Bahlman *et al*, 1972; Dunlop *et al*, 1987; Steffey *et al*, 1900a). In the horse this "recovery" of cardiac function and circulation appears to be related to an increase in cardiac output. It begins thirty minutes after the administration of halothane commences, but is not statistically significant until one and a half hours of gaseous anaesthesia (Dunlop *et al*, 1987; Steffey *et al*, 1990a). Why there is an improvement of both ventilatory and circulatory variables during prolonged halothane anaesthesia is not known. Carbon dioxide has known sympathetic stimulatory effects (Price, 1960), but in this study the slow rise in arterial carbon dioxide tension did not correlate statistically with the mean arterial blood pressure increase. However, this does not necessarily mean that carbon dioxide tensions were not to some degree involved in the improvement

in cardiovascular function. Current theories on the cause of this involve the development of metabolic acidosis, hypoxaemia, or increased effect of epinephrine. According to Fourcade *et al* (1972), the most plausible explanation may be related to a change in chemical or hormonal levels of substances that stimulate the cardiorespiratory areas such as norepinephrine, or some halothane metabolites.

The use of intravenous fluids during surgery and anaesthesia is routine at Massey Veterinary Clinic and was also applied in the study to simulate clinical conditions as closely as possible. The value of a flow rate of 2 l/hr in maintaining or elevating blood pressure is questionable in the horse considering its large blood volume. However, the advantage of using fluids, even at this low rate, is that a patent venous catheter is always present so that drugs or fluids in emergency situations may be given rapidly.

As found in this study, and recorded elsewhere, arterial carbon dioxide levels tend to increase with time under halothane anaesthesia when the patient is spontaneously breathing (Fourcade *et al*, 1972; Steffey *et al*, 1990a). The hypoventilation that causes this $PaCO_2$ increase appears to be due to central respiratory depression and reduction in tidal volumes, minute volumes and respiratory deadspace (Hall, 1971). It can be reversed with mechanical ventilation (Hodgson *et al*, 1986). The higher $PaCO_2$ tension at 60 minutes in horses induced with glycerol guaiacolate and thiopentone is probably a reflection of the persistent hypoventilatory effect of the acetylpromazine premedication, which may last up to eight hours (Parry *et al*, 1982). The inability of a horse to respond to hypercapnia after acetylpromazine premedication (Muir and Hamlin, 1975), may also contribute to the higher carbon dioxide tensions. Why the horses induced with glycerol guaiacolate/ketamine combinations after acetylpromazine premedication failed to show a similar significant increase in $PaCO_2$ remains unclear. It may be that the central nervous system stimulatory effects of ketamine negate , to some extent, the respiratory centre depression of acetylpromazine.

When combined with water, carbon dioxide acts as a weak acid. Therefore the changes in pH reflect to some extent the levels of $PaCO_2$. However other

factors such as the rise in serum lactate seen during anaesthesia with halothane (Taylor, 1989), which was not measured in this study, may influence pH. The cause of this rise in lactate appears to be multifactorial with increased muscle glycogenolysis, reduced muscle perfusion and hypoxaemia all being incriminated (Hall *et al*, 1978; Weaver *et al*, 1984; Taylor, 1989). Whether or not these changes in blood lactate are enough to alter pH significantly has not been determined.

The PaO_2 level during anaesthesia apparently depends on the size of the animal and its position. In general, ponies have a higher PaO_2 than horses and this is attributed to the difference in size between the two (Hall, 1971). Additionally, the PaO_2 gradually decreases as the horse is moved from the lateral to dorsal position (Hall, 1971; Nyman *et al*, 1988). The small alveolar-arterial oxygen tension difference (PAO_2 -PaO_2) present in conscious standing horses increases markedly when they are anaesthetised and become recumbent. This increase in PAO_2-PaO_2 reflects the development of a large pulmonary shunt and some ventilation perfusion mismatch during anaesthesia (Hall, 1971; Nyman *et al*, 1990). Although none of the horses in this study displayed arterial hypoxaemia (PaO_2 < 60 mmHg), their PaO_2 levels were less than expected. There was no persistent rise or fall in PaO_2 over the 60 minute monitoring period in this study, a finding also noted by others (Steffey *et al*, 1990a).

There appears to be an inability to clinically predict the magnitude of the respiratory changes that occur during general anaesthesia and recumbency. Thus even the healthiest of horses which demonstrate very little respiratory embarrassment during anaesthesia may show large irregularities between predicted and actual PaO_2 levels on investigation of blood gas sample results. This indicates the very real value of monitoring blood gas values at regular intervals during anaesthesia.

2. RECOVERY

Achievement of a problem free recovery is a primary goal of equine anaesthetists as self injury and damage to the surgical site by the horse during

the period of anaesthetic recovery are a constant hazard. Many major operations in horses take a considerable time to perform. To mimic this situation as closely as possible, recoveries were analysed after one hour of light surgical anaesthesia.

A number of environmental, physiological and pharmacological factors are known to influence recovery from anaesthesia in the horse. The intention of this study was to focus on the effects on recovery of various sedative and anaesthetic induction agents. To achieve this, the same environment, the same horses and a comparable anaesthetic maintenance technique was used throughout the experiment.

Gross differences in the manner and duration of recovery were found between the four groups of horses studied. These differences were seemingly due to the pharmacological effects and pharmacokinetics of the sedative and induction drugs used.

(i) Recovery Quality

Because a halothane in oxygen mixture was used to maintain anaesthesia in all horses in this study, it was assumed that the effect it had on recovery was similar in each group. The available information indicates that the effect of halothane on the length and smoothness of recovery is negligible (Vasko, 1962; Steffey and Howland, 1978; Steffey *et al* 1990a). Recovery lengths are usually less than one hour and only mild ataxia is observed once the horse is standing and walking (Vasko, 1962; Steffey and Howland, 1978; Steffey *et al*, 1990a)

Recovery from inhalation anaesthesia can be defined as the rate at which alveolar anaesthetic concentration decreases with time. The two major variables affecting alveolar anaesthetic concentration are solubility and ventilation (Stoeling and Eger, 1969). The more soluble an anaesthetic gas, the slower the alveolar clearance and so the slower the recovery. Regardless of solubility, the greatest decrease in alveolar concentration, and therefore the fastest recovery, is always seen with the greatest alveolar ventilation

(Stoeling and Eger, 1969). No recovery measurements of cardiopulmonary variables were made in this study and so it is not known if blood flow to, and ventilation within, pulmonary parenchyma were significantly different from one group to another. The data recorded during anaesthetic maintenance indicated that halothane was the principal determinant of cardiovascular function after one hour of halothane anaesthesia. This would imply that the perfusion of the lungs during recovery in this study, may not be considered a major variable between groups. In contrast, ventilatory capacity differed slightly between groups with group 1 horses showing higher $PaCO_2$ levels at 60 minutes indicative of a degree of hypoventilation. It may be that this greater degree of hypoventilation impaired, to some extent, the exhalation of halothane and therefore slowed recovery. This may help explain why the recoveries of group 1 horses were significantly longer than those of the other groups. While decreased ventilation may slow the decline in alveolar concentration of halothane and thus lengthen the duration of recovery, it should not adversely affect the quality of the recovery.

It is the differing combinations of premedication and induction drugs that appear to be involved in the obvious differences of the quality and duration of recovery. One of the most striking findings in this study was the association between ultrashort acting barbiturate administration and poor anaesthetic recoveries. The recoveries following thiopentone use were consistently bad; horses showed excitement, difficulty standing, poor coordination and marked ataxia with muscle fasciculations after standing. This persisted irrespective of the use of acetylpromazine or xylazine as premedicants. What causes this association of thiopentone with poor recoveries is not known, but it may be linked to its pharmacokinetics. The plasma half-life of thiopentone has been determined in other species and varies from 3-4 hours in the sheep (Toutain *et al*, 1983) to over seven hours in the dog (Brandon and Baggot, 1981). The clinical duration of anaesthetic effect is 5-8 and 15-20 minutes in the sheep and dog respectively; thus subanaesthetic concentrations of thiopentone exist for a much longer time than the anaesthetic duration suggests (Price *et al*, 1957; Brandon and Baggot, 1981; Toutain *et al*, 1983). In monogastric animals it is principally redistribution of thiobarbiturates to fat that determines anaesthetic duration;

the rate of recovery depends upon metabolism. Metabolism is slow. In the dog it is 10-15% per hour (Booth and McDonald, 1988) and recovery from a single dose of thiopentone can take up to two hours (Chenoweth and van Dyke, 1969).

It is not known how long, and at what levels, ultrashort acting barbiturates, particularly thiopentone, remain in equine plasma following intravenous injection. However, it is likely that the metabolism of thiopentone is slow and that subanaesthetic levels of thiopentone are present for some time in the horse, and probably persisted into the recovery period of this experiment.

It is possible that residual barbiturate levels affect the central nervous system during recovery in 2 ways :

Firstly, there may be a continuation of their sedative effect that results in a reduced ability to control motor, and perhaps sensory, function in the recovery period. Chenoweth and Van Dyke (1969), have shown that marked ataxia and incoordination occurs in dogs that are stimulated in the early phase of recovery from thiopentone anaesthesia. Additionally, the recovery of horses from thiopentone anaesthesia alone is marked by ataxia and poor coordination (Jones *et al*, 1969; Taylor, 1989), both of which may result from persistent sedative effects of thiopentone.

Secondly, residual barbiturate levels may also influence recovery by altering the level of pain perception (Clutton-Brock, 1960). Dundee (1960), found that during recovery from thiopentone (and pentobarbitone) anaesthesia, humans displayed a markedly increased awareness of pain. This became evident as soon as the hypnotic effect of barbiturates began to wane, but was clinically most obvious in the post anaesthetic period when gaseous anaesthetic agents did not mask the pain response. This increased sensitivity to pain persisted up to five hours. As a result of this discovery, Dundee postulated that subanaesthetic levels of barbiturates have an anti-analgesic effect. It is possible that a similar anti-analgesic effect exists after thiopentone anaesthesia in horses, and that a heightened perception of pain affects the quality of recovery.

The results of Taylor's (1986) study, however, appear to refute this hypothesis. Taylor found that the administration of pethidine at the termination of glycerol guaiacolate/thiopentone with halothane/oxygen anaesthesia, had no effect on the quality or duration of recovery. However, Dundee (1960), had shown that in man, subanaesthetic levels of thiopentone antagonised the analgesia produced by pethidine administration. The extent of this antagonism was affected by the dose of each drug. Also, knowing that analgesics are more effective if given before pain begins (Anon, 1978), and that Taylor used low intramuscular doses of pethidine (Baggot and Cooper, 1980) at the end of anaesthesia, it is possible that pethidine administration in her study, was not clinically effective as an analgesic. No attempt was made in Taylor's study to assess analgesic efficacy.

The presence of residual thiopentone levels enhancing the awareness of pain, and thereby having a detrimental effect on the quality of anaesthetic recovery, in this present study, is a possibility that needs further investigation.

In contrast to the poor anaesthetic recoveries seen after thiopentone use, those following the use of ketamine combinations were smooth and coordinate, and the horses showed little ataxia once standing. Whether these recoveries are a result of the presence, or lack of, residual ketamine levels affecting the central nervous system is not known.

Rapid and extensive redistribution of ketamine following intravenous administration causes the short duration of, and abrupt recovery from, anaesthesia. When the anaesthetic effect ends, approximately 40% of the injected dose still remains in plasma. Approximately 1.6 hours after ketamine injection, 10% of the dose given is predicted to persist in plasma, with 1% of ketamine remaining as long as 4 hours after administration (Kaka *et al*, 1979). Additionally, the presence of halothane may delay ketamine elimination still further, as has been demonstrated in the rat (White *et al*, 1977).

The stimulatory action of ketamine on the limbic and thalamic areas of the brain is well documented (Ferrer-Allado, 1973), and Muir *et al* (1977), attribute the excited and very badly coordinated recoveries seen after the use

of high doses (6.6 mg/kg) of ketamine to this effect. It is possible that the presence of residual ketamine levels for some hours after intravenous administration affects the central nervous system in a positive manner. The result could be that horses become alert sooner and so attain rapid, coordinate recoveries. These orderly recoveries are still seen when xylazine/ketamine combinations are followed by up to 90 minutes of halothane/oxygen anaesthesia (Taylor and Hall, 1985). However, Hall and Taylor (1981), note that although recoveries from xylazine/ketamine followed by halothane and oxygen are good, they are not as good as those seen after xylazine/ketamine use alone. This is presumably the result of the mild sedative influence of halothane on recovery.

It is however, equally possible that, in the present study, when the horses stood approximately one and a half hours after ketamine administration, that any residual ketamine in plasma had no clinical effect and thus the smooth quality of recovery was largely a reflection of the halothane/oxygen maintenance. Regrettably, previous descriptions of recoveries from halothane induced and maintained anaesthesia in horses (Steffey and Howland, 1978; Steffey *et al*, 1990a and b), lack detail and so cannot be compared with those observed following ketamine combinations used in this study.

The use of glycerol guaiacolate in combination with thiopentone and ketamine appears to have had little effect on recoveries. Its combination with ultrashort acting barbiturates has been advocated as it reduces the barbiturate dose (and therefore depressant respiratory and cardiovascular effects), smooths induction and recovery and provides good muscle relaxation (Roberts, 1968; Heath and Gabel, 1970; Funk, 1973; d'Iteren, 1976; Bishop, 1978; Hubbell *et al*, 1980; Brouwer, 1985 a and b). Presumably its combination with ketamine was introduced to overcome the increased muscle tone following ketamine use (Muir *et al*, 1977; Muir *et al*, 1979b; Booth and McDonald, 1988). The duration of clinical effect of glycerol guaiacolate is approximately 15-30 minutes (Westheus, 1955; Roberts, 1968; Davis and Wolff, 1970). Thus for longer anaesthetics than this, the influence of glycerol guaiacolate on recovery should be minimal. This is demonstrated in this study where, after an hour of gaseous anaesthesia, the poor recoveries from glycerol

guaiacolate and thiopentone appear to resemble the recoveries of thiopentone alone (Jones *et al*, 1960), or acetylpromazine and thiopentone (Taylor, 1989). Also, the better recoveries from glycerol guaiacolate and ketamine showed no difference to those of xylazine/ketamine.

(ii) Recovery Length

The duration of recovery appears to be influenced strongly by the premedicant chosen, and its interaction with the induction drug used. In both barbiturate and ketamine combinations, acetylpromazine premedication resulted in a longer recovery than when xylazine was used.

Acetylpromazine usually produces up to two hours of effective sedation after administration (Dodman, 1980; Taylor, 1985). However, mild degrees of sedation that on their own are not clinically important, may persist up to 24 hours (McKenzie and Snow, 1977; Parry *et al*, 1982). It seems likely therefore, that a residual sedative effect of acetylpromazine persists during recovery from anaesthesia resulting in longer recovery times. The longer recoveries following glycerol guaiacolate/thiopentone compared to glycerol guaiacolate/ketamine use after acetylpromazine premedication, may be attributed to the additive sedative effect of phenothiazines and barbiturates (Booth and McDonald, 1988).

There is some dispute among authors as to the influence of xylazine on recovery. Brouwer *et al* (1980), found that recoveries after ketamine, methohexitone and thiopentone, with xylazine premedication, were smooth and occurred within fifty minutes (ketamine recoveries being significantly shorter than thiopentone). However, in Brouwer's study, no gaseous anaesthesia was used to prolong anaesthesia. In contrast, Hoffman (1974), stated that recoveries from a variety of induction drugs after xylazine premedication were fast and smooth if anaesthesia was short; but recovery was rapid and often violent when anaesthesia was prolonged for 45 minutes or more. In both instances, the recoveries were rapid, and the difference in recovery quality can be explained by the duration of action of xylazine.

Xylazine has a much shorter duration of sedative effect than acetylpromazine. Clinically the length of sedation is related to the dose and route of administration. The two doses used in this experiment, 0.2 mg/kg iv and 1.1 mg.kg iv , last less than thirty and 45-60 minutes respectively (Clarke and Hall, 1969; Tronicke and Vocke, 1970; Hoffman, 1974; Garcia and Villar, 1981; Taylor, 1985). Because all horses in this experiment did not attempt to stand till at least 86 minutes after the administration of xylazine, it is unlikely that xylazine affected the duration of recovery.

It is interesting to note that with both thiopentone and ketamine combinations followed by gaseous anaesthesia, the use of premedicants did not affect the quality of recovery. In the light of this, and the knowledge of the severe arrhythmias caused by xylazine that are potentially fatal when halothane is also administered (Steffey *et al*, 1985), the practice of some veterinarians of administering small doses of xylazine at the termination of anaesthesia to "smooth" recovery, is to be discouraged.

In summary, after one hour of halothane/oxygen mixtures to maintain anaesthesia, acetylpromazine, but not xylazine, used as a premedicant prolongs the duration of recovery. The use of barbiturates as induction drugs in the horse modifies the recovery and this may be due to the sedative, and perhaps anti-analgesic, effect of subanaesthetic levels of barbiturates during the recovery period. The recoveries following barbiturates are poorer and longer in duration than ketamine combinations. Glycerol guaiacolate has negligible effect on recovery after at least one hour of inhalation maintenance of anaesthesia whereas the role of ketamine is poorly understood. Ketamine may, or may not, have a stimulatory effect during the anaesthetic recovery period.

3. MUSCLE ENZYMES

Serum biochemical analysis, to measure the levels of CPK and SOT, were used in this study to determine if significant degrees of muscle damage were occurring following anaesthesia. In agreement with other studies (Trim and Mason, 1973; Grandy *et al*, 1987), a general trend of CPK and GOT increase

was observed. This trend was demonstrated in horses from every induction group but was of insignificant magnitude to indicate severe muscle damage, and no clinical evidence of post anaesthetic myopathy was found.

Nevertheless, it was interesting to note that the two groups of horses which had received acetylpromazine as a premedicant, had significantly higher post anaesthetic CPK levels than the remaining groups. The cause of this increase in serum CPK is not clear but could be due to several factors. It may be that acetylpromazine selectively affects blood flow to skeletal muscle. It could also be the result of the capacity of acetylpromazine to lower haematocrit level (Ballard *et al*, 1982; Parry and Anderson, 1983). The decrease in packed cell volume may be a much as 50%, persists up to 12 hours, and is primarily the result of the sequestration of red blood cells. The lowered haematocrit may decrease the oxygen supply to tissues, including muscle, which could result in muscle cell damage.

The ability of acetylpromazine to increase the duration of recovery may also be detrimental to muscle blood flow and oxygenation. Although, in this experiment, no relationship was found between the recovery times and CPK or GOT levels, the duration of recumbency has been incriminated as one of many contributing factors to post anaesthetic myopathy (Grandy *et al*, 1987). Others (Richey *et al*, 1990), suggest that duration of recumbency is important only if there are concurrent periods of arterial hypotension. Since, in this study, halothane was probably the principal determinant of blood pressure after ten minutes of anaesthesia and no group differences in arterial blood pressure were noted from this time onwards, it is unlikely that hypotension was involved in the rise of CPK following the use of acetylpromazine.

The statistical lack of difference in muscle enzyme levels between the first and fourth anaesthetic of every horse, suggests that multiple anaesthetics one week or more apart, contribute little to muscle damage or the possible occurrence of post anaesthetic myopathy.

4. CRITICAL EVALUATION OF THE EXPERIMENT

(i) Experimental design and limitations.

The scope of this study was limited by cost. For this reason it was necessary to minimise animal differences and attempt to maximise repeatability of results. This was achieved by using all 4 anaesthetic techniques on each of the 10 horses. Also, to minimise the effects of variations between horses, group means were calculated and the statistical analysis performed only on these figures.

A possible criticism of the experiment is that serial anaesthetics on the horses may have influenced the data obtained. Scattergraphs constructed to examine this possibility did not reveal any such influences. However, it has been shown that halothane anaesthesia causes significant changes in serum levels of glucose, lactate, nonesterified fatty acids, cortisol, catecholamines and adrenocorticotrophic hormone (ACTH). Such changes indicate a substantial stress response to anaesthesia (Robertson, 1987; Taylor, 1989 and 1990). Whether or not this stress response wanes sufficiently over the period of a week has not been studied. It did not appear to affect the parameters measured in this study, but there may have been other undetected effects.

The information gained from this experiment relates only to horses which have been anaesthetised for 1 hour and positioned in lateral recumbency. The differences in results obtained if the duration of anaesthesia or the horse's body position was changed, can only be speculated. It is assumed that differences would be found as drug pharmacokinetics and clearance are a function of time.

A further limitation to this experiment is that no physiological data was collected during the recovery period. Pulmonary blood pressure measurements and blood gas values if monitored, would have indicated the efficiency of pulmonary function and therefore provided more information on the rate of clearance of halothane during the recovery period. Mason *et al* (1987), found that hypoxia, without hypercarbia, developed in all horses recovering from anaesthesia that did not receive oxygen supplementation. This was not due to inadequate ventilation, but was apparently related to the

persistence of a pulmonary shunt and ventilation perfusion mismatching that were established during anaesthesia. The occurrence of this pulmonary dysfunction in recumbent anaesthetised horses is probably due to recumbency and anaesthetic drug use (Hall, 1971; Hall, 1984; Rugh *et al*, 1984; Nyman and Hedestierna, 1989; Nyman *et al*, 1990). Whether or not this affects halothane clearance to any degree has not been determined, and whether or not there are specific drug differences in the degree of pulmonary dysfunction that occurs, has also not been investigated.

(ii) Clinical assessment of induction techniques

The opinion expressed by authors on the efficacy and desirability of xylazine/ketamine combinations from a practical and clinical point of view is varied (Ellis *et al*, 1977; Butera *et al*, 1978; Hall and Taylor, 1981; Taylor and Hall, 1985). Butera *et al* (1978), list the disadvantages of this induction drug combination as : excitement during induction, insufficient duration of anaesthesia with abrupt recovery, rigidity of extensor muscles and incoordination of recovery. These disadvantages are a reflection of the extrapyramidal effects of ketamine that may be manifested if there is inadequate sedation (Hall and Taylor, 1981). It is necessary therefore to ensure a strong sedative effect is present after xylazine administration before ketamine is given. This may entail waiting 4-5 minutes after xylazine administration, and, if sedation does not appear adequate at this time, the use of incremental doses of xylazine (upwards of 50 mg) to obtain maximum sedation. This was not a technique adhered to in this experiment. It is also important not to stimulate the horse in any way in the first few minutes after recumbency is achieved. If the horse is left to settle quietly once recumbent, a deeper level of anaesthesia will be reached (Hall and Taylor, 1981). Any attempt to forcibly restrain the horse at this time will result in struggling (Fisher, 1984).

The abrupt recovery following xylazine/ketamine combinations was overcome, in the present study, by the use of high inspired concentrations of halothane for the initial 10-15 minutes of gaseous maintenance. This abrupt recovery must be anticipated by the anaesthetist as there have been reports of horses attempting to rise from surgical tables due to inadequate surgical depth

during procedures (R.Machon, personal communication). The use of xylazine/ketamine, ketamine, xylazine, glycerol guaiacolate, methohexitone, thiopentone or halothane to prolong anaesthesia has been recorded (Hall and Taylor, 1981; Fisher, 1984; Trim *et al*, 1987). It appears that, of these drugs, halothane in oxygen is the most predictable and reliable means of prolonging anaesthesia.

The observations on which depth of equine anaesthesia following ketamine is based, vary slightly from those used for barbiturates. The eye commonly remains open, lacrimation and nystagmus are common, and some horses show occasional spontaneous limb movements at a depth of anaesthesia suitable for surgical manipulation (Hall and Taylor, 1981). However the eye position and palpebral reflex remain reliable monitors of depth, but the presence or absence of response to surgical stimulation is the surest guide (Campbell and Lawson, 1954; Hall and Taylor, 1981).

Of concern are several reports by clinicians of the failure of xylazine/ketamine combinations to induce anaesthesia in the horse (Fisher, 1984; Trim *et al*, 1987). The reason for complete lack of anaesthesia following ketamine administration, even after adequate xylazine sedation, is not known. It does not appear to be related to faulty drug storage, incorrect intravenous injection or miscalculated doses (Trim *et al*, 1987). No such incidences were observed in this study. Also of concern are anecdotal reports from clinicians of an increase in the number of anaesthetic deaths, within fifteen minutes of halothane administration, following the use of xylazine/ketamine combinations. The cause of this is not known, but it may be related to unfamiliarity of the drug combination and its effects, overdosing with halothane, or the arrhythmogenic effects of halothane and xylazine on cardiac function. Thus the use of xylazine and ketamine combinations for equine anaesthesia requires care and attention during the induction and early maintenance period. However, the lack of significant cardiovascular or respiratory depression following induction, the normal systemic arterial pressure during anaesthesia and the superior recoveries, make xylazine/ketamine combinations an attractive drug choice.

The use of glycerol guaiacolate/ketamine combinations also provides a smooth, excitement free recovery. Although the cardiopulmonary parameters measured were not as good as seen with xylazine/ketamine use, there was no difficulty in maintaining adequate anaesthetic depth with halothane, and glycerol guaiacolate/ketamine combinations do not appear to have any untoward results (Muir *et al*, 1978 and 1979b). Thus it may prove to be a superior choice to xylazine/ketamine combinations.

A major disadvantage with ketamine use in horses is its cost. At current prices it is approximately twice as expensive as glycerol guaiacolate/thiopentone. However, this must be balanced against the total cost of an hours duration (or more) of anaesthesia and the potential advantage to the wellbeing of the animal.

In contrast,glycerol guaiacolate/thiopentone combinations with short term halothane/oxygen maintenance, appear to have severe limitations. The initial severe cardiovascular depression coupled with the occasional stormy induction, require constant vigilance by the anaesthetist in the first twenty minutes of anaesthesia. The very poor recoveries after one hour of gaseous maintenance in comparison to ketamine combinations are disturbing and present a major problem if orthopaedic surgery has been performed.

CHAPTER 5

CONCLUSIONS

After one hour of halothane/oxygen anaesthesia, there is a statistically better chance of obtaining smoother and more coordinate recoveries if xylaxine/ketamine or aetylpromazine/glycerol guaiacolate/ketamine rather than thiopentone combinations have been used as anaesthetic induction agents.

More rapid recoveries occur with greater frequency following xylazine/ketamine induction, even after one hour of gaseous anaesthesia, than with the other drug combinations used.

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APPENDIX 1

EQUINE ANAESTHETIC RECOVERY CHART

Horse number : . . . . . .

Age : . . . . . .

Sex : . . . . . .

Height: . . . . . .

Weight: . . . . . .

Breed: . . . . . .

History

Ownership: . . . . . .

Past Illness/Accidents: . . . . . .

Diet/Appetite: . . . . . .

General Environment: . . . . . .

Clinical Examination

Pre-anaesthesia: . . . . . .

T° . . . . . .

HR: . . . . . .

RR: . . . . . .

Musculoskeletal system: . . . . . .

Respiratory system: . . . . . .

Cardiovascular system: . . . . . .

Details of abnormalities: . . . . . .

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Clinical chemistry

- routine haematology
- BUN
- liver enzymes
- muscle enzymes
- barbiturate levels

Anaesthetic technique

Premedication (mg/kg): . . . . . .

Induction agent (mg/kg): . . . . . .

Time from standing to recumbency: . . . . . .

Inhalation agent: . . . . . .

Character of induction

Smooth

Mild excitement (extensor rigidity of limbs, nystagmus)

Extreme excitement (paddling, head movements)

Depth of anaesthesia on induction

1. Medium surgical (eyeball ventral, mild palpebral, constructing pupil)
2. Light surgical (eyeball medial, stronger palpebral)
3. Non-surgical (nystagmus, strong palpebral, dilated pupil

HR	5	10	15	20	25	30	35	40	45	50	55	60
RR												
BP- mean												
- systolic												
- diastolic												
BG - pH												
- CO_2												
- O_2												
T°												
Anal tone												
Nystagmus												
Halothane %												
O_2 flow												

HR, RR every 10 minutes
BP at 10, 30, 60 minutes
Anal tone - + barely present
- ++ present
- +++ pronounced
every 20 minutes.
Nystagmus - presence or absence

Comments: . . . . . .

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Recovery

Time: to extubation (ears back, swallow on removing tube): . . . . . .

to lifting head: . . . . . .

to standing: . . . . . .

Number of attempts to stand: . . . . . .

Degree of motor co-ordination on standing

0	very poor	many (>3) attempts to stand; rolling; excitement; collapse of more than 2 limbs on standing.
1	poor	more than two attempts to stand; considerable ataxia, partial collapse of limbs on weight bearing.
2	fair	one or two attempts to stand; muscle fasiculations, mild ataxia.
3	good	standing on first attempt; muscle tremors, knuckling on one leg.
4	excellent	standing at first attempt; no ataxia.

Comments: . . . . . .

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APPENDIX 2

TABULATED RAW DATA

Time taken for induction of anaesthesia (seconds)

HORSE NO.	Experimental Group			
	I	II	III	IV
1	15	40	120	75
2	20	28	80	32
3	25	24	75	25
4	32	30	50	50
5	18	21	65	50
6	25	85	135	31
7	35	25	135	32
8	20	24	85	30
9	17	120	83	60
10	22	50	110	35
MEAN	**22.9**	**44.7**	**93.8**	**42.0**

Depth of anaesthesia following induction

HORSE NO.	EXPERIMENTAL GROUP			
	I	II	III	IV
1	2	2	2	3
2	1	2	2	1
3	1	1	2	2
4	1	2	3	3
5	2	1	2	2
6	1	2	3	1
7	1	2	3	1
8	1	1	2	3
9	2	3	3	3
10	1	2	3	1
MEAN	**1.3**	**1.8**	**2.5**	**2.0**

1. Medium surgical (eyeball ventral, mild palpebral reflex, constructing pupil).

2. Light surgical (eyeball medial, stronger palpebral).

3. Non-surgical (nystagmus, strong palpebral, dilated pupil).

Heart Rate (per minute) during maintenance of anaesthesia

Experimental Group	I					II					III					IV				
Time interval (min)	5	10	15	30	60	5	10	15	30	60	5	10	15	30	60	5	10	15	30	60
HORSE NO.																				
1	42	44	40	41	36	42	38	37	42	38	36	36	36	36	32	42	42	42	42	38
2	44	42	44	44	48	36	36	35	40	42	40	36	42	40	40	44	44	40	44	40
3	39	38	37	40	38	44	40	40	40	42	32	32	32	30	30	40	41	42	42	40
4	52	44	44	40	30	48	44	42	37	34	36	36	36	33	32	42	42	38	34	34
5	44	38	40	42	40	46	44	44	40	36	30	40	36	44	42	40	40	38	36	42
6	44	48	54	50	48	44	44	44	56	48	36	32	34	40	38	50	51	52	56	48
7	40	32	40	32	36	42	41	40	44	42	40	36	36	36	36	36	36	34	36	36
8	40	40	40	38	40	40	32	36	36	34	40	44	40	36	36	43	42	40	36	42
9	48	48	45	48	40	56	48	44	44	40	36	38	39	38	36	48	46	42	49	37
10	44	40	40	44	40	42	38	40	40	36	32	33	32	33	31	36	36	36	36	36
MEAN	43.7	41.4	42.4	41.9	39.6	44.0	36.1	46.2	41.9	39.2	36.4	36.3	36.3	36.6	35.3	42.1	42	40.4	41.1	39.3

Respiratory Rate (per minute) during maintenance of anaesthesia

Experimental Group	I					II					III					IV				
Time interval (min)	5	10	15	30	60	5	10	15	30	60	5	10	15	30	60	5	10	15	30	60
HORSE NO.																				
1	4	4	4	4	4	4	3	4	5	5	5	6	6	6	10	4	6	5	5	5
2	4	4	6	7	5	4	4	3	3	3	2+	6	8	6	6	5	6	7	6	5
3	7	8	9	9	9	9	7	8	7	8	5	8	9	8	8	4	8	7	12	12
4	5	3	2	4	5	4	5	7	5	8	6	8	6	9	12	4	4	6	8	8
5	4	6	6	6	8	2	4	8	9	9	8	10	8	10	12	3+	8	8	11	18
6	4	4	4	9	6	2	3	4	12	6	2	2	5	6	6	4	4	4	8	8
7	5	6	6	8	7	10	9	10	11	12	9	9	15	12	15	3	4	8	9	11
8	8	6	8	6	6	5	6	6	4	4	6	7	6	7	7	7	8	7	7	10
9	4	3	2	4	6	1	1	2	4	5	4	4	4	4	12	9	6	7	6	7
10	2+	2	3	4	3	2	4	4	5	5	6	7	4	8	9	4	4	4	4	7
MEAN	**4.7**	**4.6**	**5**	**6.1**	**5.9**	**4.3**	**4.6**	**5.6**	**6.5**	**6.5**	**5.3**	**6.7**	**7.1**	**7.6**	**9.7**	**4.7**	**5.8**	**6.3**	**7.6**	**9.1**

+ = Intermittent positive pressure ventilation

Mean Arterial Blood Pressure during maintenance of anaesthesia

Experimental Group	I			II			III			IV		
Maintenance period (min)	10	30	60	10	30	60	10	30	60	10	30	60
HORSE NO.												
1	60	88	99	50	62	85	75	80	74	55	74	97
2	60	63	79	47	60	79	81	60	62	43	70	56
3	63	96	97	48	79	72	82	77	91	55	80	73
4	44	63	65	59	84	81	49	55	55	54	67	68
5	52	84	81	63	92	83	78	54	54	77	92	80
6	57	77	74	62	133	126	74	85	84	79	96	98
7	54	57	76	31	48	60	74	72	82	55	78	99
8	53	71	77	41	58	79	79	57	69	53	56	59
9	58	79	68	43	40	74	73	56	57	50	52	60
10	58	75	92	42	52	73	72	63	64	49	66	74
MEAN	55.9	75.3	80.8	48.6	70.8	81.2	73.7	65.9	69.2	57.0	73.1	76.4

Partial pressure of arterial carbon dioxide ($PaCO_2$) at 10, 30 and 60 minutes (mmHg)

Experimental Group	1			2			3			4		
Time Interval (min)	**10**	**30**	**60**	**10**	**30**	**60**	**10**	**30**	**60**	**10**	**30**	**60**
HORSE NO.												
1	58.7	60.6	59.0	49.4	62.0	62.8	54.2	59.0	62.7	61.7	58.8	58.5
2	57.7	61.3	65,0	67.6	72.6	75.8	59.2	70.5	69.2	56.1	65.9	69.4
3	56.4	61.7	63.2	53.4	55.7	51.8	55.0	52.2	49.2	46.92	52.5	56.7
4	58.5	63.4	64.8	56.4	56.9	58.2	55.5	62.8	59.6	58.9	62.2	63.9
5	60.8	62.7	68.2	59.4	63.1	65.2	56.9	55.2	65.5	51.6	53.0	59.7
6	52.7	58.8	80.3	63.0	54.7	63.9	56.2	63.1	63.4	72.6	65.0	74.3
7	54.6	62.9	74.2	56.6	62.2	66.2	59.9	57.4	65.7	57.0	57.0	60.7
8	55.1	65.4	74.9	51.4	55.1	64.4	54.3	63.1	68.4	54.6	55.1	68.4
9	53.0	59.0	71.6	70.0	53.2	65.9	54.7	55.0	54.2	54	52.4	53.8
10	81.8	96.2	100.8	63.7	69.3	74.6	64.2	57.8	60.2	60.3	53.4	67.8
MEAN	**58.75**	**65.20**	**72.20**	**59.09**	**60.48**	**64.88**	**57.01**	**59.61**	**61.81**	**57.35**	**57.53**	**63.32**

pH readings at 10, 30 and 60 minutes

Experimental Group	1			2			3			4		
Time Interval (min)	**10**	**30**	**60**	**10**	**30**	**60**	**10**	**30**	**60**	**10**	**30**	**60**
HORSE NO.												
1	7.2990	7.2910	7.2960	7.3310	7.2640	7.2560	7.3000	7.2900	7.2680	7.2800	7.3030	7.3060
2	7.2880	7.2970	7.2220	7.2280	7.2120	7.2110	7.3260	7.2680	7.2920	7.2620	7.2300	7.2150
3	7.2980	7.2700	7.2750	7.3100	7.3160	7.3240	7.2850	7.3220	7.3550	7.2980	7.2880	7.2550
4	7.2840	7.2600	7.2460	7.3090	7.3000	7.2950	7.3280	7.3050	7.3230	7.3020	7.2760	7.2650
5	7.2650	7.2510	7.2400	7.2810	7.2720	7.2570	7.3110	7.3320	7.2830	7.2900	7.3530	7.3070
6	7.3030	7.2720	7.1720	7.2460	7.3050	7.2540	7.3010	7.2630	7.2980	7.3260	7.2650	7.2180
7	7.3370	7.2800	7.2220	7.2450	7.2590	7.2440	7.3300	7.3380	7.3000	7.3160	7.2930	7.2870
8	7.3310	7.2720	7.2280	7.3350	7.3030	7.2410	7.3060	7.2810	7.2490	7.2920	7.2870	7.2000
9	7.2760	7.2330	7.2090	7.1930	7.2560	7.2020	7.2830	7.3980	7.2890	7.2300	7.2790	7.2720
10	7.1710	7.1130	7.1130	7.2460	7.2250	7.2000	7.2570	7.3240	7.3280	7.2890	7.3290	7.2550
MEAN	**7.2852**	**7.2539**	**7.2223**	**7.2724**	**7.2712**	**7.2484**	**7.3027**	**7.3121**	**7.2985**	**7.2885**	**7.2903**	**7.2580**

Partial pressure of arterial oxygen (PaO_2) at 10, 30 and 60 minutes (mmHg)

Experimental Group	1			2			3			4		
Time Interval (min)	**10**	**30**	**60**	**10**	**30**	**60**	**10**	**30**	**60**	**10**	**30**	**60**
HORSE NO.												
1	350.8	439.7	466.3	343.2	427.7	441.0	283.5	338.2	383.5	439.0	483.2	492.7
2	324.8	367.9	423.0	367.6	370.1	353.9	300.6	343.7	320.6	327.0	393.9	428.2
3	480.0	517.2	517.5	399.7	510.5	471.1	346.0	415.3	528.7	411.4	507.6	477.4
4	286.8	375.2	378.7	365.0	406.0	408.1	299.7	361.2	362.0	388.7	425.4	386.5
5	483.5	470.0	496.3	298.8	423.6	469.0	305.1	409.7	413.6	399.6	417.2	455.4
6	268.1	289.1	224.8	288.5	429.4	410.3	342.7	386.7	359.2	115.8	356.3	380.8
7	360.3	421.3	402.2	355.8	390.0	427.1	384.3	465.2	454.0	374.7	466.9	483.7
8	339.0	368.8	336.0	363.2	363.2	283.4	257.1	257.1	98.6	351.8	472.9	397.2
9	243.6	256.3	223.2	116.9	111.1	114.4	293.9	283.3	211.4	304.0	314.4	326.9
10	350.4	261.4	250.1	405.2	386.4	360.9	398.4	463.2	404.3	393.5	259.1	340.4
MEAN	**318.73**	**376.69**	**341.81**	**330.39**	**381.80**	**373.92**	**330.13**	**375.96**	**353.59**	**350.55**	**409.69**	**416.92**

Time taken for horse to swallow and consequent removal of endotracheal tube after discontinuation of gaseous anaesthesia (min)

HORSE NO.	EXPERIMENTAL GROUP			
	1	**2**	**3**	**4**
1	6.0	13.0	5.0	6.0
2	11.5	5.0	3.5	9.0
3	32	4.0	6.5	7.0
4	25.0	16.5	12.0	25.3
5	12.8	12.0	6.8	6.8
6	8.0	5.0	10.0	5.0
7	34.0	14.2	12.8	13.0
8	19.5	31.0	12.0	26.2
9	17.0	13.0	7.5	14.5
10	15.0	15.0	11.0	10.0
MEAN	**18.08**	**12.87**	**8.70**	**12.28**

Time taken for horse to lift head after discontinuation of gaseous anaesthesia (min)

HORSE NO.	EXPERIMENTAL GROUP			
	1	**2**	**3**	**4**
1	37.5	41.5	17.0	17.0
2	49.0	29.0	6.3	21.0
3	56.0	24.0	12.1	8.0
4	36.0	21.2	17.0	46.5
5	42.0	31.0	7.0	14.0
6	30.5	33.0	12.5	30.0
7	44.0	20.3	13.3	37.0
8	32.1	51.0	37.0	65.0
9	53.0	23.0	15.0	18.0
10	34.0	47.2	13.0	27.0
MEAN	**41.41**	**32.11**	**15.02**	**28.35**

Time taken for the horse to achieve sternal recumbency after discontinuation of gaseous anaesthesia (min)

HORSE NO.	EXPERIMENTAL GROUP			
	1	2	3	4
1	54.5	45.5	27.0	21.0
2	59.5	33.0	17.0	37.0
3	58.5	28.0	14.2	10.0
4	41.0	28.8	18.3	59.3
5	45.0	31.0	13.5	14.0
6	31.0	35.0	13.1	33.0
7	67.0	20.6	13.3	37.0
8	58.0	73.0	37.0	65.0
9	75.0	44.0	15.5	20.0
10	73.0	47.0	17.0	41.0
MEAN	**56.25**	**38.59**	**24.89**	**33.73**

Time taken for horse to stand after discontinuation of gaseous anaesthesia (min)

HORSE NO.	GROUP			
	1	**2**	**3**	**4**
1	67.0	58.5	55.0	40.0
2	60.0	41.0	29.0	37.3
3	60.25	28.0	29.5	12.0
4	48.0	41.8	44.0	59.5
5	47.0	31.5	15.8	24.5
6	60.0	52.0	27.4	39.0
7	85.0	34.2	17.5	52.0
8	72.0	76.0	37.2	65.3
9	91.0	53.0	23.3	26.8
10	77.0	60.0	17.0	62.0
MEAN	**66.73**	**47.60**	**29.56**	**41.84**

Number of attempts of each horse to stand after discontinuation of gaseous anaesthesia

HORSE NO.	GROUP			
	1	**2**	**3**	**4**
1	2	2	1	1
2	2	4	1	2
3	3	2	1	2
4	4	1	1	1
5	2	3	2	1
6	3	1	1	1
7	2	4	2	1
8	2	4	1	1
9	3	5	1	2
10	2	2	1	1
MEAN	**2.5**	**2.8**	**1.2**	**1.3**

Recovery grade

HORSE NO.	EXPERIMENTAL GROUP			
	1	**2**	**3**	**4**
1	1	2	4	3
2	2	0	3	2
3	1	2	4	1
4	0	3	3	3
5	2	1	2	4
6	1	3	4	4
7	2	1	2	4
8	2	0	4	4
9	1	0	4	2
10	2	2	3	4
MEAN	**1.4**	**1.4**	**3.3**	**3.1**

CPK Levels before and 3 hours after anaesthesia (IU/l)

	EXPERIMENTAL GROUP											
Time Interval	**1**			**2**			**3**			**4**		
HORSE NO.	*Pre*	*Post*	*Diff*	*Pre*	*Post*	*Diff*	*Pre*	*Post*	*Diff*	*Pre*	*Post*	*Diff*
1	84	197	113	84	153	69	92	119	27	124	374	250
2	91	316	225	100	146	46	133	146	13	142	295	153
3	97	319	222	98	115	17	100	153	53	114	590	476
4	122	221	99	142	193	51	170	282	112	124	292	168
5	65	225	160	136	124	12	89	143	54	81	103	22
6	160	314	154	92	147	55	118	245	127	166	277	111
7	195	421	226	199	312	113	173	380	207	170	469	299
8	173	346	173	131	173	42	136	185	49	147	325	178
9	165	514	349	117	417	300	130	263	133	138	581	443
10	109	269	160	169	276	107	97	226	129	111	291	180
MEAN	126.1	314.2	188.1	126.8	205.6	81.2	123.8	214.2	90.4	131.7	359.7	228.0

GOT levels before and 24 hours after anaesthesia (IU/l)

	EXPERIMENTAL GROUP											
Time Interval	**1**			**2**			**3**			**4**		
HORSE NO.	*Pre*	*Post*	*Diff*	*Pre*	*Post*	*Diff*	*Pre*	*Post*	*Diff*	*Pre*	*Post*	*Diff*
1	143	138	5	133	151	18	148	166	18	136	131	5
2	164	196	21	154	166	12	239	277	38	164	176	12
3	191	199	8	176	174	2	179	224	45	280	318	38
4	171	189	18	142	170	28	181	242	61	151	194	43
5	164	186	22	141	151	10	189	196	7	161	174	13
6	227	250	23	164	161	3	174	204	30	161	164	3
7	154	171	17	161	191	30	164	207	43	156	166	10
8	181	212	31	126	108	18	131	146	15	161	185	24
9	141	222	81	133	143	10	166	196	30	169	189	20
10	126	166	40	154	148	6	156	154	2	141	164	23
MEAN	166.2	192.9	26.6	148.4	156.3	13.7	172.7	201.2	28.9	168.0	186.1	19.1

APPENDIX 3

Example of Two-Way Analysis of Variance

Two-way Analysis of variance of time to attain sternal recumbency

Source	DF	SS	MS
Group	3	5232	1744
Horse	9	4129	459
Error	27	6674	247
TOTAL	39	16035	2450

F value = $\frac{\text{MS trtmt}}{\text{MS error}}$ = 7.06 > than 2.96 = $p<0.05$

LSD = $2.052 \times \sqrt{1/5} \times \text{S.D.}$ = 12.4 for 5% significance

Difference in group means	
Group 1 - 2	17.67*
1 - 3	13.36*
1 - 4	22.5*
2 - 3	13.7
2 - 4	4.86
3 - 4	-8.84

* significant $p<0.05$

APPENDIX 4

Example of Regression Analysis and corresponding Scattergraph (MINITAB)

Regress CPK (C34) on Number of Attempts to Stand (C31)

The fitted equation is: C34 = 123 + 12.5 C31

Column	Coeff	SD (coeff)	t-value
Constant	122.55	36.78	3.33
C31	12.50	16.53	0.76

The residual standard deviation about the model is s = 112.0 with 39-1 = 38 degrees of freedom.

R-squared = 1.48%

5% level of significance: t >2.02

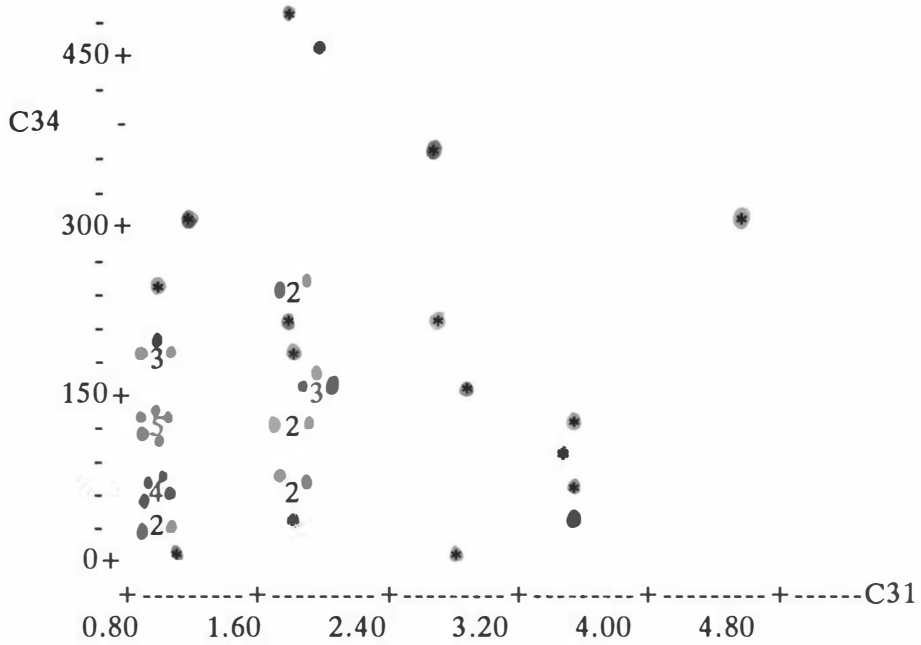
Analysis of Variance

Due to	DF	SS	MS = SS/DF
Regression	1	7174	7174
Residual	38	476590	12542
Total	39	483765	

Unusual Observations

Obs	C31	C34	Fit	St.dev.Fit	Residual	St. Residual
12	2.00	476.0	147.6	17.7	328.4	2.97R
34	5.00	300.0	185.1	53.4	114.9	1.17x
36	2.00	443.0	147.6	17.7	295.4	2.67R

Scattergraph of CPK (y-axis) and number of attempts to stand (x-axis)



Key: 1st anaesthetic
2nd anaesthetic
3rd anaesthetic
4th anaesthetic