WARMING AND HUMIDIFICATION OF INSPIRED GASES: ITS EFFECTIVENESS IN MINIMIZING HYPOTHERMIA IN ANAESTHETIZED CATS

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ABSTRACT

Body temperature is governed by a complex, highly integrated control system which carefully balances heat production and heat loss. Heat is produced as a byproduct of metabolism, and as the result of muscular work, shivering and chemical thermogenesis; while heat is lost from the body via the channels of heat exchange - radiation, conduction, convection and evaporation. General anaesthetic agents interfere with the normal mechanisms of temperature control by reducing heat production in the face of increased heat loss.

Six adult domestic short-haired cats were included in a randomized cross-over study, to evaluate the effectiveness of warming and humidification of inspired gases in the prevention of anaesthetic induced hypothermia. General anaesthesia was maintained with halothane in 100% oxygen, delivered via a Mapelson type E non-rebreathing anaesthetic circuit. Both passive and active methods of inspired gas warming and humidification were investigated in this study: the passive technique evaluated the effectiveness of a human neonatal Heat and Moisture Exchanger (HME), while the active technique used an electrical heating unit to supplement the warming capabilities of the HME.

Rectal and oesophageal temperatures continued to fall throughout each of the 120 minute experimental periods. Body temperature did not vary significantly between the three trials. The effectiveness of the HME in preserving normothermia in anaesthetized animals has not been reported previously. Despite the success of similar techniques in human neonates and infants, the results of this study indicate that warming and humidification of inspired gases is ineffective in minimizing hypothermia in halothane anaesthetized cats.

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TABLE OF CONTENTS

FIGURES AND TABLES

INTRODUCTION

"The most effective way of cooling a man is to give him an anaesthetic"

Pickering, *Lancet* 1958.

It has long been recognized that general anaesthesia markedly impairs the body's ability to maintain a normal temperature. Von Kappeler first reported the problem in 1880, describing a case-series of 20 human patients who experienced a decrease in body temperature during general anaesthesia. Over the following quarter of a century, numerous references to the cause and incidence of this phenomenon were published in the medical literature (Newman, 1971), and today, interest in the basic mechanisms of temperature control, and the ways in which general anaesthesia interferes with this, remains high.

Is hypothermia a significant problem in veterinary anaesthesia? Human literature documents that the body temperature of children, especially neonates, falls rapidly during general anaesthesia and surgery. Yet despite obvious similarities in patient size, and the use of common anaesthetic agents and techniques, the actual incidence and significance of intraoperative hypothermia in small animals has received little attention (Stead and Stead, 1972; Waterman, 1975). However, there is little question that anaesthetized animals become "cold". Hypothermia is a common clinical finding in cats and dogs recovering from surgery, and the difficulty of trying to maintain a normal body temperature during general anaesthesia has been the subject of several research studies published in the veterinary literature (Evans, Sawyer and Krahwinkel, 1973; Haskins and Patz, 1980; Haskins, 1981; Raffe and Martin, 1983).

It is well known that intraoperative hypothermia induces a complex array of physiological changes that may, in certain circumstances, jeopardize patient safety. However, more than 100 years after Von Kappeler's initial observation, hypothermia continues to be a common and potentially serious complication of general anaesthesia

and surgery (Sessler, M°Guire and Sessler, 1991).

The purpose of this review is to highlight the importance of the recognition, management and prevention of hypothermia during general anaesthesia in small animals. But in order to fully appreciate the dramatic impact of anaesthetic agents on the body's ability to regulate temperature, and the profound physiological consequences of this insult to homeostasis, it is essential to firstly consider **normal** temperature control. Therfore, this reveiw opens with an introduction to current theories of the highly complex mechanisms of thermoregulation, focusing in particular on heat loss and the body's response to this.

1 TEMPERATURE REGULATION

1:1 The Thermal Steady State

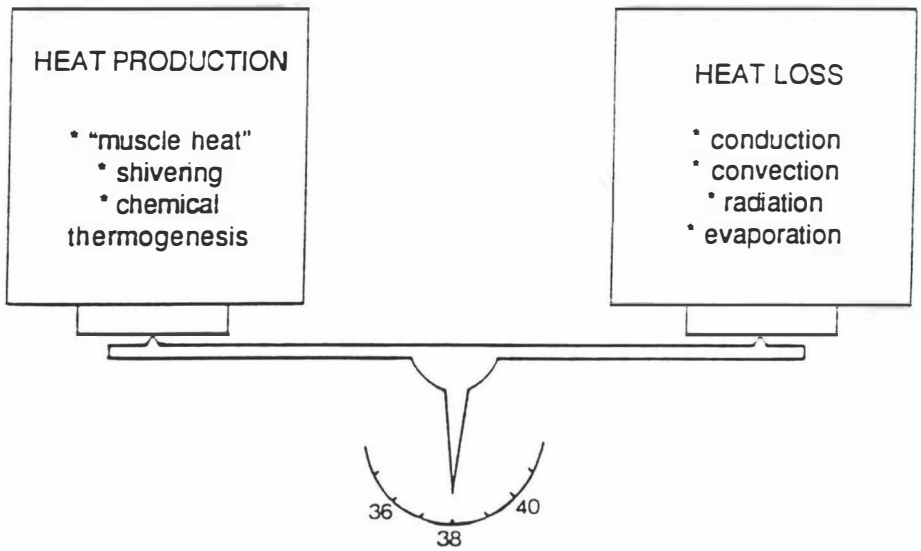
Body temperature is regulated by a complex process which, like any control system, consists of three essential components. Firstly, a measuring device to detect changes relevant to the system; secondly, a mechanism for integrating and assessing these changes; and finally, an effector mechanism which responds to the instructions of the integrator and alters the behaviour of the control system in an appropriate manner (Richards, 1973). Changes in body temperature are detected by peripheral thermoreceptors and thermosensitive neurons located in the central nervous system. Thermal information is then modified at the spinal cord, hind and midbrain levels prior to final processing and assessment in the central temperature control centres.

Major body systems (particularly the cardiovascular, musculoskeletal and respiratory systems) are employed by these thermoregulatory centres to modify body heat by means of complex mechanisms that increase heat production, or minimize heat loss, or aid in heat dissipation.

Clearly, the maintenance of a constant body temperature is the achievement of a dynamic, multi-faceted, highly integrated control system. In the simplest terms however, the process of thermoregulation can be viewed as a delicate set of scales, see-sawing to maintain a relatively uniform body temperature by balancing heat production and heat loss (Figure 1). Therefore, a thermal "steady state" can exist only when the net effect of the body's heat production is balanced by the net effect of body heat loss. But why is it so important for the body to maintain this thermal "steady state" ?

The maintenance of a constant body temperature is of profound physiological importance because metabolic capacity is closely allied to temperature. Within the narrow range of temperatures tolerated by an organism, metabolic rate increases with

Figure 1. **The "Thermal Balance"**



increasing temperature and decreases with decreasing temperature in a very regular fashion (Keeton, 1980). According to the laws of thermodynamics, the rate of a chemical reaction varies with its temperature. This basic law is applicable to enzyme controlled intracellular chemical reactions, however, a change in temperature also changes the **character** of these complicated biological processes. Protein denaturation (and therefore enzyme breakdown), begins at about 42^{0}C in mammalian species, while ice-crystal formation occurs at -1^{0}C. However vital organ function fails at internal temperatures significantly higher than freezing (Imrie and Hall, 1990). As the optimal performance of body enzymes is confined to a very narrow temperature range, normal body function is dependent on the maintenance of a precise internal temperature (Ganong, 1983). When this temperature deviates significantly from "normal", metabolic function deteriorates and death may ensue. How to maintain this near constant body temperature in the face of dramatic temperature changes in their environment is a common problem facing all animals. Different groups of animals have evolved remarkably different solutions to this common predicament of balancing heat production and heat loss.

1:2 Endothermy

The intracellular oxidation of carbohydrates, fats and proteins in the formulation of adenosine triphosphate (ATP) produces energy, most of which is released in the form of heat. The vast majority of organisms promptly lose most of this heat to their environment, however a small number of animals (principally mammals and birds) have evolved to utilize metabolic heat to maintain a relatively high, almost constant body temperature. Unlike poikilotherms, more accurately known as **ectotherms**, (organisms with variable body temperature) whose activity is rigorously regulated by temperature changes in their environment, these animals maintain a high metabolic rate and thus a high level of activity, independent of environmental temperature fluctuations. This ability to harness internally produced heat to help maintain a precise, relatively high internal temperature is referred to as **endothermy**. Organisms that approach the problem of balancing heat production and heat loss in this manner are known as **endotherms** or **homeotherms** (Keeton, 1980).

Endothermy offers many advantages, but to think of ectotherms as extremely simple, "cold blooded" creatures incapable of thermoregulation is a greatly oversimplified view. Despite the fact that the remainder of this introduction will only discuss thermoregulation in endotherms (by far the majority of small animal patients seen in companion animal veterinary practice e.g. dogs, cats, small rodents and birds), it is extremely important to realize that ectotherms are capable of maintaining their body temperature within a fairly narrow range and that some ectothermic lizards actually maintain an internal temperature 2-3^{0}C higher than their distant "warm-blooded" relatives. Endotherms and ectotherms **both** employ sophisticated physiological and behaviourial mechanisms to regulate heat production and heat loss. The manner in which endotherms achieve this will be discussed next.

1:3 Heat Production

A variety of basic chemical reactions continually contribute to body heat production. **Metabolism** simply refers to the sum of chemical reactions occurring in the cells of the body (Keeton 1980), but because all the energy released by metabolic processes eventually becomes heat, **metabolic rate** can be considered as a measure of the heat liberated by these reactions. Therefore, factors that increase or enhance cellular chemical activity also increase metabolic rate and thus heat production. Such factors include the simple effect of temperature on cellular enzyme activity and the release of certain hormones and neurotransmitters, (e.g. thyroxine, epinephrine and norepinephrine) (Guyton, 1991).

Although heat is continually produced as a by-product of nutrient oxidation, this is not the body's major heat source. The main provider of the heat required to sustain high levels of metabolism is skeletal muscular activity (Ganong, 1983).

1:3 (i) *"Muscle" Heat*

The skeletal muscle system is capable of generating vast amounts of heat. During exercise (i.e. muscular work), more than 80 per cent of the body's heat content is produced in skeletal muscle, but even the simple maintenance of normal muscle tone contributes significantly to body heat production (Andersson, 1977). The cleavage of the ATP molecule to adenosine diphosphate (ADP) with the release of the high energy phosphate bond provides energy for muscular activity, but is in fact, a highly inefficient process. Less than 20 per cent of a muscle's energy input is converted into work; the remainder is liberated as heat. Much of the energy required for normal muscular contraction is simply to overcome the viscosity of the muscles themselves and the viscosity of other body tissues so that movement can occur. This in turn produces friction within these tissues which yields additional heat (Guyton, 1991).

When normal heat production is exceeded by heat loss to the environment, supplementary heat can be generated in the skeletal muscle mass through the activation of shivering.

1:3 (ii) *Shivering*

While muscular work refers to the voluntary, controlled movement of muscle groups, shivering is the repeated synchronous contraction of both flexor and extensor muscles resulting in an involuntary muscle "tremor". Shivering is a powerful, involuntary response to cold. It is an autonomic process which utilizes the skeletal muscles normally under voluntary control to produce a sharp rise in metabolic rate, oxygen consumption and most importantly, heat production (Bligh, 1973; Noxon, 1983). As oxidation is the most important cellular metabolic process, it is possible to determine an animal's heat production indirectly by measuring the consumption of oxygen (Ousey, 1990). During sudden exposure to cold, shivering provides the major contribution to the rapid production of heat, increasing oxygen consumption (and thus body heat production) by up to 400 per cent (Andersson, 1977).

1:3 (iii) *Non Shivering Thermogenesis and Enhanced Cellular Metabolism*

An increase in heat production in animals exposed to cold may also occur in the absence of shivering or voluntary muscular activity due to so-called "**non-shivering thermogenesis**" (Andersson, 1977). Heat released by non-shivering thermogenesis is a product of fatty-acid oxidation and is believed to result, at least partially, from the ability of epinephrine and norepinephrine to uncouple oxidative phosphorylation in various "thermogenic tissues" (principally muscle and brown adipose tissue) (Guyton, 1991). During normal oxidative phosphorylation, enormous amounts of energy are "trapped" in the phosphate bonds of ATP molecules. When mitochondria are stimulated to oxidize nutrients in an uncoupled manner, ATP formation is negligible and almost all of the released energy immediately becomes heat. The relative

contribution of non-shivering thermogenesis to total body heat production is debatable and appears dependent on species, degree of maturity and extent of cold acclimatization (Bligh, 1973). When an unacclimatized adult human is exposed to cold, only a small rise in heat production attributable to non-shivering thermogenesis (e.g. 10-15 per cent) may occur. However in human neonates, uncoupled oxidative phosphorylation in musculature and brown fat, may increase metabolism and thus the rate of heat production by as much as 100 per cent (Bligh, 1973; Guyton, 1991).

Metabolic heat production increases progressively during cold exposure due to an increase in cellular metabolic rate mediated via the sympathetic nervous system. The release of norepinephrine by sympathetic nerve endings and to a lesser extent, the adrenal release of epinephrine, results in an almost instantaneous rise in cellular metabolism in many body tissues. Heat production is increased as consequence of free fatty acid production, blood glucose concentration and the effect of catecholamines on cell membrane permeability.

Catecholamine enhanced lipolysis results in the release of free fatty acids from white adipose tissue, while blood glucose concentrations increase as a result of hepatic glycogenolysis and gluconeogensis stimulation. Neither of these events liberate vast amounts of heat, but they are crucial to an overall increase in heat production because they generate the substrates for enhanced cellular metabolism in other tissues. In contrast, the catecholamine mediated changes in cell membrane permeability can directly generate large quantities of heat. Catecholamines selectively increase the permeability of many cell membranes to the passage of cations. This has a direct calorigenic effect in smooth muscle, where the resultant Na^+ and K^+ flux leads to cellular depolarization and a concomitant increase in the tone and rhythm of these tissues. But more importantly, heat is generated in many tissues as a result of increased active transport. In order to maintain normal concentration gradients the Na^+/K^+ active transport mechanism must now work harder to "pump" Na^+ out of the cell and K^+ into the cell across the catecholamine induced "leaky" membrane. The energy required to

drive the sodium-potassium pump is derived from the conversion of ATP to ADP. As previously discussed, the cleavage of the ATP molecule is a highly inefficient process. Only a small proportion of the released energy is used to power the pump; the remainder is liberated as heat (Webster, 1974).

Cold exposure indirectly stimulates an increased output of thyroxine by the thyroid gland. Thyroxine also has a calorigenic effect, increasing the rate of nutrient oxidation and potentiating the calorigenic effects of catecholamines (Bligh, 1973). However this aspect of thermogenesis involves a much more delayed increase in cellular metabolic heat production, with cellular enzyme systems taking up to several weeks to show an increased level of activity following thyroxine stimulation (Guyton, 1991). The action of catecholamines and thyroxine on cellular activity is referred to as **chemical thermogenesis**; heat production due simply to enhanced cellular metabolism. But if endotherms are to maintain a thermal steady-state, the body's net heat production must be balanced by an equivalent heat loss.

1:4 Heat Loss

Heat is lost from body surfaces, principally the skin and lungs, via the following processes: **conduction, convection, radiation and evaporation** (Richards, 1973; Andersson, 1977; Ganong, 1983; Guyton, 1991). In addition, small amounts of heat are lost with the voiding of faeces and urine. The methods of heat loss, also known as "channels of heat exchange", may be explained as follows:

1:4 (i) *Conduction*

Conduction refers to heat exchange between objects at different temperatures that are in direct contact with one another.

The amount of heat transferred by this channel is proportional to the temperature difference between the objects, known as the **thermal gradient**. Under normal circumstances, conduction to other objects accounts for only minor losses but conduction to air represents a sizeable proportion of the body's total heat loss (about 15 per cent in man) (Guyton, 1991). Heat is carried by conduction when molecules of substances collide with one another. If air temperature is cooler than the skin, this energy can be transferred down the thermal gradient to the air immediately adjacent the body's surface. Once the two temperatures equilibrate, no further heat transfer can occur via this route unless the heated air moves away from the skin, allowing unheated air to take its place thus re-establishing the thermal gradient. This phenomenon is known as **convection.**

1:4 (ii) *Convection*

Natural Convection occurs when air molecules in direct contact with the skin are warmed (via conduction) causing them to expand and decrease in density. As the air rises it is replaced by new, unheated air. This movement of air molecules results in the production of "**convection currents**". In contrast, **forced convection** results from an external force or pressure (e.g a fan) increasing the flow of air past the body surface with heat loss increasing accordingly (Richards, 1973). Convection currents not only carry heat away directly but also increase the loss by evaporation, and this process will be explained following a brief discussion of radiation.

1:4 (iii) *Radiation*

Radiation refers to the transfer of heat in the form of infrared electromagnetic waves, between objects not in contact with one another. All objects that are not at absolute zero temperature radiate "heat waves" in all directions. Thus an animal not only emits long wavelength radiant energy but also receives it from objects in its environment, in addition to short wavelength energy from the sun. However as long as body

temperature is greater than that of the surroundings, the net transfer of heat is away from the animal. In man, radiation accounts for nearly 60 per cent of normal heat loss (Guyton, 1991). The proportion of total heat loss occurring by this channel depends not only on the thermal gradient between the body surface and the environment but also the effective radiating area (Richards, 1973).

1:4 (iv) *Evaporation*

Under normal conditions, nearly 25 per cent of the heat produced by man at rest is lost via the evaporation of water from the skin and respiratory tract. If the temperature of the surrounds is less than that of the body, heat will be lost **passively** as an inevitable consequence of breathing. Cool dry inspired air is warmed to body temperature and saturated with water vapour as it flows through the upper respiratory tract.

The humidification of inspired gas is particularly important with respect to evaporative heat loss as the conversion of water from the liquid to the gaseous phase requires considerable energy in the form of heat. This "latent heat of vaporization" consumes approximately 0.58 Calories of heat per gram of water vaporized. A certain amount of water is vaporized at all times. Its loss is termed "insensible" and cannot be controlled for the purposes of thermoregulation because it results from the continual diffusion of water molecules through the mucous membranes of the respiratory tract, regardless of body temperature.

The rate of evaporation is dependent on the vapour-pressure gradient that exists between the animal and its environment. Lack of air movement impedes effective evaporation in a manner similar to that which reduces effective cooling by conduction. Once the air immediately adjacent the to body surface becomes saturated with water, the vapour-pressure gradient ceases to exist preventing further evaporation. Convection currents enhance evaporation by removing moisture-saturated air and allowing unsaturated air to come in contact with the evaporative surfaces of the body (Richards, 1973; Guyton,

1991).

Thus in simple terms, the physical forces governing the channels of heat loss depend largely on the presence of thermal and vapour pressure gradients between the body surface and the environment. A thermal steady-state can exist only when heat production and heat loss are in balance; there must be an equilibrium between the heat continuously generated as a by-product of metabolism and that which is continuously lost to the environment by the processes described.

The flow of heat away from its site of production obviously depends on the presence of a significant thermal gradient. As heat flows to body surfaces **before** it is lost to the environment, substantial thermal gradients must also exist **within** the body. Differences in temperature between the various organs and tissues exist simply because different sites are subject to widely varying conditions of heat production and heat loss (Bligh, 1973; Richards, 1973). But with so many different temperatures throughout the various parts of the body which of these is representative of "normal body temperature"?

1:5 Body Temperature

Variations in body heat content make it impossible to assign a single value to "normal temperature". Factors responsible for the fluctuations in body temperature resulting in a normal temperature **range** include; environmental temperature, circadian rhythms, age, sex and level of activity (Andersson, 1977). Therefore the term "body temperature" is somewhat misleading because it implies a precise numerical value for all tissues, which in reality can not be measured (Richards, 1973). As previously explained, the body is not "thermally homogeneous" but is characterized by substantial thermal gradients between the deep organs and the skin. This concept can be used to divide the body into two compartments : a **core** of deep tissues and a **shell** of peripheral tissues.

1:5 (i) *The Core and the Shell*

Although variations in temperature have been demonstrated within the deep tissues of the body, the differences are small and in practical terms the deep organs and structures of the head, neck and trunk may be considered as a single thermal region referred to as the **core**. This is principally a region of **heat production**, the temperature of which is considered to be fairly uniform and stable. The rest of the body - the coat of hair or feathers, the skin and superficial tissues of the entire body and all the tissues of the limbs, forms the **shell** which is characterized by steep thermal gradients (Bligh, 1973; Richards, 1973). Temperature here varies with blood-flow, air temperature, relative humidity and wind velocity and may fall to nearly environmental temperature in an attempt to conserve body heat (Reuler, 1978). Clearly, "constancy of body temperature" - the hall-mark of endotherms, does not apply to the tissues of this thermal region. This is important in the light of studies which indicate that in man greater than 50% of the body may function as "shell"(Richards, 1973). The shell is thus a region of **heat-flow** which acts to protect the near constant temperature of the core (and therefore the thermal steady-state necessary for normal body function) by modulating heat loss to the environment.

Although the core-shell theory greatly simplifies the difficult concept of heat-flow and distribution within the body, it still fails to adequately solve the problem of measuring "normal body temperature". As the region of the shell is neither constant nor uniform it becomes extremely difficult to accurately define the area of the core (and thus the region of near constant temperature), simply because there is no sharp division between the two compartments. Likewise, it is impossible to assign a single value to "core temperature" because this abstract value relates to the unmeasurable means of many different temperatures : mean core temperature is no more measurable than mean body temperature (Bligh, 1973). However it is possible to accurately measure the temperature of precise body sites. Could one of these measurements serve as a meaningful representation of mean body or core temperature?

1:5(ii) *Representative Body Temperatures*

In terms of thermoregulation, the single most significant body temperature is probably that of arterial blood as it leaves the heart. The venous return to the right side of the heart has two principal thermal components : the first draining from the heat-producing core tissues, and the second, draining from the peripheral or shell regions which are more involved in body heat loss. Significant thermal "streams" are present in the great veins and the right atrium but have not been detected in the well mixed blood of the pulmonary artery. The temperature of the blood at this site acts as an index of the mean temperature of the venous return to the heart and is therefore, a near ideal representation of "mean body temperature" (Bligh, 1973).

Could this "mean body temperature" act as a reference point for thermoregulatory studies? It has been shown that the temperature of arterial blood is modified almost immediately after leaving the heart and that appreciable thermal gradients are present along the major arteries of the body (Horvath, Rubin and Foltz, 1950). In addition, blood entering the aortic arch has passed through the lungs - a suspected site of heat exchange. Therefore, the temperature of arterial blood just as it leaves the left side of the heart may be the single most significant representation of "body temperature". But how does this relate to the temperature of blood in the pulmonary artery?

During the 19th century the nature of temperature changes in the blood induced by its passage through the pulmonary circulation, was a subject of raging controversy. Many early reports claimed that blood gained heat as it passed through the pulmonary vascular system, while the majority of later investigators spoke of "cooling in the lungs" - a term still occasionally encountered in the literature. In fact, it would appear that there is **no** difference between the temperature of the well mixed venous return to the heart and that of arterial blood entering the aortic arch. Investigations in the early 1950's demonstrated that near maximal warming and humidification of inspired gases and therefore near maximal heat loss via the latent heat of vaporization, occurs in the **upper**

respiratory tract with negligible heat exchange at the alveolar level. Simultaneous measurements in the pulmonary artery and the aortic arch failed to reveal any change in blood temperature across the lungs (Mather, Nahas and Hemingway, 1953).

The temperature of arterial blood just as it enters the aortic arch is not only a meaningful index of "normal" body temperature; due to its well-mixed contributions from the core and the shell, the temperature of blood at this site is also **rapidly** responsive to **changes** in heat balance resulting from fluctuations in heat production and heat loss. However, the measurement of the temperature of arterial blood leaving the left side of the heart, is clearly impractical and is impossible without extensive and invasive surgery.

To monitor **thermal balance** it is necessary to record both core **and** peripheral temperatures in order to estimate **total** body heat. This is rarely done. In nearly all clinical situations and in the majority of experimental studies, temperature is assessed by placing a thermosensitive measuring device within a natural body orifice (e.g. mouth, rectum, oesophagus), with the purpose of gaining an estimate of core temperature. In the past, physiologists have argued that the single most significant measurement of core temperature is that of the hypothalamus, due to the central role of this structure in thermoregulation. Classical experiments (Hellstrom and Hammel, 1967) demonstrated that local warming or cooling of the anterior hypothalamus resulted in appropriate physiological responses for heat loss or heat gain. Based on these findings, it was thought that hypothalamic temperature per se was the critical temperature or "set point" for thermoregulation. More recently, the concept of the hypothalamus as the sole sensor of core temperature has given way to a theory of multiple thermal sensors distributed throughout the body. Nonetheless, hypothalamic temperature remains a significant representation of **core** temperature, and in recent years the temperature of the hypothalamus has often served as the standard against which other indicators of core temperature are assessed (Cork, Vaughan and Humphrey, 1983). Therefore it is important to understand the relationships between these

temperatures, hypothalamic temperature and that of the blood entering the aortic arch.

1:5 (ii)(a) *Oral Temperature*

In man, oral temperature is generally 0.5^0C lower than rectal temperature but is markedly affected by many factors including the recent ingestion of foods or fluids, mouth-breathing and speaking (Ganong, 1983). The mouth is obviously an unsuitable site for temperature assessment in conscious animals, while inadequate isolation from the outside air, possible gas leakage about the endotracheal tube, and accidental displacement of temperature probes all leading to inaccurate readings, precludes the use of this site in anaesthetized patients (Hall, 1978).

1:5 (ii)(b) *Rectal Temperature*

The most easily obtained index of body temperature in the majority of veterinary patients is of course, rectal temperature. Under steady-state conditions rectal temperature is generally 0.2-0.5^0C higher than that of blood in the aortic arch. It would seem logical to assume that most core tissues have temperatures which are in fact, slightly higher than that of the blood leaving the heart, because aortic temperature (or "mean body temperature") is influenced by cool thermal streams returning from the sites of heat loss in the shell. Thus under normal conditions, rectal temperature is quite possibly a truer representation of mean **core** temperature (Bligh, 1973; Andersson, 1977).

Assessment of rectal temperature is not without some disadvantages; thermometers can perforate the rectal mucosa, and as a temperature gradient exists within the rectum it is important to insert the thermometer to a constant depth and to position the sensor against the rectal wall to avoid inaccuracies due to temperature differences between the rectum and faecal mass (Andersson, 1977). More importantly, during a state of thermal imbalance with resultant changes in body temperature, there is a delay before

a change in the temperature of blood leaving the heart is reflected in the temperature of the rectum. When body temperatures are falling, this delay causes rectal temperature to "lag behind" that of the blood in the aortic arch, effectively **increasing** the temperature difference between the two sites. During periods of rapid cooling e.g. controlled hypothermia in cardiovascular surgery, lags in rectal temperature of up to 3-4^{0}C have been reported in the literature (Trede, Foote and Maloney, 1961). The delayed responsiveness of rectal temperature to changes in other core temperatures makes this site less suitable for dynamic thermoregulatory studies.

Under these circumstances, the use of rectal temperature as an indication of core temperature has been cited as "a major reason for the lack of progress in the understanding of thermoregulatory physiology" (Hall, 1978). However rectal temperature continues to serve as a meaningful representation of deep body temperature under steady-state conditions.

1:5(ii)(c) *Oesophageal Temperature*

Various clinical and experimental trials in both humans (Whitby & Dunkin, 1968 & 1971; Holdcraft & Hall, 1978) and companion animals (Trede et al, 1961; Shanks, 1974) have shown deep oesophageal temperature to be a reliable representation of "mean body temperature." Although the intervening tissues impose some degree of temperature lag during rapid fluctuations in body heat content, deep oesophageal temperature in the nearest approximation to aortic temperature that can be obtained without surgical intervention (Bligh, 1973). However the temperature of the oesophagus is not constant along its length. There is a small but progressive increase in temperature from the upper to the lower oesophagus in conscious humans, while marked temperature variations may be found along the length **and** breadth of the oesophagus in the anesthetized and intubated patient. These temperature differences, which are thought to be due to the cooling effect of inspired gases, decrease in the lower one-third of the oesophagus, with the least variation occurring in the lower one-

fourth (Whitby & Duncan, 1968).

Kaufman (1987) reported on the relationship between the oesophageal temperature gradient and heart and lung sounds as heard by an oesophageal stethoscope in anesthetized people. The position of best sounds (defined as the position within the oesophageal lumen providing the best combination of breath **and** heart sounds) is a fairly cool location. Accurate oesophageal temperature is measured with the thermistor probe positioned behind the heart (i.e. retrocardiac), 12-16 cm deeper than the position of best sounds. Similar studies, comparing oesophageal temperature gradients with heart and lung sounds in companion animal species, have not been published.

1:5(ii)(d) *Tympanic Membrane Temperature*

The temperature of the tympanic membrane has proven to be an accurate and rapidly responsive estimate of hypothalamic temperature in people (Cork, Vaughan & Humphrey, 1983; Imrie & Hall, 1990, Sladen, 1990). Conceptually the tympanic membrane is an excellent site for measurement of core temperature, since it is readily accessible and receives its blood supply from a portion of the same vasculature that perfuses the hypothalamus (i.e. the internal carotid artery) (Shinozaki, Deane & Perkins, 1988).

Contact-type temperature probes can be used to assess core temperature in sedated patients prior to induction, but must be inserted carefully in order to obtain accurate readings and to avoid injury. Reports of patient discomfort and damage to the tympanic membrane (including perforation & haemorrhage) have been published, precluding the use of these probes in alert patients.

An infrared tympanic membrane thermometer has been described recently (Shinozaki et al, 1988). The device determines temperature by measuring infrared radiation emitted by a warm object. It is non-invasive, non-traumatic and appears consistently

accurate over the narrow temperature range (34^0 to 39.5^0C) investigated by the authors.

1:5(ii)(e) *Bladder Temperature*

Temperature probes incorporated in indwelling urinary catheters have been used to measure bladder temperature as an estimate of body temperature in anaesthetized or sedated human beings (Cork et al, 1983; Horrow & Rosenberg, 1988; Imrie & Hall, 1990; Sessler, 1990). The bladder wall is in close proximity to the rectum and would be expected to approximate rectal temperature and therefore be subject to the same temperature "lag" problems seen during rapid changes in body heat content. Under conditions of low urine output this is indeed the case, however bladder temperature is strongly influenced by the amount of urine being produced. When urinary flow is high, urinary catheter temperature closely approximates other indicators of "core" temperature including oesophageal (retrocardiac) measurements (Cork et al, 1983; Horrow & Rosenberg, 1988). Urinary catheter temperature is thought to reflect core temperature because urine is a filtrate of core blood. During conditions of rapid change in body heat content and providing urine production remains high, lags in urinary catheter temperature remain small because the urine has little time to equilibrate with the "cooler" tissues of the bladder wall.

Although urinary thermocouple readings are more accurate than rectal probe measurements, urinary thermocouples are expensive, invasive and are subject to the same problems of temperature lag if urine output is low.

1:5(ii)(f) *Pulmonary Artery Temperature*

Thermistor tipped pulmonary artery catheters enable continuous and highly accurate assessments to be made of core temperature. The placement of a pulmonary arterial catheter is applicable only under special circumstances; the method is invasive, proper placement requires skilled technique and the probes are expensive.

Which of these sites provides the most suitable measurement of "body temperature" in anaesthetized animals?

Cork et al (1983) assessed the precision and accuracy of several commonly employed sites for the measurement of body temperature during general anaesthesia in adult humans. When compared to tympanic membrane temperature (considered as the "true" value of core temperature for the purpose of this trial), oesophageal and bladder temperature measurements provided the best combination of accuracy and precision. The use of these sites was recommended in preference to the tympanic membrane, in order to avoid possible trauma to the ear drum. Similar studies comparing these temperature monitoring sites in domestic animals have not been published. However, the lower fourth of the oesophagus (with the thermistor probe positioned behind the heart) is perhaps "the site of choice" (Whitby & Duncan, 1971) for measuring mean body temperature and assessing rapid fluctuations in body heat content.

1:6 Control of Body Temperature

Body temperature is normally maintained within very narrow limits through the coordinated actions of the sensory, integrative and effector components of the thermoregulatory systems.

1:6(i) *Thermoregulatory Sensors*

Temperature information is obtained from thermally sensitive cells distributed throughout the body. Cells specifically sensitive to either cold or warmth are located in a variety of tissues including the skin, mucosal surfaces, skeletal muscle, deep abdominal structures and spinal cord, as well as numerous areas of the brain stem (Imrie & Hall, 1990; Sessler 1990). The relative density and distribution of these cells in the different tissues in largely unknown, however cold receptors are thought to predominate in more peripheral tissues, particularly the skin. Whilst thermal receptors

have been localized anatomically, their precise histological appearance has not yet been characterized. Some studies suggest that cutaneous thermal receptors are in fact small, unmyelinated "free" nerve endings (Simon, Peirau & Taylor, 1986; Spray, 1986). It would appear that warm "impulses" are conveyed by C fibres whereas cold signals travel primarily via A-delta fibres, although this is not absolute (Sessler, 1990). Cutaneous cold-sensitive cells increase their firing rates as skin and environmental temperatures cool and are inhibited by warmth; the converse is true for warmth receptors. The exact mechanism by which these receptors transduce thermal stimuli into nervous impulses is also unclear but is thought to involve a temperature dependent electrogenic sodium pump, or possibly a temperature dependent variant of the well known sodium/potassium pump. It is known that thermal receptors transduce information on both steady-state and transient temperatures, thus the response to a thermal stimulus is a function of the absolute temperature as well as the rate of temperature change (Simon et al, 1986).

Even less is known about the nature and exact location of deep body-thermal receptors. However, warm sensitive splanchnic and both warm and cold sensitive vagal nerve fibres have been identified in a number of mammalian species (Bligh, 1973; Simon, et al, 1986). Most ascending thermal information is carried via the spinothalamic tracts in the spinal cord, although no single tract is critical for conveying thermal signals.

The possible existence and thermoregulatory role of temperature sensitive neurons in the brain was first proposed by Bergmann in 1845 (Richards, 1973). The theory gained support when it was shown that artificial heating or cooling of the brain resulted in appropriate thermoregulatory responses. It is now known that thermosensors exist in many areas of the central nervous system including the hypothalamus (in particular the preoptic region of the anterior hypothalamus), midbrain, medulla, pons and spinal cord (Boulant & Dean, 1986). It is unknown if central thermoreception is accomplished by specific cells or if it is the result of temperature dependent changes within neural networks (Imrie & Hall, 1990).

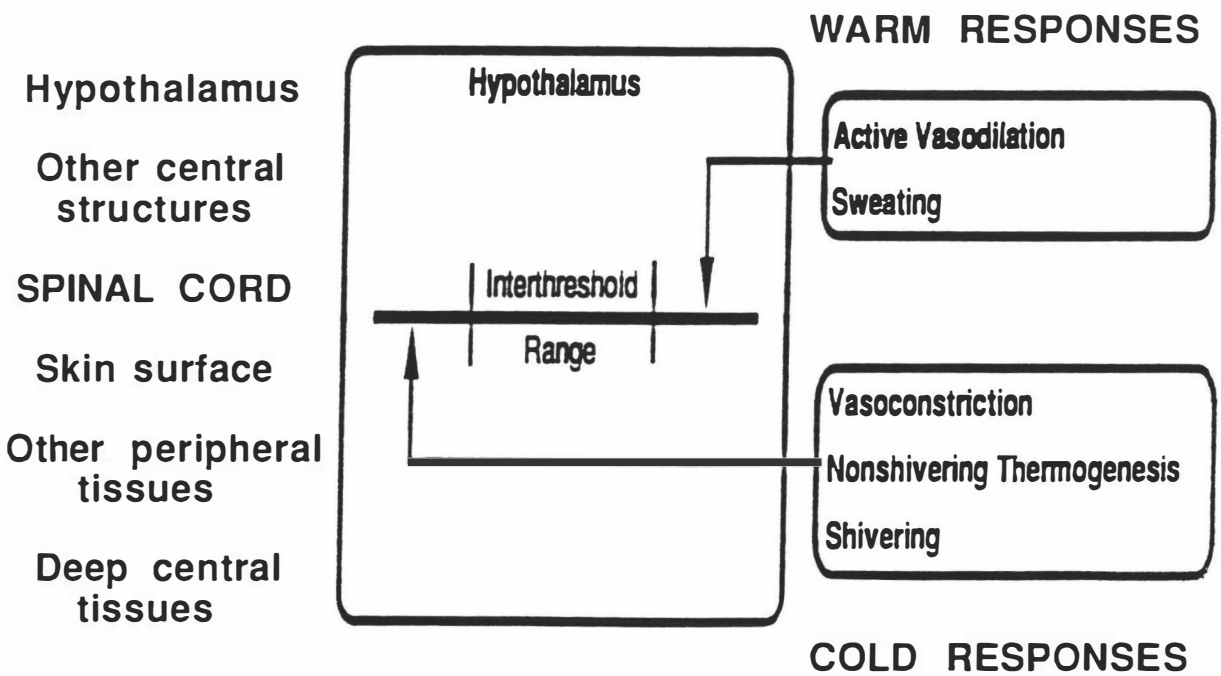
1:6(ii) *Processing and Integration of Thermal Information*

Body temperature is regulated by a complex control system which measures changes in body heat content; integrates and assesses this thermal information; and employs behavioural and autonomic mechanisms to minimize deviations from "normal." As previously discussed, variations in body heat content (as an absolute value and within the body itself) make it impossible to assign a single value to "normal" body temperature but rather, result in a normal temperature **range** which is strictly regulated. It is well known that the body is **not** "thermally homogeneous" and that specific thermosensors are located in many different tissues including tissues within those regions traditionally considered "shell" and "core". The complexity of assessing and integrating thermal information from the various parts of the body including the surface, peripheral and deep structures now becomes obvious. How does the body process, integrate and interpret the thermal information it receives?

It was thought that specific hypothalamic centres acted as the body's "thermostat", with the actual temperature of certain neurons (representing the true value of core temperature) being compared to a centrally mediated reference or "set point". Current theories now propose that endotherms assess body temperature by comparing thermal inputs from a variety of deep and peripheral tissues, with **threshold** temperatures for heat and cold. While the hypothalamus is most certainly the dominant thermoregulatory site, its own temperature per se is thought to be a relatively small fraction (perhaps as little as 20%) of the total thermal input it receives. The **interthreshold range** spans about 0.4^{0}C (Sladen, 1990; Sessler, 1991) and refers to the difference between the lowest "warm" and the highest "cold" threshold temperature values. Despite the fact that humans (and presumably other mammals) can detect minute temperature changes (people can detect temperature variants as small as 0.003^{0}C), thermoregulatory responses do not occur within this interthreshold range (Figure 2). Thermoregulatory responses are based on **mean** body temperature; - a physiologically weighted "average" reflecting the thermoregulatory importance of the different tissues and their thermal

inputs (Sessler 1990 & 1991). Thus, thermal information from different skin and peripheral regions is processed in several different ways, perhaps reflecting the importance of thermal information for regulatory purposes versus a purely perceptive function (Simon et al, 1986). How the body determines absolute threshold temperatures is unknown but the mechanism appears to be mediated by central neurotransmitters including norepinephrine, dopamine, 5-hydroxytryptamine, acetylcholine, prostaglandin E and various neuropeptides (Lipton & Clark, 1986; Sessler, 1990). Threshold temperatures vary daily and may be altered by exercise, food intake, anaesthetics and other drugs and certain endocrine diseases (notably hypothyroidism).

Figure 2. **Thermoregulatory Control: the interthreshold range and the thresholds for warm and cold responses.**



Although the hypothalamus is the dominant centre for processing of thermal data, most temperature information is **preprocessed** in the spinal cord and brain stem (Sessler, 1990). Substantial modification of thermal signals occurs at the spinal level. Dorsal horn neurons are involved in the spatial summation of converging warm and cold afferent messages which then project to the lower brain stem nuclei via spinothalamic tracts. Thermal information from skin surface areas such as the face and ears, appears to be transmitted to thalamic nuclei via the trigeminal nucleus in a relatively uninterrupted process. The thalamic, raphe and other midbrain nuclei are key sites for the processing and integration of both central and peripheral thermal stimuli. Recent studies suggest that ascending thermal information is processed in series, passing through the raphe nuclei and the thalamus before converging on the preoptic anterior hypothalamic regions (Gordon and Heath, 1986). It appears that a hierarchical system exists. Thermal information is successively processed in the spinal cord, lower brain stem and midbrain prior to reaching the temperature regulating centres of the hypothalamus, with the lower centres modifying thermal inputs to the higher, more precise regulatory control systems (Sessler, 1991).

1:6(iii) *Thermoregulatory Effectors*

With the exception of sweat glands and brown fat, there are no specific effector tissues or organ systems that function solely to regulate temperature. Instead, major body systems which normally subserve other physiological functions are employed by the central nervous system to modify heat production and environmental heat loss. These include the musculoskeletal system with involuntary shivering, the cardiovascular system for the control of skin temperature, and the respiratory system which modifies evaporative heat loss (Crawshaw, 1980; Gordon & Heath, 1986).

As previously discussed, current theories now suggest that endotherms assess "body temperature" by comparing integrated thermal inputs with threshold temperatures for heat and cold. When the total thermal input exceeds one of these thresholds,

appropriate effector responses are initiated, returning body temperature to "normal" (Sessler, 1990 & 1991). While the temperature control centres of the hypothalamus are ultimately responsible for "the orchestration of responses to distant thermal sensors" (Sessler, 1991), significant thermoregulatory efforts can be generated by other areas of the central nervous system, most notably the spinal cord.

The effector responses can be categorized into several broad groups based on the following criteria:

(i) the response effectors which control heat production versus those which control heat loss;
(ii) autonomic versus behavioural responses;
(iii) responses which operate via neuronal mechanisms as opposed to those which act via hormonal regulation.

Each thermoregulatory effector has its own threshold temperature (for activation) and response intensity, so that there is an orderly progression of responses and magnitude of response in proportion to need. In general, energy-efficient mechanisms such as peripheral vasoconstriction are maximized before metabolically expensive responses such as shivering are initiated (Sessler, 1990).

Quantitatively, behavioural thermoregulation is probably the most important effector mechanism for the maintenance of constant body temperature. All motile organisms possess the ability to respond to adverse temperatures by varying posture, insulation and choice of habitat. Behavioural responses are stimulated by a sense of thermal discomfort and therefore tend to depend more heavily on thermal information from skin and peripheral sensors, as opposed to an integrated "whole body" temperature assessment. However, behavioural thermoregulation is also initiated by changes in mean body heat content. Behavioural thermoregulatory responses such as huddling or limb extension, seeking shade or sun, wallowing and saliva spreading, can be thought

of as metabolic "cost savers". Conscious awareness of thermal discomfort coupled with an appropriate behavioural response, anticipates and minimizes the change in mean body temperature which would otherwise occur and thus "spares" the more energy expensive autonomic effector processes. Most importantly, behavioural temperature regulation greatly extends the range of environmental conditions in which an animal can survive and has allowed some species to populate regions of the world in which homeothermy could not be maintained by autonomic effectors alone (Bligh, 1973).

Hypothermia is a state of subnormal body temperature that results when heat loss from the body surpasses heat production (Wang & Peter, 1977). Normally, a body temperature lower than the cold response "threshold", triggers responses which work to minimize further heat loss and to restore body temperature to within the normal interthreshold range. However if the efficacy of these responses is reduced, tight control of mean body temperature will fail, allowing the temperature of the environment to have a more profound influence on body heat content. Accidental hypothermia has long been a recognized complication of general anaesthesia and is still a common problem. General anaesthetic agents are administered to veterinary patients for a variety of reasons including; restraint; to aid examination; to permit manipulations; and to lessen awareness, pain and muscle reflexes so that surgical procedures can be performed in a humane manner. General anaesthesia is best described as a state of unconsciousness produced by a controlled, reversible intoxication of the central nervous system. What effect does this "intoxication" have on the complex neuronal pathways of temperature control? How do the processes of surgery and anaesthesia attenuate the normal mechanisms of thermoregulation? Why do anaesthetized patients become so cold?

2. THE EFFECTS OF ANAESTHESIA ON TEMPERATURE REGULATION

Regulation of body temperature is severely impaired by the administration of general anaesthetic agents. Autonomic and behavioural responses to external and internal thermal stresses are diminished so that deviations in body temperature that elicit vigorous thermoregulatory responses in normal conscious animals, elicit diminished or no responses in anaesthetized animals (Hammel, 1988).

During surgery and anaesthesia, several factors combine to interfere with normal thermoregulation. These include the abolition of behavioural responses, diminished hypothalamic function, reduced metabolic rate, reduced effector responses, and abnormally large thermal stresses (Imrie & Hall, 1990).

2:1 Mechanisms of Perioperative Heat Loss

In the anaesthetized patient, heat production is markedly decreased due to a reduction in both metabolic and normal postural muscular activity. Conversely, heat loss (via the normal channels of radiation, conduction, convection and evaporation), is enhanced.

2:1(i) *Radiant Heat Loss*

Although radiant heat loss is not normally excessive in clothed humans or in animals with a normal hair coat, it becomes increasingly important in the anaesthetized patient. Radiation refers to the transfer of heat in the form of infrared electromagnetic waves, between objects not in contact with one another. All objects not at absolute zero temperature will radiate heat waves but as long as body temperature is higher than that of the surrounding objects, the net transfer of heat is away from the patient. Therefore, anaesthetized patients will effectively "warm up" the walls, floor and solid objects of the operating room, losing heat in the form of radiant energy (Bissonnette, 1991).

2:1(ii) *Conductive Heat Loss*

Conductive losses are equal to the temperature difference between the skin and adjacent surfaces with which the patient makes direct contact. Placing patients on cold, noninsulated operating tables; cleaning the skin with cold preparatory solutions; administering cold intravenous fluids or blood products; and flushing exposed tissues or body cavities with cold irrigating solutions, results in significant heat loss (Morrison, 1988).

An additional source of conductive heat loss occurs between the patient and the air. Morris (1971) and Morris and Wilkey (1970) concluded that ambient temperature was the major factor determining body temperature during anaesthesia. Heavily gowned surgeons are comfortable with operating room temperatures of 16^0 to 18^0C. Anaesthetized human adults however, require room temperatures of at least 22^0 to 24^0C in order to remain normothermic; children a neonates require even higher temperatures. While optimal environmental temperatures for anaesthetized animals have not been published, the chilling effects of cold operating rooms have been reported in numerous publications (Dale, Elefson and Niemeyer, 1968; Waterman, 1975; Haskins, 1981). In one study (Dale et al, 1968), normal dogs anaesthetized with sodium pentobarbital were exposed to room temperatures of 32^0, 27^0, 21^0, 16^0 and 10^0C. Rectal temperatures were measured at 30 minutes intervals. Hypothermia was apparent in all dogs exposed to air temperatures less then 27^0C. Decreases in rectal temperature ranged from one to five degrees at room temperatures of 27^0, to ten to eighteen degrees at room temperatures of 10^0C. When exposed to the coldest environmental temperatures (10 & 16^0C), hypothermia was progressive and frequently fatal.

2:1(iii) *Convective Heat Loss*

Air currents greatly increase the transfer of heat from skin, and exposed muscles and viscera to air, by continually removing the warmed air immediately adjacent to the patient. Modern surgical suites have room air exchanges of 15 to 30 times per hour, effectively creating a continuous "draft". Energy transfer via convection accounts for 25 to 35% of total intraoperative heat losses in anaesthetized people (Morrison, 1988).

2:1(iv) *Evaporative Heat Loss*

Insensible water loss accounts for nearly 25% of the total heat dissipated in anaesthetized adult humans (Bissonnette, 1991). Serosal evaporation of extra cellular fluid from the pleura, peritoneum and exposed viscera, can be a dramatic source of heat loss (Sladen, 1990). In fact evaporative heat loss from a large surgical incision may be equivalent to all other sources of intraoperative heat loss. Additional evaporation occurs as preparatory solutions (in particular, alcohol based solutions) vaporize from the skin.

Insensible losses from the respiratory tract seldom account for more than 5 to 10% of the total heat dissipated during surgery and anaesthesia in human adults (Bissonnette, 1991), however these losses may be dramatically increased in small children and neonates. Heat is lost when cold dry anaesthetic gases are warmed and humidified by water evaporating from the tracheobronchial epithelium. Because minute ventilation on a per kilogram basis is higher in smaller patients (e.g. neonates), respiratory losses may be highly significant, amounting to approximately one-third of the total heat loss. Anaesthetized patients less than 5 to 10 kilograms in body weight, are often maintained on non-rebreathing anaesthetic circuits. These circuits have no carbon dioxide absorbants and instead rely on high fresh gas flows to effectively "flush" the circuit, preventing rebreathing of expired gases. Patients maintained on these circuits are therefore exposed to large volumes of cold, dry anaesthetic gases which must be

warmed and humidified by the respiratory tract.

2:2 Thermoregulation During Anaesthesia

The pattern of temperature change during anaesthesia is well documented. It consists of an initial precipitous fall in body temperature which occurs during induction and the first hour of anaesthesia, with a slower reduction in mean body temperature thereafter (Imrie & Hall, 1990; Bissonnette, 1991). In anaesthetized dogs and cats, the most dramatic decreases in body temperature are seen to occur in the first 20 minutes following induction (Waterman, 1975). This is not unexpected considering the relative contributions of radiant, conductive, convective and evaporative heat loss to the overall loss of heat from the body and when these channels of heat loss would be operating maximally.

The loss of consciousness during general anaesthesia abolishes thermal sensation but it is generally believed that thermoreceptor **sensitivity** is not impaired. Similarly, the maximum **intensity** of thermal responses (e.g. vasoconstriction and shivering) appears to be well preserved in the anaesthetized patient. However, all general anaesthetic agents (with the possible exceptions of ketamine and ether) impair thermoregulation, presumably by attenuating hypothalamic function, particularly the coordination of neural elements in the preoptic and hypothalamic nuclei that subserve temperature regulation (Hammel, 1988; Imrie & Hall, 1990; Sessler, 1990 & 1991). The overall effect is to decrease the thermoregulatory threshold for hypothermia, effectively **widening the interthreshold range** over which no thermoregulatory responses occur. Within this range, changes in body temperature are passively determined by the difference between metabolic heat production and heat loss to the environment (Sessler, 1990). In this setting, anaesthetic induced decreases in tissue metabolism, the absence of muscular activity (particularly if the patient is being mechanically ventilated) and exposure to the thermal stresses of the operating room environment, rapidly tilt the scales of thermal balance in favour of hypothermia.

The fact that thermoregulatory responses are still possible during general anaesthesia has been known for some time. Early attempts to intentionally induce hypothermia (to aid neurosurgery), were limited by severe patient shivering, prior to the common administration of neuromuscular-blocking agents (Imrie & Hall, 1990). Active peripheral vasoconstriction has been shown to occur in hypothermic, but not normothermic, anaesthetized patients. Peripheral vasoconstriction occurred at body temperatures significantly lower than those seen in conscious humans, demonstrating a decrease in the normal thermoregulatory threshold for this response (Sessler, Olofsson, Rubinstein & Beebe, 1988). In spite of near normal intensity, the activation of such responses is insufficient to actively warm the patient although these mechanisms may reduce and even prevent further heat loss. Thermal steady state requires that metabolic heat production equals environmental heat loss. Therefore, patients must increase heat production and/or decrease heat loss to prevent further hypothermia. Heat loss from the patient to the environment is a function of the difference between skin and ambient temperatures. Heat loss therefore, decreases passively as patients become increasingly hypothermic. Peripheral thermoregulatory vasoconstriction decreases heat loss by 10 to 15% in anaesthetized adult humans. The roles of thermoregulatory mechanisms such as vasoconstriction and initiation of nonshivering thermogenesis have not been reported in animals (Bissonnette, 1991).

2:3 The Effects of Anaesthetic Agents on Temperature Regulation

Anaesthetic agents may have a direct effect on thermoregulation. Quantitatively, behavioural thermoregulation is probably the most important effector mechanism for the maintenance of constant body temperature. Obviously, general anaesthetic agents completely abolish this mechanism, however it is important to remember that any anaesthetic drug with central nervous system depressant effects will also blunt normal behavioural responses. Drugs such as the phenothiazines, butyrophenones, benzodiazepines, alpha-2 agonists and opioids (alone or in combination), are frequently given preoperatively and will result in impaired thermoregulation which may be marked

in the very old or the very young.

Agents with vasodilatory effects (e.g. the phenothiazines, halothane and isoflurane) redistribute body heat to the peripheral tissues and increase the potential for heat loss to the environment (Imrie & Hall, 1990). The initial rapid decrease in core temperature immediately following induction of general anaesthesia appears to be related largely to redistribution of heat within the body. This redistribution of heat does not immediately change **mean** body temperature (Bissonnette, 1991) but by shifting heat to the vasodilated peripheral tissues likewise increases the potential for heat loss.

The volatile inhalational anaesthetic agents also depress normal thermoregulatory responses. Halothane depresses the threshold for peripheral vasoconstriction in human adults by approximately 2.5^{0}C (although this is somewhat dose dependent) (Sessler, Olofsson, Rubinstein & Beebe, 1988). Isoflurane decreases this same threshold by 3^{0}C per percent of isoflurane, measured as the end-tidal concentration (Sladen, 1990). By promoting vasodilation these agents increase radient conductive and evaporative heat loss. By promoting muscle relaxation, they impede heat production.

Neuromuscular blocking agents ("muscle relaxants") contribute to heat loss by reducing muscle tone and abolishing shivering. Opioids with potent sympathomimetic effects (e.g. fentanyl, sufentanil and alfentanil), impede the normal sympathetically driven responses to hypothermia (Sladen, 1990). Despite its lack of potency, nitrous oxide has been shown to inhibit behavioural thermoregulation in mice (Bissonnette, 1991).

Local anaesthetic agents, when used to provide regional anaesthesia (e.g. epidural or spinal blockade) will also contribute to the development of hypothermia. Peripheral vasoconstrictor responses are impeded by sympathetic blockade, while heat generation from normal postural muscle activity is reduced by muscle relaxation. Spinal thermoregulatory and thermosensitive neurons may be depressed while the transfer of

neuronal messages from peripheral thermal receptors may also be blocked (Sladen, 1990).

Therefore, most general anaesthetic agents depress or abolish normal thermoregulatory responses. However, the dissociative anaesthetic agents such as ketamine and tiletamine, have been shown to have less depressant effects on temperature regulation. Rhesus monkeys anaesthetized with ketamine, were able to maintain thermal balance in a manner similar to the unanesthetized state when exposed to ambient temperatures of 18^0, 29^0 and 38^0C (Hunter, Holmer & Elizondo, 1981). A thermal steady state was maintained by appropriate thermoregulatory mechanisms such as peripheral vasoconstriction, shivering, and increased metabolic rate, even though behavioural responses were eliminated.

Ketamine produces a so-called "dissociative" anaesthetic state, a unique form of anaesthesia described as a functional and electrophysiological dissociation between the thalamoneocortical and limbic systems (White, Way & Trevor, 1982). It may be that this drug leaves hypothalamic function relatively untouched, thus allowing normal thermoregulatory processes to proceed unhindered.

Hypothermia occurs commonly during surgery and anaesthesia, due to abolition of normal behavioural responses, anaesthetic induced inhibition of thermoregulatory mechanisms, and exposure of the patient to the thermal stresses of the cold operating room environment. But is this decrease in body temperature detrimental to the patient? What effect does hypothermia have on the body?

3. HYPOTHERMIA AND ITS EFFECTS ON THE BODY

Hypothermia causes a complex array of physiological changes. The initial response of an endothermic organism exposed to a cold environment is to minimize heat loss and increase heat production. Vasoconstriction is profound, oxygen consumption increases, ventilation accelerates, heart-rate, stroke volume and arterial blood pressure increase, and cardiac output is enhanced - all the result of catecholamine release and intense sympathetic nervous system stimulation. As previously discussed, each thermoregulatory effector has its own threshold temperature and response intensity, resulting in an orderly progression of responses and magnitude of response in proportion to need. In general, energy-efficient mechanisms are maximized before metabolically expensive responses are initiated. But if these mechanisms fail, or if they are prevented by the administration of central nervous system depressant drugs (e.g. general anaesthetic agents), mean body temperature will continue to decrease. Mild hypothermia (33 to 34^{0}C) is generally well tolerated in the anaesthetized patient. Although progressive changes in cardiovascular, renal, central nervous system, hepatic and coagulation function are occurring, these changes are not readily apparent until a core temperature of 32 to 33^{0}C is reached (Rupp & Severinghaus, 1986; Morrison, 1988).

3:1 The Effect of Hypothermia on Metabolism

As the body cools, metabolism decreases at a rate of 8 per cent per degree centigrade fall in mean body temperature, decreasing to about 50% of normal at 28^{0}C (Reuler, 1978; Rupp & Severinghaus, 1986). Cooling slows oxygen consumption and carbon dioxide production reflecting the decrease in basal metabolism. Low metabolic rates permit tissue metabolism to remain aerobic, even in the face of a compromised oxygen supply, and minimize toxic waste production.

Carbohydrate metabolism is reduced and hyperglycemia is common. Many factors contribute to the increase in blood glucose levels including decreased insulin release and lowered peripheral utilization. Activation of the stress response promotes glycogenolysis and gluconeogenesis via the release of adrenal catecholamines and glucocorticoids. Renal clearance of glucose is compromised and the enzyme hexokinase, which is inhibited by cold, fails to catalyze hexose transfer across cell membranes.

Protein and fat metabolism are also affected. Body stores of fat and protein are depleted (especially during accidental hypothermia), in response to the release of cortisol, glucagon, epinephrine, norepinephrine and other stress hormones (Wong, 1983).

3:2 The Effect of Hypothermia on the Cardiovascular System

The effects of hypothermia on the cardiovascular system have been studied intensively because of the application of clinical hypothermia in cardiac surgery.

3:2(i) *The Heart*

If the initial sympathetic response to hypothermia is suppressed by general anaesthesia, progressive cooling results in a decrease in heart rate, cardiac output and mean arterial blood pressure, with little change in stroke volume (Wong, 1983). Although the speed of myocardial contractions decreases during hypothermia, the actual force of contraction is not depressed: - in fact contractility actually increases as temperature decreases, reaching a maximum force at about 28^0C (Rupp & Severinghaus, 1986). With continued cooling contractility fails. Heart rate slows to about 50% of normothermic levels at 28^0C and about 20% of normothermic levels at 20^0C in both laboratory animals and people.

Hypothermia leads to progressive changes in myocardial electrical conduction (Wong, 1983; Morrison, 1988; Sessler, 1990). At temperatures less then 28^{0}C, sinoatrial pacing becomes erratic and ventricular irritability increases. At these temperatures dysrhythmias become increasingly common and nodal rhythms, premature ventricular contractions, atrioventricular blocks or ventricular fibrillation may occur spontaneously. The electrocardiogram shows prolongation of the PR & QT intervals and widening of the QRS complex. The ST segment may be elevated or a secondary wave - known as the J or Osborn wave - rising steeply from the S wave, may appear. The J wave has been reported in humans and in many domestic species including the dog (Zenoble & Hill, 1979): it is considered pathognomonic for hypothermia. During any degree of hypothermia, additional factors such as acidosis, hypoxaemia, electrolyte imbalances or sympathetic stimulation, may be sufficient to trigger arrhythmias which would normally be associated with more profound decreases in mean body temperature (Morrison, 1988). Ventricular fibrillation and asystole - when associated with hypothermia - are relatively unresponsive to electrical defibrillation, atropine, electrical pacing and other forms of cardiac resuscitation (Rupp & Severinghaus, 1988).

3:2(ii) *The Circulatory System*

Regional blood flow decreases during hypothermia. Skin, skeletal muscle and the tissues of the extremities show the largest reduction in flow, followed by decreases in the renal and splanchnic beds as the body attempts to maintain flow to the heart and brain (Rupp & Severinghaus, 1986). At a mean body temperature of 20^{0}C, splanchnic flow is decreased to 40% of normal while renal flow falls to less then 8% of normothermic values. Thus the kidneys have the largest proportional reduction in blood flow of all the major organs.

Plasma volume decreases by 25% at 25^{0}C with a corresponding increase in plasma protein concentration. Transcapillary "leakage" results in additional free fluid in all vascular beds and effectively increases the oxygen diffusion distance. Blood viscosity

is also affected. A reduction in temperature from 37 to 25^{0}C in the dog will increase viscosity 173 percent. Haematocrit concentrations increase as intravascular water is lost to the extracellular space. Blood viscosity is an important determinant of peripheral vascular resistance and adequacy of microcirculatory flow. Consequently, intravascular rouleaux formation, red blood cell aggregation and microvascular sludging may become a problem (Morrison, 1988), resulting in cessation of flow to certain areas of the microvasculature.

3:3 The Effects of Hypothermia on the Respiratory System

Cooling has surprisingly little effect on respiratory control. However under anaesthesia, the carbon dioxide tension tends to increase, pH tends to fall, and the patient may become hypoxaemic (Rupp & Severinghaus, 1986). Respiratory strength is diminished at central temperatures less than 33^{0}C. The ventilatory response to carbon dioxide is only minimally affected but experimental evidence suggests a loss of the hypoxic ventilatory drive in hypothermic patients.

Hypothermia alters normal pulmonary function. Bronchomotor tone decreases, producing an increase in both physiological and anatomical deadspace volume. Pulmonary static compliance falls and surfactant production is impaired. Hypoxic pulmonary vasoconstriction is attenuated by hypothermia, while non-specific pulmonary vasoconstriction is enhanced resulting in increased pulmonary vascular resistance. The pulmonary exchange of oxygen and carbon dioxide is not significantly affected by hypothermia, although carbon monoxide diffusion capacity falls significantly at core temperature of 25^{0}C in the dog (Wong, 1983).

3:4 The Effects of Hypothermia on the Central Nervous System

In conscious unmedicated individuals, hypothermia results in an initial phase of sympathetic stimulation and excitement followed by progressive sedation and central

nervous system impairment. Cerebral function is well maintained until central temperatures reach about 33^{0}C. Sedation progressing to a "clouded sensorium" occurs at 31^{0}C, with "cold narcosis" and loss of consciousness occurring at core temperatures below 28^{0}C (Rupp & Severinghaus, 1986; Sessler, 1990). Motor function is similarly impaired. Higher nervous functions, such as locomotion, voluntary movements, hearing and sight are affected first. The more primitive reflexes such as the gag, pupillary constriction and monosynaptic spinal reflexes remain intact until about 25^{0}C.

Experimental evidence suggests that low grade hypothermia (core temperatures of 34^{0}C) protects brain function during episodes of ischaemia and/or anoxia, by reducing metabolic demands for oxygen and glucose. Cerebral blood flow is reduced, however this decrease in flow is proportionate to the reduction in cerebral metabolic rate. Therefore, oxygen requirements are met, high-energy intracellular substrates (e.g. ATP, ADP and phosphocreatine) are preserved, tissue pH is kept within normal limits, and lactic and levels remain low. Unlike general anaesthetic agents which decrease cerebral metabolic rate by depressing neuronal function, hypothermia appears to reduce not only those energy requirements related to function but also the metabolic expenditure necessary for maintenance of neuronal structural integrity (Rupp & Severinghaus, 1986). This is the main reason for the numerous reports of survival (often with normal neurological function), after 25 to 30 minutes of cold-water drowning and submersion; and for the improved survival rates in cardiac surgery when cardiopulmonary bypass techniques are supplemented with deliberate hypothermia.

3:5 The Effects of Hypothermia on Neuromuscular Function

Temperature induced impairment of neuromuscular transmission is well described. Nerve conduction decreases and the release of acetylcholine at the neuromuscular junction is progressively reduced as the body cools. However, peripheral muscle tone increases, resulting in rigidity and myoclonus at core temperatures of 26^{0}C.

3:6 The Effects of Hypothermia on Hepatic and Renal Function

Hypothermia decreases whole body metabolic rate by approximately 8 percent per degree Celsius fall in body temperature, resulting in a marked reduction in hepatic function. **Total** liver blood flow is reduced: hepatic arterial flow falls in proportion to the cold induced decrease in cardiac output, but portal flow is reduced to a lesser extent. Therefore, during hypothermia, the liver is often increased in size with a higher than normal blood volume. This is probably a consequence of the generalized shift in circulating blood volume (from the extremities to the splanchnic beds), that occurs in the presence of an abnormally low body temperature (Rupp & Severinghaus, 1986).

Renal blood flow also decreases with progressive cooling although this reduction is far in excess of that expected solely from the lowered cardiac output. Glomerular filtration rate is reduced by up to 60% at body temperature of 25^{0}C, resulting in a progressive fall in urine output. The ability of the kidney to concentrate or dilute urine decreases as tubular transport of sodium, chloride and water slowly fails, so that urinary composition and osmolality approach that of plasma.

In general, the kidneys appear to function well following episodes of intentional hypothermia (e.g. cardiac bypass surgery) despite the marked reduction in renal perfusion that occurs with cooling. However progressive oliguria and renal failure have been reported in a small percentage of such patients (Rupp & Severinghaus, 1986). Acute renal failure is a more frequent complication of accidental hypothermia (Hudson & Conn, 1974).

3:7 The Effects of Hypothermia on Fluid, Electrolyte and Acid-Base Status

Hypothermia results in a mild metabolic acidosis. Although the exact cause is unknown, tissue hypoxia seems unlikely, despite the reduction in cardiac output and the alterations in regional blood flow. Inefficient renal-tubular resorption of bicarbonate

may play a small role in the production of this metabolic acidosis, but the prominent cause is more likely related to an abnormal flux of ions across cell membranes, due to the effect of decreasing temperature on ionic pumps and membrane channels.

Haemoglobin dissociation is also altered by a reduction in body temperature. Hypothermia shifts the oxyhaemoglobin dissociation curve to the left (Reuler, 1978) reducing oxygen delivery. This is generally not clinically significant due to the concomitant decrease in tissue oxygen requirements and the cold induced increase in blood and tissue oxygen solubility.

In the absence of central nervous system depressants, the initially increased metabolic response to hypothermia draws fluid into cells, resulting in cellular swelling. Loss of water from the vascular space contributes to haemoconcentration and increased plasma protein levels. With the onset of "cold narcosis" water moves out of cells into the extracellular space resulting in haemodilution and oedema formation (Rupp & Severinghaus, 1986; Morrison, 1988).

3:8 The Effects of Hypothermia on Coagulation

Increased bleeding tendencies may be seen in association with hypothermia. Abnormal decreases in body temperature adversely affect platelet function and distribution, plasma clotting factors, and coagulation inhibitors. Progressive thrombocytopaenia occurs as platelets are sequestered in the portal circulation, particularly the liver, with platelets effectively disappearing from the peripheral vasculature at core temperatures of 20^{0}C (Rupp & Severinghaus, 1986). Platelet aggregation is also impaired.

Hepatic function is directly depressed by cooling. Coagulation degradation products are cleared less rapidly and this, in combination with increased blood viscosity, red blood cell aggregation, and microvascular sludging, may result in thrombus formation. In extreme cases (eg. prolonged accidental hypothermia), massive tissue damage,

platelet dysfunction and widespread microthrombosis may result in fulminant disseminated intravascular coagulation. Serum clotting factors are consumed in thrombus formation and are destroyed by the fibrinolytic system which is activated primarily to break down the microthrombi. As platelet numbers and clotting factor concentrations continue to decline - as a result of this hypercoaguable process in addition to the effects of hypothermia, - normal clotting mechanisms fail and significant haemorrhage may occur (Goto, Nonami, Hamasaki, Zucker, Unruh and Arakawa, 1985).

3:9 The Effects of Hypothermia on the Immune System

There is a general concern that hypothermia may render patients more susceptible to infection. Leukopaenia is a consistent finding during hypothermic episodes with up to eighty per cent of circulating neutrophils disappearing from the peripheral circulation of dogs at core temperatures of 23^0C (Rupp & Severinghaus, 1986). Decreased phagocytic ability has also been reported, particularly in polymorphonuclear leukocytes and reticuloendothelial phagocytic cells. Cooling also slows bacterial replication, however most studies indicate that hypothermia compromises host defenses to a far greater extent.

3:10 The Effects of Intraoperative Hypothermia on the Anaesthetized Patient

As previously discussed, **mild** intraoperative hypothermia is generally well tolerated in the normal healthy anaesthetized patient. Despite this, all the changes in organ and body system functions that occur as a direct result of hypothermia, are happening to some degree in the anesthetized patient. Unless some effort is made to conserve body temperature on-going heat loss will dramatically increase the significance of these changes. The effects of intraoperative hypothermia on the anaesthetized patient can be divided into two broad categories: those that occur intraoperatively and those that take place during the recovery period.

3:10(i) *The Intraoperative Period*

It is essential to remember that anaesthesia of itself, has a significant effect on normal body function. Anaesthetic agents are frequently respiratory depressants. They may induce quite profound changes in blood pressure, heart-rate and cardiac contractility, and may sensitize the heart to the effects of circulating catecholamines. Certain agents may alter regional blood flow or cause sequestration of red blood cells. Many drugs require extensive metabolism. Some agents are toxic. Therefore, when the physiological effects of hypothermia are superimposed upon the stresses already placed on the body by the administration of general anaesthetic agents, the consequences of mild hypothermia in the surgical suite may be very different to those observed in the experimental laboratory. In addition, many patients present for surgery with a variety of pathophysiological disorders, all of which may reduce the patient's tolerance of intraoperative hypothermia.

The effect of hypothermia on individual organ and body systems has already been discussed, however, some equally important consequences of hypothermia relate to the effects of cooling on drug action and metabolism. The tissue solubility of volatile inhalational anaesthetic agents is inversely proportional to temperature (Flacke & Flacke, 1986). Therefore tissue uptake will be greater in a hypothermic patient, effectively increasing the potency of these drugs. Cooling itself produces progressive central nervous system depression. Consequently, the minimum alveolar concentration (MAC) of the volatile agents decreases as body temperature falls (Regan & Eger, 1966). This may result in anaesthetic overdose and prolonged recovery times.

Cold induced changes in haematocrit and total plasma protein concentrations may affect the amount of free or unbound drug available to interact with cell membrane receptors. Changes in regional blood flow may significantly alter the amount of drug carried to the brain or the heart. Cold induced neuromuscular depression may potentiate the action of non-depolarizing neuromuscular blocking agents (Morrison, 1988).

Hepatic degradation and excretory functions are greatly reduced, inhibiting drug metabolism and dramatically prolonging the half-life (i.e. duration of action) of these agents. Renal blood flow and metabolism are also impaired. In particular, distal tubular function begins to fail, significantly prolonging the renal clearance of water-soluble drugs and drug metabolites.

Thus hypothermia may have profound effects on the **potency** and specific **action** of anaesthetic agents in addition to altering the ways in which the body normally responds to these drugs.

3:10(ii) *The Postoperative Period: The Metabolic Cost of "Shivering"*

Hypothermia is common during general anaesthesia. It results from a number of factors including exposure to a cold operating environment, decreased metabolic heat production, redistribution of heat within the body, and increased heat loss. In addition, general anaesthesia produces central nervous system depression and, as a direct consequence of this depression, dose-dependent inhibition of normal thermoregulatory responses.

Recovery from general anaesthesia is frequently accompanied by involuntary muscular activity. Post-anaesthetic tremor has been attributed to a broad range of aeteologies including uninhibited spinal reflexes; pain; decreased sympathetic activity; pyrogen release; adrenal suppression; respiratory alkalosis; and most commonly, simple shivering in response to intraoperative hypothermia (Sessler, Israel, Pozos, Pozos and Rubinstein, 1988; Sessler, Rubinstein and Moayeri, 1991). However, the actual mechanism of this tremor remains unknown.

Generalized shivering refers to involuntary muscle tremors or oscillations, involving the muscles of the extremities, neck, pectoral and abdominal regions (Horvath, Spurr, Hutt & Hamilton, 1956). Increased muscular tone generally proceeds the oscillations

(Andersson, 1977) which display a synchronous waxing and waning pattern (Sessler et al, 1988). In contrast, three distinct patterns of post-anaesthetic muscular activity have been identified in human studies. The first is a "tonic stiffening" that occurs in both hypothermic and nomothermic patients. This pattern appears to be a direct effect of the anaesthetic agent (isoflurance) and is not related to body temperature. Comparable non-thermoregulatory tonic muscle activity has also been reported in cats recovering from halothane anaesthesia (Schmeling, Kampine and Warltier, 1989). The second pattern resembles normal shivering. This pattern is seen in hypothermic patients and is generally proceeded by vasoconstriction, supporting the proposal that this is a genuine thermoregulatory response. A spontaneous clonic pattern is the final form of muscular activity observed in the immediate post-anaesthetic period. Clonus occurs when descending cortical control fails to inhibit spinal reflex arcs. During recovery from general anaesthesia, abnormal reflexes such as nystagmus can often be elicited suggesting that there is some anaesthetic induced inhibition of descending control of spinal reflexes. Cortical function is more sensitive than the gamma motor neuron system to the effects of anaesthetic agents, and thus at low concentrations (as would be seen during recovery), the brain may still be "asleep" while the spinal cord is "awake" resulting in increased spinal reflex activity (Sessler et al., 1988). This final pattern is also thought to be thermoregulatory. As spinal cord thermoreceptors have been demonstrated in every mammal and bird so far examined, it may be that this spontaneous clonic pattern of muscular activity is simply a modification of normal shivering or a **normal** thermoregulatory response initiated by the brain stem or spinal cord but **blunted** by residual amounts of anaesthetic agent (Sessler et al, 1988; Sessler et al 1991).

While the "tonic stiffening" pattern of post-anaesthetic muscular tremor does not appear to be a direct thermoregulatory response (i.e. a coordinated central response to a change in body heat content), **any** repetitive muscular activity is thermogenic and will therefore help to normalize body temperature in hypothermic patients recovering from general anaesthesia. However, "shivering" is a remarkably inefficient process, incapable of

maintaining total body heat content for prolonged periods of time. More importantly, post-anaesthetic muscular activity (including true shivering) places huge metabolic demands on the patient which may, in the long-run, be far more detrimental than all the effects of hypothermia discussed so far.

Postoperative shivering is always potentially serious because of the dramatically increased requirements for oxygen to fuel muscular activity. Shivering in conscious human volunteers has been shown to increase oxygen consumption by 300% (Horvath et al, 1956) to over 800% (Benzinger, 1969) and changes of similar magnitude have been recorded in hypothermic patients recovering from general anaesthesia (Bay, Nunn and Prys-Roberts, 1968). Increased oxygen demand requires increased oxygen delivery to the tissues. The only means by which the postoperative patient can increase oxygen transport is to increase cardiac output and therefore, myocardial work. If cardiac output increases sufficiently, the balance between the body's oxygen demand and supply will be met. If not, the concentration of oxygen in the blood will decrease resulting in hypoxemia, tissue acidosis and the start of a vicious and dangerous cycle which may lead to cardiovascular collapse (Flacke & Flacke, 1986).

Other problems related to anaesthesia such as anaemia, hypovolemia, drug-induced hypoventilation and atelectasis, may also be of critical importance in hypothermic patients. Arterial oxygen content is a function of haemoglobin concentration, haemoglobin saturation and the partial pressure of oxygen in the blood (PaO_2). Unlike cardiac output, arterial oxygen content cannot be increased by autonomic nervous system activity. Shivering tissues will extract larger than normal amounts of oxygen from arterial blood resulting in lower than normal levels of oxygen in mixed venous blood. A certain percentage of venous (desaturated) blood will always bypass the lungs; this is referred to as physiological shunt. In the case of a shivering patient, venous blood is desaturated to a greater extent than normal and this effectively magnifies the influence of physiological shunting on arterial oxygen content. The normal response to this phenomenon in conscious hypothermic people, is an increase

in minute respiratory volume usually manifested as hyperventilation (Bay et al, 1968). Patients recovering from anaesthesia may not be able to mount this response: many anaesthetic agents cause dose related respiratory depression, and atelectasis (which increases physiological shunting), is common. If ventilation is not increased, acute respiratory acidosis and arterial hypoxemia will result.

Obviously, the majority of healthy normal patients, are capable of adequately meeting the huge metabolic and physiological demands of post-anaesthetic muscular activity. Other patients are far less tolerant of hypothermia and the body's attempt to increase heat production by means of shivering. In the very old, the very young, and patients with compromised cardiovascular and/or respiratory function, the demands of shivering (in addition to such anaesthetic-induced problems as atelectasis, residual central respiratory depression, alveolar hypoventilation, decreased cardiac output, depressed myocardial function and metabolic substrate exhaustion), may well exceed the capability of these patients to adapt. The final result is systemic acidosis, arterial hypoxemia, cellular substrate starvation and eventual cardiovascular collapse and death (Flacke & Flacke, 1986; Morrison, 1988).

Excessive shivering has also been reported to disrupt wounds, promote bleeding, increase intracranial and intraocular pressure, and result in patient injury (Sladen, 1990).

4: PREVENTION OF INTRAOPERATIVE HYPOTHERMIA

Anaesthetized patients become hypothermic when heat loss to the environment exceeds metabolic heat production. The initial rapid decrease in core temperature which accompanies the induction of anaesthesia, is largely related to a redistribution of heat **within** the body: it is therefore difficult to prevent. Vasodilation allows cool "peripheral" blood to mix with warm "central" blood, decreasing **core** temperatures by 0.5 to 1.0^{0}C (Sessler, 1990). Redistribution of heat does not immediately change **mean** body temperature and of itself, is of little thermoregulatory consequence. However, by shifting heat to the vasodilated peripheral tissues, the potential for heat loss is dramatically increased. Therefore, any technique that limits environmental heat loss will help conserve metabolically derived heat and will minimize the development of intraoperative hypothermia (Bissonnette, 1991; Sessler, 1991).

The classic channels of heat exchange (radiation, conduction, convection and evaporation) and their relative contributions to the development of hypothermia have already been discussed. Techniques for the prevention of intraoperative hypothermia are aimed at reducing the loss of heat occurring via one or more of these channels. Most techniques are **passive**. Heat loss is reduced by raising microenvironmental temperatures (e.g. of the skin or upper airway) to approximate that of the patient's tissues, thereby reducing the patient-to-environment thermal gradient and slowing heat flow. It is rarely possible to **actively** transfer heat **to** the patient, because this requires the presence of a significant thermal gradient between the patient and the heat source; a thermal gradient which is near impossible to achieve without causing burns (Sessler, 1990).

4:1 Controlling Radiant Heat-Loss

4: 1(i) *Control of Environmental Temperature*

Environmental temperature is the single most important factor in determining the **rate** and **degree** of heat loss in an anaesthetized patient (Morrison, 1988; Sessler, 1990; Bissonnette, 1991). Heat "flow" is dependent on the presence of a thermal gradient. Raising room temperature will reduce this gradient and is therefore one of the most simple and effective methods of minimizing heat loss. As previously discussed, adult humans require ambient temperatures of $>21^{0}C$ in order to maintain normothermia during general anaesthesia. Anaesthetized infants and neonates require much higher temperatures, possibly as high as $26^{0}C$. Optimal room temperatures for the maintenance of normothermia in anaesthetized small animals have not been published.

Radiant heat loss is not only dependent on the presence of a thermal gradient: the **size** of the effective radiating area is also very important. Therefore, any measure which limits the extent of the patient's effective radiating area will also limit the amount of heat lost via this channel. Both radiative and convective losses are dramatically decreased by even a single covering layer. Thus a towel, blanket or even simple surgical drapes placed to cover the patient, can considerably increase thermal comfort (Bissonnette, 1991).

4:2 Controlling Conductive Heat-Loss

Direct contact between exposed skin or tissues and colder objects such as the operating table, skin preparatory solutions, irrigation solutions or intravenous fluids, results in the transfer of heat away from the patient via conduction. An additional source of conductive heat loss occurs between the patient and room air; therefore, control of environmental temperature will also help minimize heat lost via the conductive channel.

4:2(i) *Heating Blankets (Mattresses)*

Heating blankets (or mattresses) are commonly used in an attempt to prevent intraoperative hypothermia. Circulating warm-water blankets and electric heating pads have been evaluated repeatedly, and have generally been found to be ineffective in preventing the development of hypothermia in anaesthetized humans (Imrie & Hall, 1990), dogs and cats (Haskins, 1981; Evans, Sawyer and Krahwinkel, 1983; Hubbell, Muir & Harrison, 1985). When used in a conventional manner (i.e. placed under the patient) heating pads are fairly effective in reducing heat transfer from the patient to the operating table. However, their overall efficiency is minimal due to the small degree (less than one-third of body surface area) of patient contact (Sladen, 1990). Circulating warm-water blankets may be more effective when draped over the patient. Haskins (1981) demonstrated a "cocooning" technique (wrapping the patient in a circulating warm-water blanket) to be superior to the use of "space blankets" (reflective metal blankets), infrared heat lamps and hot-water bottles, for the prevention of hypothermia in pentobarbital anaesthetized cats. Unfortunately, cocooning techniques are of limited use during the majority of surgical procedures but may be of benefit in the post-operative period.

Numerous reports have cautioned against the use of electric heating pads, due to the increased incidence of tissue injury and burns seen with this type of heated mattress (Fox, Goring and Probst, 1986). Although considered safer, circulating warm-water blankets have also been reported to malfunction, resulting in patient burns (Crino & Nagel, 1968).

4:2(ii) *Fluid Warmers*

Heat loss due to the infusion of cold intravenous fluids, becomes significant when large volumes of cold crystalloid solutions or blood products are administered to anaesthetized patients (Sessler, 1990). Although these fluids are rapidly warmed to

body temperature (as they mix with blood), this is only achieved at the expense of a considerable amount of metabolic energy. The infusion of one litre of crystalloid solution at room temperature (25^{0}C) to normal human adults, results in the loss of 16 kcal of energy and can decrease core temperature by 0.5^{0}C (Morrison, 1988). Fluid warmers significantly reduce these losses and when combined with other methods of thermal support are effective in minimizing intraoperative hypothermia in anaesthetized humans. Similar studies have not been reported in anaesthetized animals.

4:2(iii) *Additional Methods of Controlling Conductive Heat Loss*

Other methods of reducing conductive heat loss include the use of warmed preparatory solutions, warmed irrigation/lavage fluids, and placing hot-water bottles or hot-water filled surgical gloves next to the patient. The use of warmed preparatory solutions and irrigation fluids minimizes additional sources of heat loss and is helpful when combined with other warming techniques. As with electric heating pads, hot-water bottles and/or hot-water filled gloves should only be used with extreme caution in anaesthetized patients. Due to the high risk of burns associated with their use, these devices should always be insulated from direct contact with the patient's skin and should never be heated to $>45^0$C (Dunlop, Daunt & Haskins, 1989). Furthermore, hot-water bottles/gloves cool rapidly and must be replaced: - if left in contact with the patient the now-cool water will only serve as an additional avenue of heat loss as heat flows down the thermal gradient from the patient's skin to the container.

4:3 Controlling Convective Heat-Loss

As described earlier, most modern surgical suites have room air exchange of 15 to 30 times per hour: - effectively placing the patient in a continuous draft and promoting ongoing heat loss via the phenomenon of convection. Controlling room (i.e. "air") temperature is the single most effective method of minimizing convective (as well as radiative) losses, however good patient "insulation" will provide additional heat loss

protection. An enveloping cover, such as a towel, blanket, plastic sheeting etc. will provide insulation by creating a layer of stagnant air adjacent to the skin. Some heat will be lost as energy is transferred down the thermal gradient from the skin to this air layer but once the two temperatures equilibrate, no further heat dissipation will occur via the convective route. The usefulness of this technique is limited by the type of surgical procedure being performed as its success requires insulation of well over 60% of the body's total surface area (Morrison, 1988).

4:4 Controlling Evaporative Heat-Loss

Evaporation of water from the skin surface and lungs (the so-called "insensible water loss"), results in the loss of heat because the water must undergo a change in state from liquid to vapor - a process requiring energy. Ventilation of the lungs with cool dry anaesthetic gases results in heat loss via two main mechanisms: warming of the inspired gases, and humidification.

4:4(i) *Airway Warming and Humidification*

The heat capacity (i.e. specific heat) of gases is low (Parbrook, Davis & Parbrook, 1991); consequently, only a small amount of energy is needed to warm gases from ambient to body temperature (Bissonnette, Sessler & LaFlamme, 1989). Warming of inspired gases accounts for only 2% of the patient's total heat loss and is of little importance in the development of intraoperative hypothermia. Humidification of dry gases however, consumes a significant amount of heat, which may account for up to 15% of the total heat loss. When water changes from the liquid to a gaseous state heat must be supplied, even though this change of state takes place at a constant temperature. The heat or energy required for this change in state is known as the latent heat of vaporization. This is a measure of energy "input" and is dependent on the temperature at which the change of state occurs: the lower the temperature, the more latent heat required to vaporize the substance. Therefore the amount of heat lost in the

humidification of inspired gases is inversely proportional to the temperature of the gases. The loss of heat via evaporation is also heavily dependent on the water-vapor pressure gradient between the mucous membranes of the respiratory tract and the air. Thus, humidification of cool dry inspired gases (via the evaporation of moisture from the patient's respiratory epithelium), is a far more significant source of heat loss than that needed to warm these gases (Parbrook, Davis & Parbrook, 1991).

Heat loss due to the warming and humidification of anaesthetic gases can be minimized by adding a heater-humidifier device to the anaesthetic circuit. Such a device may be either active or passive.

4:4(ii) *Active Warming and Humidification of Inspired Gases*

Active heater-humidifiers are electrically heated devices which deliver gases to the patient at 37-40^{0}C with 100% relative humidity, containing 44mg H_2O/litre - the equivalent of tracheal air (Sladen, 1990). The potential advantages of such a system include conservation of heat, prevention of post-operative shivering, and a decreased incidence of post-anaesthetic pulmonary complications. Warming and humidification of inspired gases has been shown to result in many patient benefits including a reduction in the incidence of post-operative atelectasis, the maintenance of near normal tracheal ciliary function, the prevention of significant respiratory water loss, and the facilitation of the mucociliary transport system (Fonkalsrud, Calmes, Barcliff & Barrett, 1980). In addition, heating and humidification has been shown to have no adverse effects on the alveolar uptake of anaesthetic gases such as nitrous oxide and halothane (Zeller and Fonkalsrud, 1978). However active heater-humidifiers are not without risk. They are expensive, often bulky, and have been associated with various complications including bacterial/fungal contamination; condensation or "rain-out", causing the failure of valves within the anaesthetic circuit or tubing obstruction; and inadvertent tracheal injury (Morrison, 1988). Tracheal burn or "hot-pot tracheitis" has been reported in patients receiving humidified gases warmed to $>41^0$C. This is due to the low heat

capacity of air which makes it difficult to actively transport large amounts of heat to the patient via the respiratory tract, without risking thermal injury (Bissonnette, Sessler and LaFlamme, 1989). Near complete humidity increases the amount of heat transferred to the trachea and thus the likelihood of burn (Morrison, 1988), due to the high specific heat of water. In addition, the use of ultrasonic nebulizer-humidifiers may result in water overload or intoxication (especially in neonates) (Sladen, 1990; Parbrook et al, 1991), ventilation and perfusion mismatching resulting in hypoxia due to overhumidification (Haskins & Patz, 1980), and increased airway resistance (Parbrook et al, 1991).

Active heater-humidifiers have been shown to be effective in the prevention of anaesthetic induced hypothermia in human infants and neonates (Fonkalsrud et al, 1980). Despite isolated case reports championing the success of this method in human adults, controlled experimental studies have shown heating and humidification of inspired gases to be ineffective when used as the **sole** method of thermal support (Sladen, 1990). Sessler (1991) states that the clinical impression of the technique's success under these circumstances, most likely results from artifactual warming of improperly positioned oesophophageal thermometers; stressing the importance of appropriate temperature monitoring. Airway heating and humidification is more effective in neonates than adults because a greater fraction of neonatal metabolic heat is lost via respiration (Sessler, 1991). In anaesthetized adults, the heater-humidifier is overwhelmed by other sources of heat loss, especially that lost via evaporation in surgical wounds. These losses must be controlled by additional methods of thermal support in order to minimize intraoperative hypothermia and maximize the benefits of airway warming and humidification. The effect of active warming and humidification of inspired gases in the prevention of anaesthetic induced hypothermia has been evaluated in both cats (Haskins & Patz, 1980) and dogs (Raffe & Martin, 1983). In each report the authors concluded that although active heating and humidification slowed heat loss, when used alone, the technique was insufficient to prevent hypothermia.

4:4(iii) *Passive Warming and Humidification of Inspired Gases*

Passive warming and humidification of inspired gases can be achieved effectively with the use of a heat and moisture exchanger; commonly known as an HME or "artificial nose." The early forms of this device consisted of an inlet and outlet screwed together with a mesh of metal sandwiched in between. When connected to the endotracheal tube adaptor, expired water vapor condensed on the metal mesh simultaneously warming the mesh above ambient room temperature. During inspiration the reverse process occurred; the warmed mesh effectively heating the inspired gas while the condensed moisture evaporated, providing some degree of airway humidification.

In more efficient forms of the HME the metal mesh is replaced by a well of paper, foam-sponge or fibrous material, impregnated by a hygroscopic substance such as calcium chloride, lithium chloride or silica gel (Parbrook et al, 1991). As seen with the original metal-mesh, the hygroscopic well absorbs warm water during expiration, allowing this moisture to warm and humidify cool dry gases during inspiration. The amount of water absorbed depends on the type of well (or membrane) and its size. Generally speaking, these devices are capable of warming and humidifying air to a state similar to that produced by the nasopharynx, i.e. 25-30^{0}C with a relative humidity of 50-70% and containing 30mg H_2O/litre (Sladen, 1990). Because the hygroscopic well can become saturated before a large expiration is complete, heat and moisture exchangers are most effective when tidal volumes are small (Bissonnette, Sessler & LaFlamme, 1989). For this reason they may be particularly useful in children and in small domestic animals.

The advantages of the HME include its simplicity, small size, ease of use and cost. The HME appears to be a reasonable alternative to active airway humidification in human adults and children, however the "artificial nose" cannot warm an already hypothermic patient (Bissonnette, Sessler & LaFlamme, 1989; Sladen, 1990). The disadvantages of this device include bacterial contamination and plugging of the well

or membrane with respiratory secretions, effectively increasing airway resistance. The effectiveness of heat and moisture exchanges in the prevention of intraoperative hypothermia in anaesthetized small animals is unknown.

SUMMARY

Body temperature is governed by a complex, highly integrated control system which carefully balances heat production and heat loss. Heat is produced as a byproduct of metabolism, and as a result of muscular work, shivering and chemical thermogenesis; while heat is lost from the body via the channels of heat exchange - radiation, conduction, convection and evaporation. General anaesthetic agents interfere with the normal mechanisms of temperature control. Anaesthetized patients become cold simply because they experience reduced heat production in the face of significant heat loss. Furthermore, hypothermia imposes large physiological stresses on patients who may already be compromised as a result of their age, physical condition or disease process.

Intraoperative hypothermia is well recognized as a common and potentially hazardous complication of general anaesthesia in human patients. While the problem has received little attention in veterinary anaesthesiology, there is little doubt that animals, like their human counterparts, may also experience a complex array of physiological changes as a direct consequence of hypothermia. The management of intraoperative hypothermia must be based on a sound knowledge of the normal mechanisms of thermoregulation, in addition to a thorough understanding of how general anaesthesia interferes with this process. Only then is it possible to understand the significance of hypothermia in anaesthetized patients and to investigate possible means of temperature conservation.

The aim of the following study was to investigate warming and humidification of inspired gases as a means of minimizing the development of hypothermia in anaesthetized cats. Recent successes with the use of Heat and Moisture Exchangers in the human literature, prompted interest in the use of a similar technique in small animal anaesthesia.

MATERIALS AND METHODS

The effectiveness of warming and humidification of inspired gases in the prevention of hypothermia during general anaesthesia was evaluated in six adult, domestic short-haired cats. The cats were anaesthetized using a common induction technique and maintained in a manner common to private veterinary practice within Australia and New Zealand. Prior to inclusion in the study, normal health was evaluated by clinical and laboratory examination : a jugular blood sample being collected for routine haematology and biochemical assessment of hepatic and renal function (Alkaline phosphatase, Alanine transaminase, Blood Urea Nitrogen and Creatinine levels.). The cats; five spayed females and one castrated male, with a mean body weight of 3.4 kg, were obtained from four different sources. They were housed in the Massey University Small Animal Hospital and observed daily for not less than seven days while acclimatizing to the hospital environment.

EXPERIMENTAL DESIGN

Three separate trials were designed to investigate the null hypothesis that warming and humidification of inspired gases does not prevent the development of hypothermia in anaesthetized cats.

Trial I : to evaluate the degree of hypothermia produced by the anaesthetic technique employed in this study. (n=6)

Trial II : to evaluate the effect of **passive** warming and humidification of inspired gases on body temperature in the anaesthetized cat. (n=6)

Trial III : to evaluate the body temperature response of the anaesthetized cat to **active** heating of inspired gases, in combination with the passive warming and humidification technique investigated in Trial II. (n=6).

General anaesthesia was maintained for 120 minutes. The recovery period was then monitored for a further 60 minutes. Non-breathing Mapelson type E anaesthetic circuits were used for maintenance anaesthesia; an Ayres T piece was used in Trials I and II, while in the third trial cats were maintained on the experimental warming circuit. Fresh gas was delivered to the anaesthetic systems at a flow approximating 2½ x Minute Respiratory Volume (500 ml/kg/min). General anaesthesia was maintained with Halothane[1] in 100 per cent oxygen, delivered via a precision vaporizer[2]. Room temperature was measured with a mercury-in-glass thermometer and attempts were made to keep room temperature a constant 23 to 24^{0}C for the duration of each experiment, using an electric fan heater.

Induction Technique

An identical induction technique was applied in each trial. Food was withheld for the 12 hours preceding each experiment, although water was freely available. Sixty minutes before induction each cat was weighed; the heart-rate, respiratory rate and rectal temperature recorded; and a jugular blood sample collected to determine packed cell volume (PCV) and total plasma protein (TPP) levels. Three plastic clothes pegs were placed on the cat's scruff as a handling and restraint aid whilst measurements were recorded during the pre-induction period.

General anaesthesia was induced with an intravenous injection of 1.25% Thiopentone Sodium[3] at a dose rate of 25 mg/kg body weight, administered in small increments to effect. Each cat was intubated with a cuffed endotracheal tube which was rapidly

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1 Fluothane Imperial Chemical Industries.

2 Fluotec Mark III.

3 Pentothal. Abbott Australia Pty Ltd.

connected to the appropriate gaseous anaesthetic circuit.

Passive Warming and Humidification of Inspired Gases

Passive warming and humidification of the anaesthetic gases was achieved by inserting a Heat and Moisture Exchanger[4] (HME) into the anaesthetic circuit at the level of the endotracheal tube adaptor (Figures 3a, 3b and 4). The HME allows expired air to heat and humidify inspired gases in the intubated patient. Warm, water-saturated air expired from the lungs passes over the cooler surface of the microwell paper within the HME. Moisture condenses and is absorbed by the hydroscopic paper surface. Inspired gas passing over the warm, moistened paper, carries a portion of this heat and moisture back to the patient. The HME used in this trial was specifically designed for use in human neonates with tidal volumes of 10-50 millilitres and so is highly suited for use in the cat. The unit has minimal deadspace (2.4 ml), low resistance to-flow (maximum of 12 mm of water at Fl/min) and is small, cheap, lightweight and simple to use.

Active Warming of Inspired Gases

Trial III evaluated the addition of active thermal support to the humidification and warming capacity of the HME.

Warmed gas begins cooling as soon as it flows beyond its heat source. As its temperature decreases, the relative humidity of the gas increases until it reaches 100 per cent, causing water vapour condensation on adjacent objects. This phenomenon occurs in the inspiratory limb of anaesthetic circuits supplying heated gases and is referred to as "rainout". Rapid falls in gaseous temperature and consequent rainout are major problems in the design and function of breathing circuits which employ warming and

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[4] Humid Vent Mini. Gibeck Respiration.

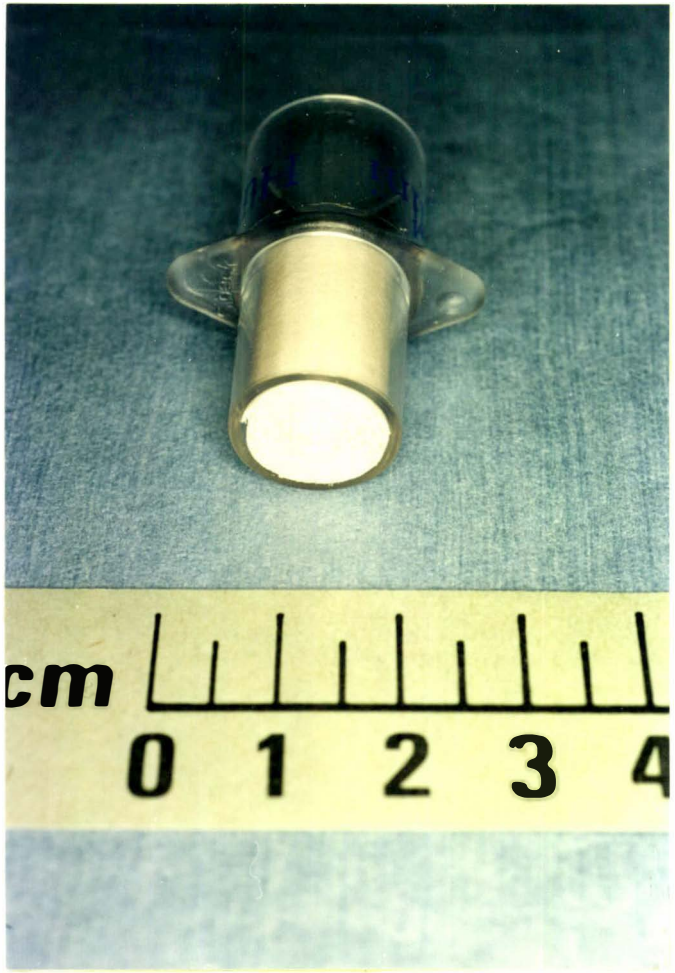

Figure 3a. **Humid Vent Mini, Heat and Moisture Exchanger.**

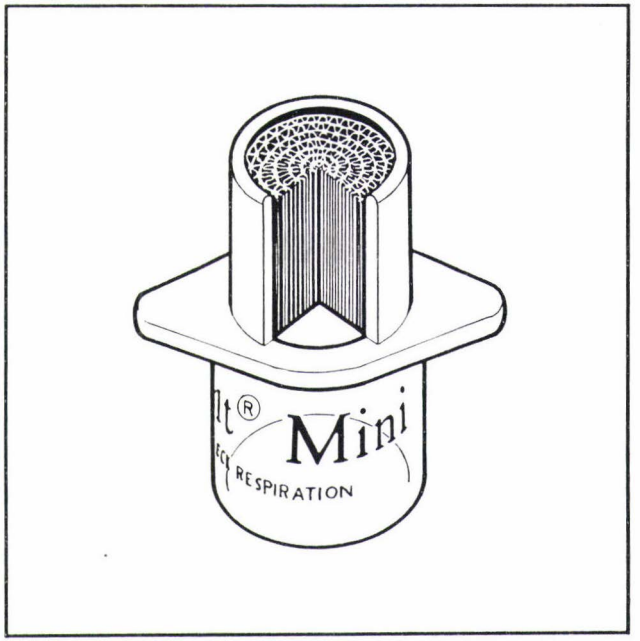

Figure 3b. **HME cutaway displaying the hygroscopic paper microwell responsible for warming and humidification of inspired gases.**

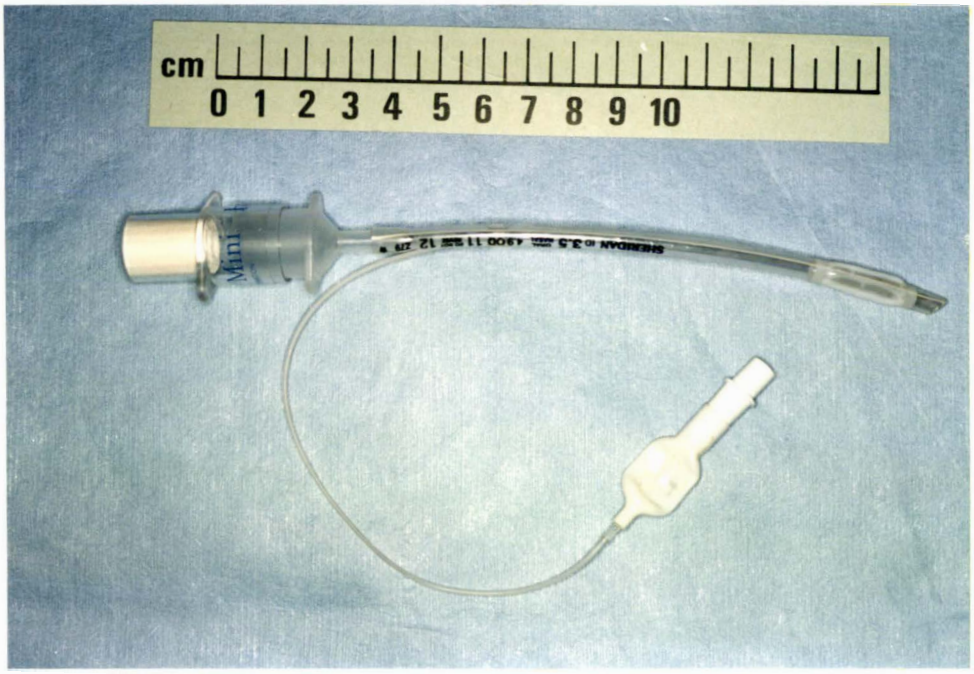

Figure 4. **Humid Vent Mini, HME attached to the endotracheal tube adaptor.**

humidification of the delivered gases. The extent of this temperature drop is determined by the length and physical characteristics of the delivery circuit, the flow rate of gas and the environmental temperature. If the relative humidity of the fresh gas is close to 100 per cent, then a relatively small fall in temperature will result in water vapour condensation. Rainout obstructs the inspiratory limb, provides a medium for bacterial and fungal growth and results in less moisture being delivered to the patient.

A simple electrical heating unit[5] was designed to actively heat the fresh gas delivered via a human neonatal Mapelson type E system (Figure 5). A low voltage, insulated electrical wire runs the length of the inspiratory limb of the circuit, effectively heating the gas as it flows towards the patient, thereby minimizing rainout.

Small, mercury-in-glass thermometers were positioned at the fresh gas outlet and at the circuit's Y-piece (Figures 6 and 7). The heater was adjusted so that the temperature of the inspired gases as they passed from the Y-piece to the cat, was confined to a narrow range (40-42^{0}C). The HME was inserted into the circuit at the level of the endotracheal tube adaptor as in Trial 11. Thirty minutes prior to induction the heating unit was switched on and oxygen delivered to the circuit to ensure that the gaseous temperature was within the experimental range when the cat was anaesthetized and connected to the system.

Patient Preparation

Once anaesthetized, each cat was positioned in dorsal recumbency on a painted metal trolley. A single hand-towel placed under the animal prevented direct contact with the metal table surface.

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5 Invent Pty Ltd, Auckland, New Zealand.

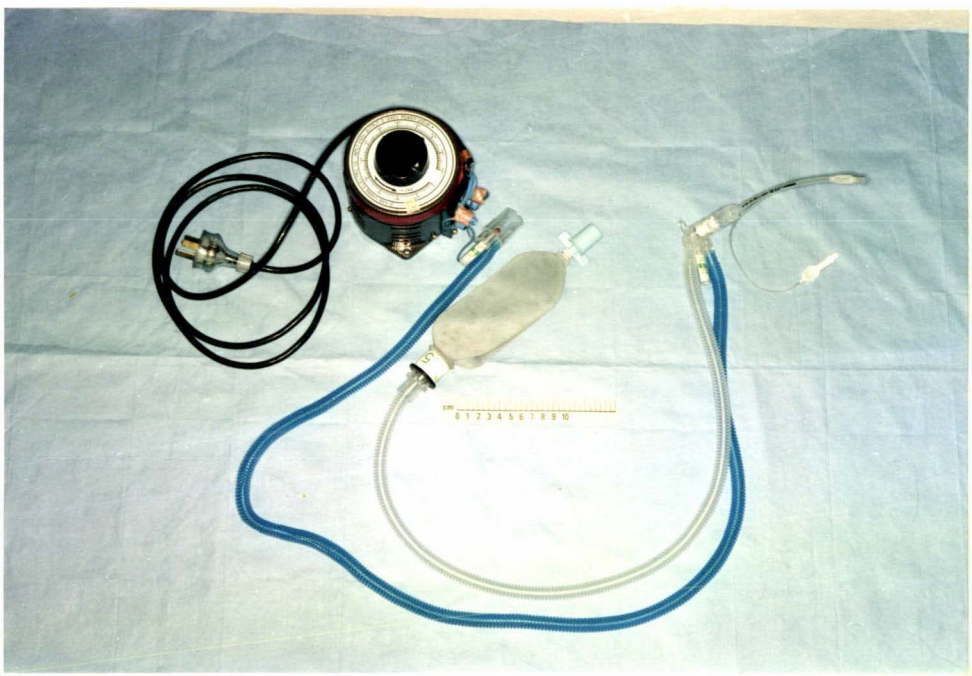

Figure 5. **The experimental breathing circuit; a human neonatal Mapleson type E system attached to the electrical heating unit.**

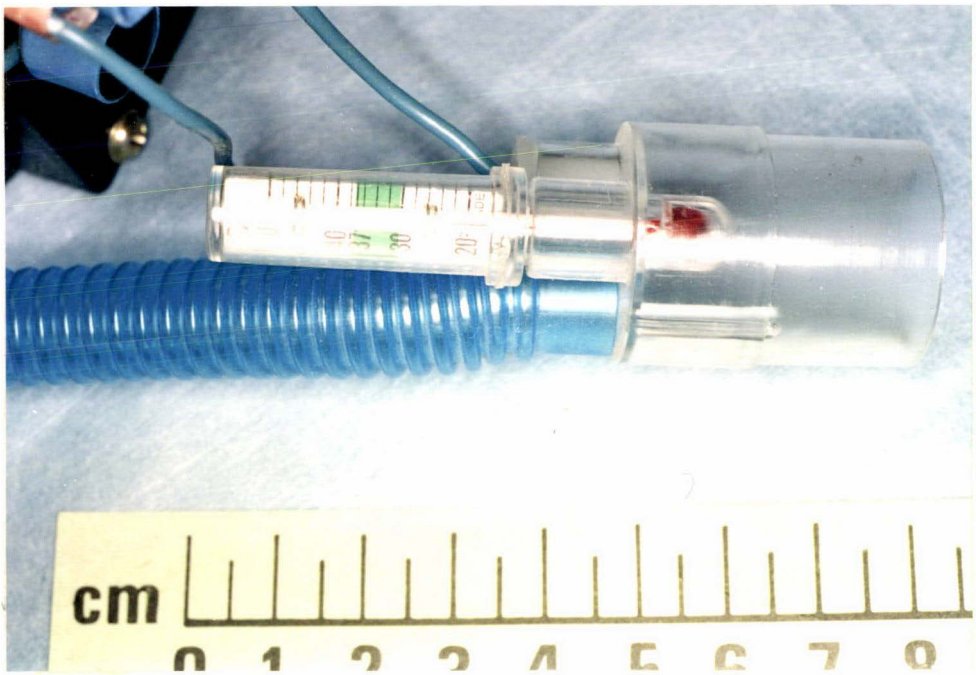

Figure 6. Mercury-in-glass thermometer positioned at the fresh gas outlet of the experimental circuit.

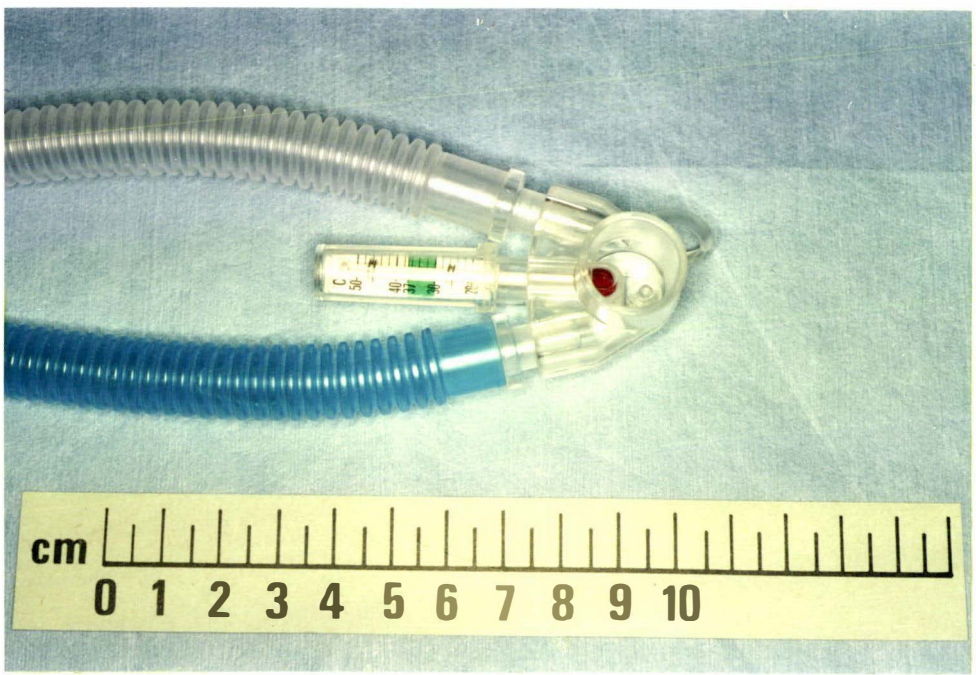

Figure 7. Mercury-in-glass thermometer positioned at the Y-piece of the experimental circuit.

A small area over the cephalic vein was clipped and aseptically prepared prior to catheterization with a 22 gauge, 2.5 cm over-the-needle catheter[6]. The catheter was capped and flushed with 0.7 ml of heparinized sterile saline (25 IU/ml).

To simulate the heat loss associated with surgical preparation of an anaesthetized patient, an area of the cat's ventral abdomen 1 cm lateral to the nipple line, 2 cm cranial to the umbilicus and 10 cm caudal to the umbilicus was clipped and prepared aseptically using a standardized technique. Five gauze swabs soaked in 20 ml of an aqueous solution of chlorhexidine gluconate[7] were used to vigorously clean the skin. This was followed with a chlorhexidine tincture preparation[8], again using five swabs soaked in 20 ml of solution. Povidone iodine[9] was applied liberally and the cat covered with a fenestrated "cat spay" drape.

The oesophageal thermistor probe was inserted taking care to ensure it was placed accurately and constantly within the caudal oesophagus by pre-measuring the distance from the tip of the nose to the 7th rib and taping the probe at this point.

The time was noted and the 120 minute experimental period of general anaesthesia recorded from this moment.

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6 Jelco. Critikon.

7 Hibitane. Imperial Chemical Industries (ICI).

8 Hibitane. ICI, 1% in 70% alcohol.

9 Biocil. Biovet, Ethical Agents Ltd.

COLLECTION OF DATA

The study was completed over six experimental sessions. Three cats were anaesthetized for each session, one cat for each of the three experimental trials, enabling Trials I, II, and III to be run concurrently.

The following data was collected from each cat during each experimental session:

Body Temperature

(i) Rectal Temperature: Rectal temperature was measured with a digital thermometer [10]. Readings were initially recorded every five minutes (0-30 mins), at the 40 minute mark and at 20 minute intervals thereafter, until the conclusion of the 120 minute trial.

(ii) Oesophageal Temperature: Mean body temperature was assessed with a neonatal rectal/oesophageal thermistor probe[11] placed in the caudal oesophagus. The oesophageal temperature was recorded at the beginning of the experimental period and at five minute intervals for the first 30 minutes of the trial. Measurements were then recorded every 10 minutes until the conclusion of the 120 minute period.

Heart Rate and Respiratory Rate

Heart and respiratory rates were recorded 60 minutes prior to induction and every 10 minutes for the duration of the experimental anaesthetic trial and recovery period. The number of heart beats and breaths per minute were respectively assessed by palpating the apex heart beat and monitoring the breathing bag of the circuit or chest movements.

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[10] Nipro Co Ltd, Tokyo Japan.

[11] Neonatal Rectal/Oesophageal Temperature Probe. Libra Medical. England

ANALYSIS OF DATA

Body Temperature

Statistical analysis was performed on a mainframe computer using the SAS[12] statistacal software package. A randomized complete block design, incorporating a two factor factorial treatment plan, was employed to determine any differences in the **absolute change in temperature** between trials and between the two sites of temperature measurement (ie. rectal vs. oesophageal). Differences were considered to be statistically significant at $P < 0.05$.

When a significant effect was detected, the data for each individual time point were then subjected to ANOVA with repeated measures using a General Linear Models procedure[12]. In this analysis each cat acted as a block, with the trial and site of temperature measurement considered as factors in the factorial treatment design. Once again, statistical significance was set at $P < 0.05$.

Heart Rate and Respiratory Rate

The data for heart rate and respiratory rate were assessed in two stages. Firstly, a repeated measures analysis, using a randomized complete block treatment design, was employed to detect any differences between the initial values (taken at time = -60 minutes) and the values obtained throughout the 120 minute experimental period. Fisher's protected LSD was used for mean comparisons between trials, and all times were compared to time = -60 minutes.

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12 SAS, Statistical Analysis System, SAS Institute Inc. Cary, NC, USA.

The data for each experimental trial were then subjected to a second repeated measures analysis, again using a randomized complete block treatment design and Fisher's protected LSD for mean comparisons between trials. Polynomial contrasts were used to test the effects of time. Differences were considered to be statistically significant at $P < 0.05$.

RESULTS

Body Temperature

Rectal temperature measured at the -60 minutes mark, had a mean value of 38.0 $\pm$ 0.1 (SEM)^{0}C, and did not vary significantly between the three trials. The patient preparation time, following the induction of general anaesthesia and prior to the collection of data at time = 0 minutes, ranged from six to 25 minutes with means of approximately 13.0, 14.0 and 14.5 minutes in Trials I, II and III respectively. During this time, rectal temperature fell by a further 0.88 $\pm$ 0.1 (SEM)^{0}C.

Body temperature did not vary significantly between the three trials. Because these results lacked statistical significance, the rectal and oesophageal temperatures for each cat are not presented here but are recorded in the appendix; (Tables IV - IX and Figures 11-16). The mean rectal and oesophageal temperatures ($\pm$ SEM) for Trials I, II and III are presented below in Tables (I-III) and Figures (8-10).

Body temperature continued to decrease throughout each of the 120 minute experimental trials. When compared with baseline data (time = 0 mins.), both rectal and oesophageal temperatures for each time point there-after, differed significantly from these initial values. The total decrease in rectal temperature across all trials, ranged from 3.9 to 6.4^{0}C with a mean of 5.2 $\pm$ 0.2 (SEM)^{0}C. The corresponding decrease in oesophageal temperatures ranged from 3.4 to 5.8^{0}C with a mean of 4.5 $\pm$ 0.2 (SEM)^{0}C. The absolute change in oesophageal temperature was significantly smaller than the absolute change in temperature measured rectally. In all trials oesophageal temperature tended to decrease in a linear fashion (approximately 0.2^{0}C per five minutes), whereas the fall in rectal temperature slowed somewhat after the 80 minute mark.

From time = 25 minutes onwards, the individual cats were a significant source of variation, however the randomized block design of the study removed this source of error from the analysis.

Heart Rate and Respiratory Rate

When measured at the -60 minute mark, the mean heart rate for Trials I, II and III was 168.0 ± 7.7 (SEM) beats per minute. At time = 0 minutes, following the induction of general anaesthesia, heart rate decreased significantly to 122.9 ± 6.9 (mean ± SEM) beats per minute. Heart rate continued to slow during the experimental periods, resulting in a significant time effect, but no significant variation between the three trials. Owing to the lack of statistical significance these results are not presented here but are recorded in the appendix; (Tables XI, XIII and XV).

The mean respiratory rate for Trials I, II and III measured at -60 minutes was 48.9 ± 3.2 (SEM) breaths per minute. Baseline values for respiratory rate measured at the commencement of the experimental period (ie. time = 0 minutes), had decreased significantly to 19.3 ± 1.6 (mean ± SEM) breaths per minute. All values for respiratory rate from this point onwards were significantly different from the initial -60 minutes measurement. There was no time effect during the trials and respiratory rate did not vary significantly between trials. These results are presented in Tables X, XII and XIV in the appendix.

Room Temperature

Room temperature ranged from 22.3 to 27.0^{0}C, with an median of 23.4^{0}C and did not vary significantly between the three trials. Although attempts were made to keep the temperature constant throughout each trial, some minor fluctuations did occur.

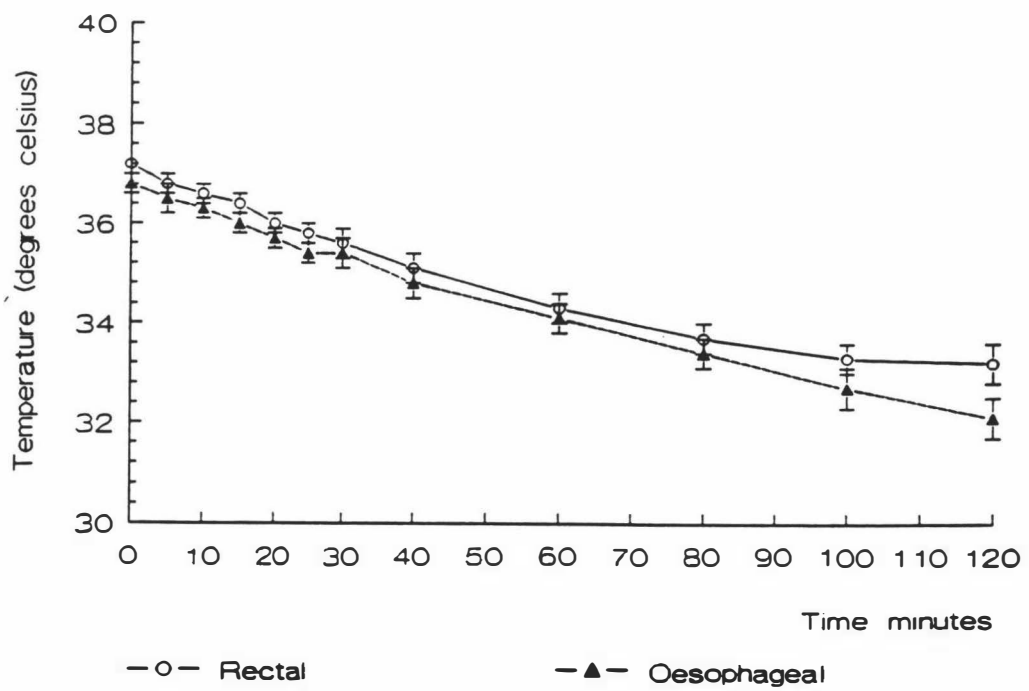
Trial I.

Table I. Mean Rectal and Oesophageal Temperatures for Trial I (^{0}C)

Time	Rectal Temperature	Oesophageal Temperature
0	37.2 ± 0.2*	36.8 ± 0.2*
5	36.8 ± 0.2	36.5 ± 0.3
10	36.6 ± 0.2	36.3 ± 0.2
15	36.4 ± 0.2	36.0 ± 0.2
20	36.0 ± 0.2	35.7 ± 0.2
25	35.8 ± 0.2	35.4 ± 0.2
30	35.6 ± 0.3	35.4 ± 0.3
40	35.1 ± 0.3	34.8 ± 0.3
60	34.3 ± 0.3	34.1 ± 0.3
80	33.7 ± 0.3	33.4 ± 0.3
100	33.3 ± 0.3	32.7 ± 0.4
120	33.2 ± 0.4	32.1 ± 0.4

* ± Standard Error

Figure 8. Mean (± SEM) Rectal and Oesophageal Temperatures Trial I (^{0}C).

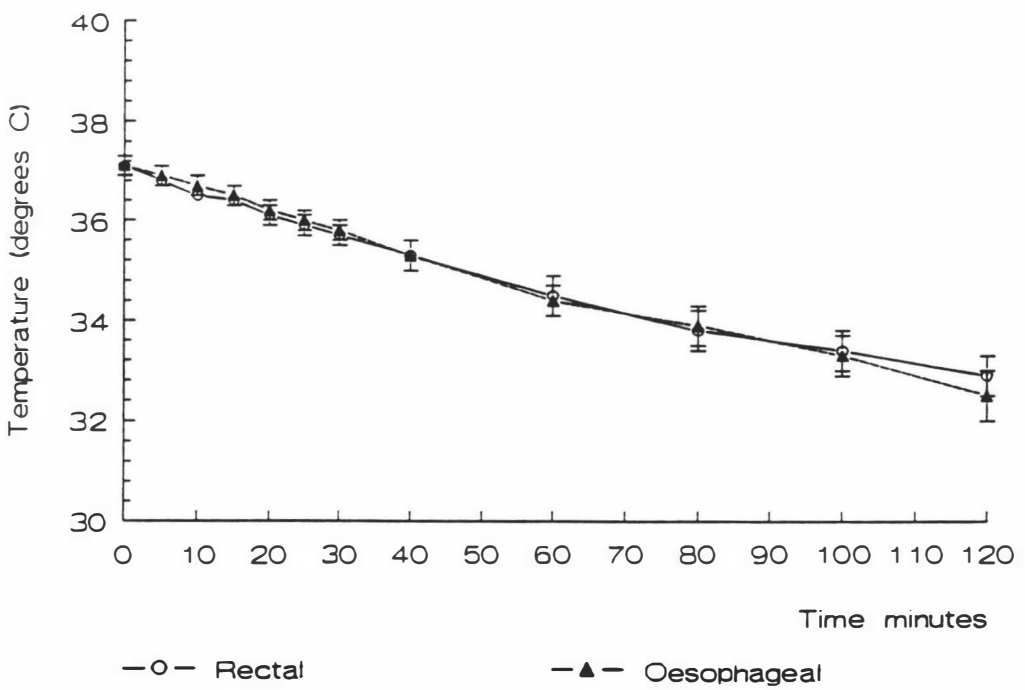


Trial II.

Table II. Mean Rectal and Oesophageal Temperatures for Trial II (°C)

Time	Rectal Temperature	Oesophageal Temperature
0	37.1 ± 0.1*	37.1 ± 0.2*
5	36.8 ± 0.1	36.9 ± 0.2
10	36.5 ± 0.1	36.7 ± 0.2
15	36.4 ± 0.2	36.5 ± 0.2
20	36.1 ± 0.2	36.2 ± 0.2
25	35.9 ± 0.2	36.0 ± 0.2
30	35.7 ± 0.2	35.8 ± 0.2
40	35.3 ± 0.3	35.3 ± 0.3
60	34.5 ± 0.4	34.4 ± 0.3
80	33.8 ± 0.4	33.9 ± 0.4
100	33.4 ± 0.4	33.3 ± 0.4
120	32.9 ± 0.4	32.5 ± 0.5
* ± Standard Error		

Figure 9. Mean (± SEM) Rectal and Oesophageal Temperatures Trial II (°C).

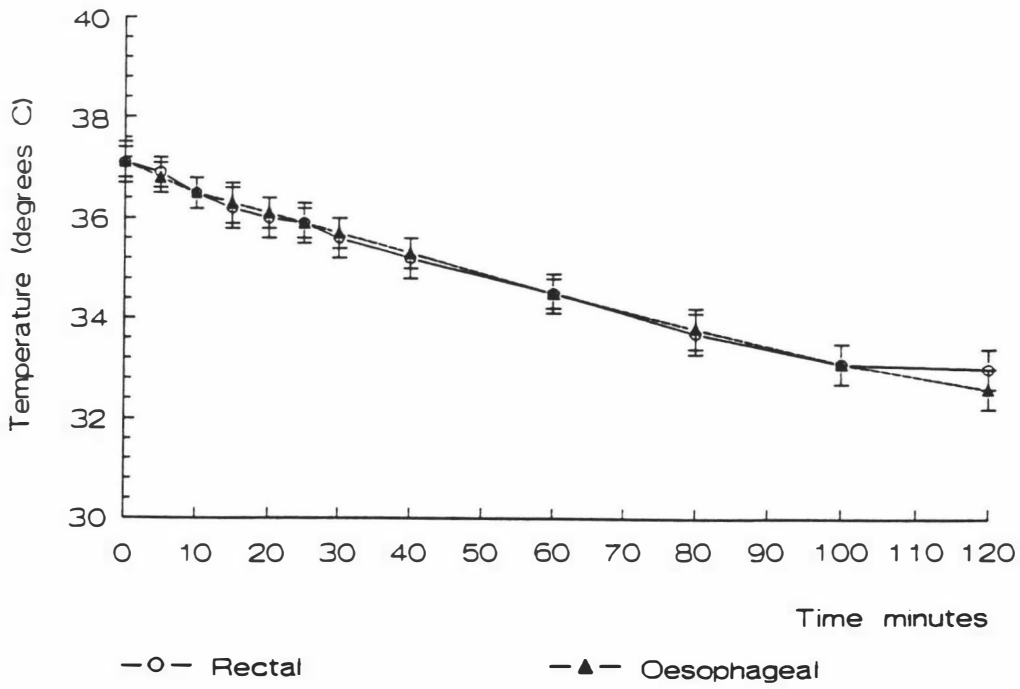


Trial III.

Table III. **Mean Rectal and Oesophageal Temperatures for Trial III (°C)**

Time	Rectal Temperature	Oesophageal Temperature
0	37.1 ± 0.4*	37.1 ± 0.3*
5	36.9 ± 0.3	36.8 ± 0.3
10	36.5 ± 0.3	36.5 ± 0.3
15	36.2 ± 0.4	36.3 ± 0.4
20	36.0 ± 0.4	36.1 ± 0.3
25	35.9 ± 0.4	35.9 ± 0.3
30	35.6 ± 0.4	35.7 ± 0.3
40	35.2 ± 0.4	35.3 ± 0.3
60	34.5 ± 0.4	34.5 ± 0.3
80	33.7 ± 0.4	33.8 ± 0.4
100	33.1 ± 0.4	33.1 ± 0.4
120	33.0 ± 0.4	32.6 ± 0.4
* ± Standard Error		

Figure 10. **Mean (± SEM) Rectal and Oesophageal Temperatures Trial III (°C).**



DISCUSSION

Intraoperative hypothermia is a common and potentially serious complication of general anaesthesia. Heat is lost from the respiratory tract when cold dry gases are warmed and humidified by water evaporating from the respiratory epithelium. Because 65 to 85% of this heat loss is insensible (resulting from water's high latent heat of vaporization), the actual humidification of inspired gases is the more important source of heat loss. The potential for heat transfer across the respiratory tract is considerable, and human studies have shown that intraoperative heat loss may be minimized by incorporating a heater-humidifier within the anaesthetic circuit (Morrison, 1988; Sessler, 1990; Bissonnette, 1991). However, active heater-humidifiers are not without their complications. In contrast, passive warming and humidification of anaesthetic gases can be achieved with the use of a Heat and Moisture Exchanger (HME) (Weeks and Ramsey, 1983). Although HMEs contribute only slightly to the preservation of a normal body temperature in anaesthetized human adults (Goldberg, Jan, Gregg, Berko, Marr and Larijani, 1988), favorable results have been attained with the use of these devices in sedated and anaesthetized children (Fonkalsrud et al, 1980; Bissonnette and Sessler, 1989; Bissonnette, Sessler and LaFlamme, 1989). The effectiveness of the HME in preserving normothermia in anaesthetized animals has not been reported previously. However, despite the success of similar techniques in human neonates and infants, the results of this study indicate that warming and humidification of inspired gases is ineffective in minimizing hypothermia in halothane anaesthetized cats.

These results agree with previously reported findings on the use of active airway warming and humidification techniques in rabbits (Marfatia, Donahue and Hendren, 1975) and dogs (Raffe and Martin, 1983), and are similar to the findings of Haskins and Patz (1980) who evaluated the effectiveness of an active heater-humidifier in the prevention of hypothermia in cats anaesthetized with pentobarbital.

Interestingly, Haskins and Patz recorded a variation in oesophageal temperature (between control and treatment trials), which became significant after 45 minutes of anaesthesia. They reported that cats receiving airway warming and humidification "exhibited a positive heat balance through the respiratory tract" and concluded that although all cats became hypothermic, the inspired air heating technique was significantly beneficial in minimizing heat loss during general anaesthesia: a finding contrary to the results of the present study.

It may be that active airway humidification is simply far superior to the relative humidification achieved by a passive device such as the HME. Although the inspired gas temperature was carefully monitored and maintained between 40 to 42^{0}C throughout each trial, no attempt was made to monitor actual airway humidity. Because of this, it is impossible to calculate the net passage of water (and therefore heat), across the respiratory tract of the cats and thus determine "respiratory heat balance". However, both laboratory (Weeks and Ramsey, 1983) and clinical studies (Bissonnette et al, 1989) report that HME devices identical to those used in this project generate $>50\%$ relative humidity, which is comparable to the degree of humidification achieved by the upper respiratory tract. Furthermore, with ongoing use, the relative humidity attained with an HME may increase to 80%, a value not greatly different from that achieved with active humidification (Bissonnette et al, 1989).

A more likely explanation for the variation in oesophageal temperatures seen by Haskins and Patz (1980), resides in the question of correct temperature probe positioning. The authors reported that thermistor probes were placed in the "lower" oesophagus, but did not document the actual site of temperature measurement. It is possible that their findings result from artifactual warming of improperly positioned thermistors; a problem that was hopefully resolved by the protocol used in this present investigation.

Various explanations have been offered for the failure of airway warming and humidification to preserve normal body temperatures in anaesthetized cats and dogs. Differences in species, anaesthetic technique, surgical procedure and additional aspects of patient management, have all been cited as contributing to the disparity of experimental results seen with the use of airway warming and humidification in people versus small animals (Raffe and Martin, 1983). In particular, Raffe and Martin (1983) state that animals, in general, have a greater body surface area per unit mass than people, and conclude that this provides an avenue of heat loss which far exceeds the benefits of warming and humidification of inspired gases. Differences in the body surface area to mass ratio between small domestic animals and human adults are considerable, however this observation does not account for the well documented success of this technique in human neonates, who also possess a relatively large body surface area.

Perhaps the answer lies (at least in part), in neonatal respiratory physiology. Because minute-ventilation on a per kilogram basis, is higher in the very young (Bissonnette, 1991), humidification of inspired gases is more effective in neonates than adults. Furthermore, heat and moisture exchangers are most effective when respiratory tidal volumes are small; another factor supporting the success of this technique in children. Based on this premise, the relatively small tidal volumes of the cat would seem ideally suited to this type of thermal support. However, as in humans, minute ventilation in adult cats is significantly lower than that in kittens (Grandy and Dunlop, 1991). Like their human counterparts, other sources of heat loss probably exceed the contributions of the HME to thermal balance in mature cats.

As previously discussed, the low heat capacity of gases makes it difficult to actively transfer significant amounts of heat to patients via the respiratory system without risking burns (Bissonnette et al, 1989). Obviously, the thermal gradient generated by the combination of active heating and the HME was too small to minimize the development of hypothermia in the halothane anaesthetized cats. However, tracheal injury has been

reported in human patients receiving gases humidified to 100% and warmed to $>41^0$C. Near complete humidity increases the amount of heat transferred to the patient and thus the likelihood of burn, due to the high specific heat of water (Morrison, 1988). For this reason, the active heating unit in this study was carefully monitored, so that inspired gases (measured at the endotracheal tube adaptor) were kept in the range of 40 to 42^0C. The actual temperature of the inspired gases in the trachea and lower airways was not monitored, but would be expected to be somewhat cooler than these values.

Three other factors may have influenced the results of this investigation: environmental temperature; anaesthetic depth; and additional means of thermal support.

Undoubtedly, environmental temperature remains the single most important factor in determining thermal balance during general anaesthesia. Heat flow is dependent on the presence of a thermal gradient: raising room temperature will reduce the thermal gradient between the patient and their environment, minimizing heat loss. Although attempts were made to keep room temperature as constant as possible (at approximately 23 to 24^0C, with an average of 23.4^0C), this was not sufficient to prevent the onset of hypothermia in the cats examined in this report. Optimal room temperatures for the prevention of anaesthetic induced hypothermia in small animals have not been published, although Dale et al (1968) were able to show that dogs anaesthetized with pentobarbital became hypothermic when exposed to air temperatures of $<27^0$C.

Anaesthetic depth is also an important factor influencing normal thermoregulation. Deep levels of anaesthesia contribute to ongoing decreases in body temperature by depressing heat production and promoting heat loss. In particular, halothane has been shown to blunt spinal cord thermoregulatory mechanisms (Schmeling, Kampine and Warltier, 1989), and to depress thermosensitive neurons in the preoptic region of the anterior hypothalamus (Poterack, Kampine and Schmeling, 1991). Clinical anaesthetic depth was closely monitored throughout each experiment. The lack of significant variation in heart and respiratory rates between the three trials, supports the assumption that

anaesthetic depth was kept fairly constant. However, endtidal halothane concentrations were not measured, so it is impossible to accurately define the exact level of anaesthesia attained in each cat.

Part of the success of airway warming and humidification in preventing hypothermia in anaesthetized children may lie in the use of additional methods of thermal support. In this investigation, a towel was placed under each cat in an effort to provide some degree of insulation. Additionally, the covering surgical drape should have reduced some heat loss, by restricting the size of the effective radiating area. These are obviously minimal methods of thermal support, and in this case, any benefit from these measures was overwhelmed by ongoing sources of heat loss, such as that encouraged by the use of cold preparatory solutions. Warming and humidification of inspired gases may be more successful in reducing heat loss in anaesthetized small animals if it were combined with more aggressive means of temperature control.

In conclusion, the use of a Heat and Moisture Exchanger, combined with an additional source of active airway warming, was ineffective in minimizing the development of hypothermia in halothane anaesthetized cats. It may be that no single method of thermal support will prove sufficient to prevent the onset of anaesthetic-induced hypothermia in small animals. The preservation of normal body temperatures in anaesthetized veterinary patients may well require a combination of aggressive heat conservation techniques. Environmental temperature appears to be the single most important factor governing the loss of heat in anaesthetized patients. Aggressive thermal support should therefore include the control of room temperature supplemented by additional control measures such as heating pads, warmed intravenous fluids, and warming and humidification of inspired gases.

Although the HME was unsuccessful in minimizing the development of hypothermia, airway humidification may still serve a useful role in veterinary anaesthesia and critical care. Passive warming and humidification of inspired gases prevents mucosal drying,

increases tracheal mucous flow, and maintains near normal tracheal ciliary function (Fonkalsrud et al, 1980). The HME is small, cheap and simple to use. These features may benefit small animals anaesthetized for prolonged procedures, and may be of use in the management of patients requiring long term mechanical ventilation.

APPENDIX

Table IV.

Trial I. **Oesophageal Temperature ^{0}C**

Time (mins)

	-60	0	5	10	15	20	25	30	40	50	60	70	80	90	100	110	120	Fall in Temperature ^{0}C
Cat 1		36.0	35.9	35.7	35.5	35.3	35.0	34.9	34.6	34.1	33.8	33.5	33.2	32.9	32.7	32.2	32.2	3.8
Cat 2		37.2	37.2	36.9	36.6			36.3	35.8	35.5	35.3	34.8	34.5	34.1	33.7	33.4	33.1	4.1
Cat 3		37.2	36.9	36.6	36.3	36.0	35.8	35.6	35.0	34.7	34.3	33.8	33.6	33.2	32.9	32.9	32.5	4.7
Cat 4		36.3	35.9	35.7	35.3	35.0	34.7	34.4	33.8	33.8	32.9	32.4	32.0	31.5	31.1	30.8	30.5	5.8
Cat 5		37.1		36.4	36.4	36.2	36.0	35.7	35.2	35.0	34.6	34.3	33.9	33.6	33.4	32.9	32.6	4.5
Cat 6		36.7	36.5	36.3	36.0	35.8	35.4	35.2	34.6	34.0	33.7	33.2	33.0	32.6	32.3	32.0	31.7	5
Mean		36.8	36.5	36.3	36.0	35.7	35.4	35.4	34.8	34.5	34.1	33.7	33.4	33.0	32.7	32.4	32.1	

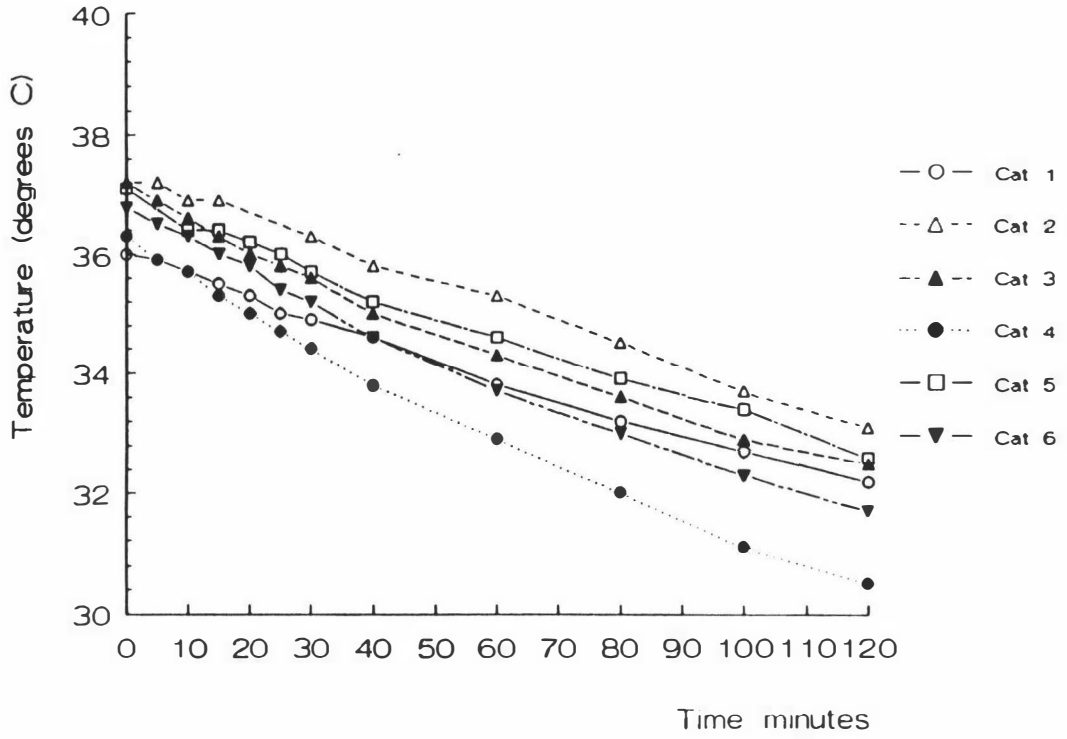


Figure 11.

Trial I Oesophageal temperature (degrees celsius)

Table V.

Trial II. **Oesophageal Temperature ^{0}C**

Time (mins)

	-60	0	5	10	15	20	25	30	40	50	60	70	80	90	100	110	120	Fall in Temperature ^{0}C
Cat 1(a)		37.6	37.4	37.3	37.1	36.9	36.7	36.5	36.1				35.2	34.9	34.7	34.4	34.2	3.4
Cat 2		36.8	36.4	36.1	35.9	35.7	35.5	35.2	34.7	34.3	33.8	33.5	33.1	32.7	32.4	32.2	31.9	4.9
Cat 3		37.1	37.0	36.7	36.4	36.0	35.8	35.5	34.8	34.4	34.0	33.4	33.0	32.5	32.2	31.7	31.3	5.8
Cat 4		37.6	37.4	37.1	37.0	36.7	36.6	36.4	36.0	35.7	35.4	35.0	34.7	34.5	34.2	34.0		3.6
Cat 5		36.5	36.3	36.1	35.8	35.7	35.5	35.2	34.9	34.4	34.1	33.8	33.5	33.3	33.0	32.7	32.5	4
Cat 1(b)		37.2	36.9	36.7	36.5	36.2	36.0	35.8	35.3	34.9	34.5	34.1	33.8	33.3	33.1	32.7	32.4	4.8
Mean		37.1	36.9	36.7	36.5	36.2	36.0	35.8	35.3	34.7	34.4	34.0	33.9	33.5	33.3	33.0	32.5	

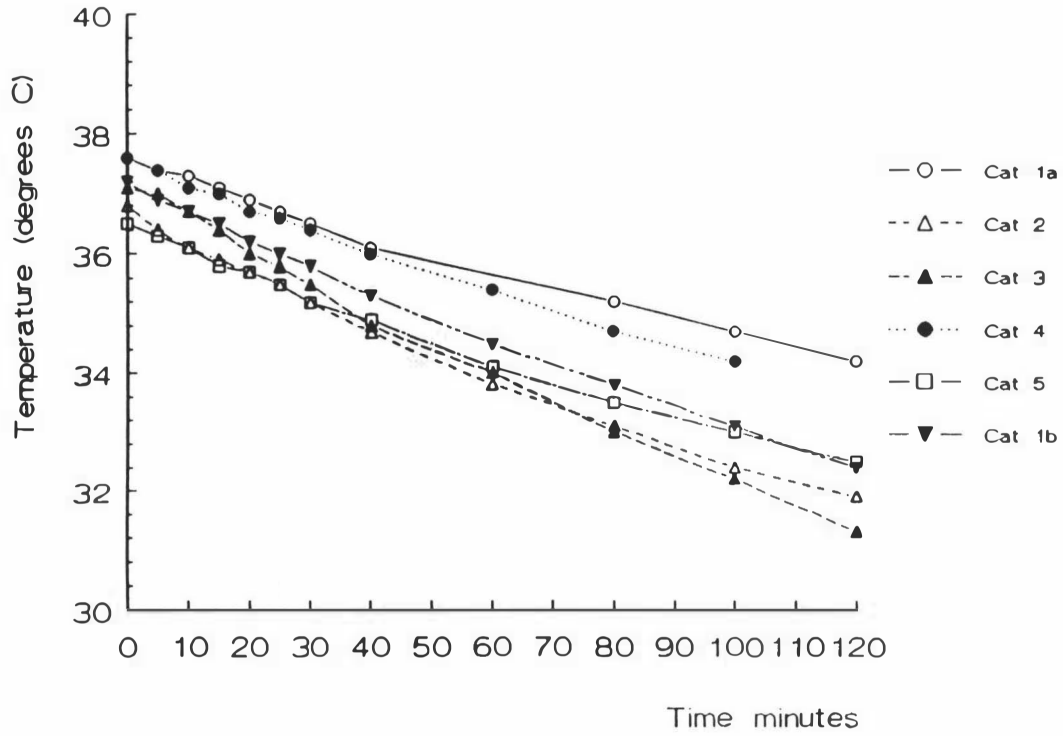


Figure 12.

Trial II Oesophageal Temperature (degrees celsius)

Table VI.

Trial III. **Oesophageal Temperature ^{0}C**

Time (mins)

		0	5	10	15	20	25	30	40	50	60	70	80	90	100	110	120	Fall in Temperature ^{0}C
Cat 1		37.0	36.8	36.5		36.4	26.2	36.0	35.7		35.0		34.3	33.9	33.6	33.4	33.1	3.9
Cat 2		36.9	36.8	36.5	36.2	35.8	35.6	35.4	34.8	34.3	33.9	33.6	33.0	32.7	32.4	32.0	31.7	5.2
Cat 3		38.5	38.3	38.0	37.8	37.5	37.2	37.0	36.7	36.3	35.9	35.4	35.3	35.1	34.7	34.5	34.1	4.4
Cat 4		36.7	36.5	36.2	36.0	35.7	35.6	35.4	35.0	35.7	34.3	34.0	33.6	33.4	33.1	32.8	32.5	4.2
Cat 5		37.0	36.5	36.2	35.9	35.7	35.4	35.2	34.7	34.2	33.8	33.1	33.0	32.7	32.3	32.0	31.8	5.2
Cat 6		36.3	36.1	35.8	35.6	35.4	35.3	35.0	34.7	34.3	34.0	33.6	33.3	32.9	32.7	32.4	32.1	4.2
Mean		37.1	36.8	36.5	36.3	36.1	35.9	35.7	35.3	35.0	34.5	33.9	33.8	33.5	33.1	32.9	32.6	

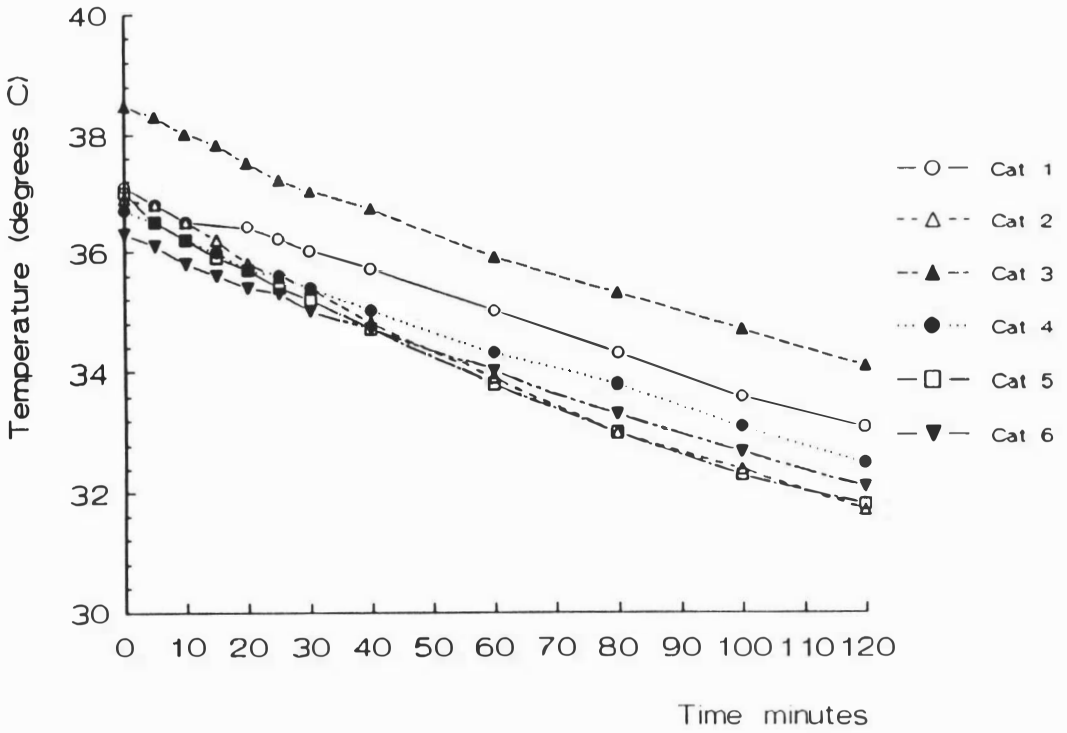


Figure 13.

Trial III Oesophageal Temperature (degrees celsius)

Table VII.

Trial I. **Rectal Temperature ^{0}C**

Time (mins)

	-60	0	5	10	15	20	25	30	40	50	60	70	80	90	100	110	120	Fall in Temperature ^{0}C
Cat 1	38.3	37.1	36.7	36.6	36.4	35.7	35.8	35.7	35.2		34.5		34		33.4		33	5.3
Cat 2	38.1	37.8	37.3	37.4	37	36.8	36.4	36.4	35.8		35		34.6		34.1		34.2	3.9
Cat 3	37.8	37.3	36.9	36.7	36.4	36.1	35.9	35.6	35.1		34.4		33.6		33		32.4	5.4
Cat 4	37.7	36.5	36.2	35.8	35.5	35.2	34.8	34.5	33.9		33.2		32.2		<32		<32	>5.7
Cat 5	37.8	37.6	37.2	37	36.7	36.6	36.3	36.1	35.8		35		34.2		33.6		33.1	4.7
Cat 6	37.7	36.9	36.6	36.3	36.1	35.8	35.6	35.2	34.8		33.9		33.3		32.6		<32	>5.7
Mean	37.9	37.2	36.8	36.6	36.4	36	35.8	35.6	35.1		34.3		33.7		33.3		33.2	

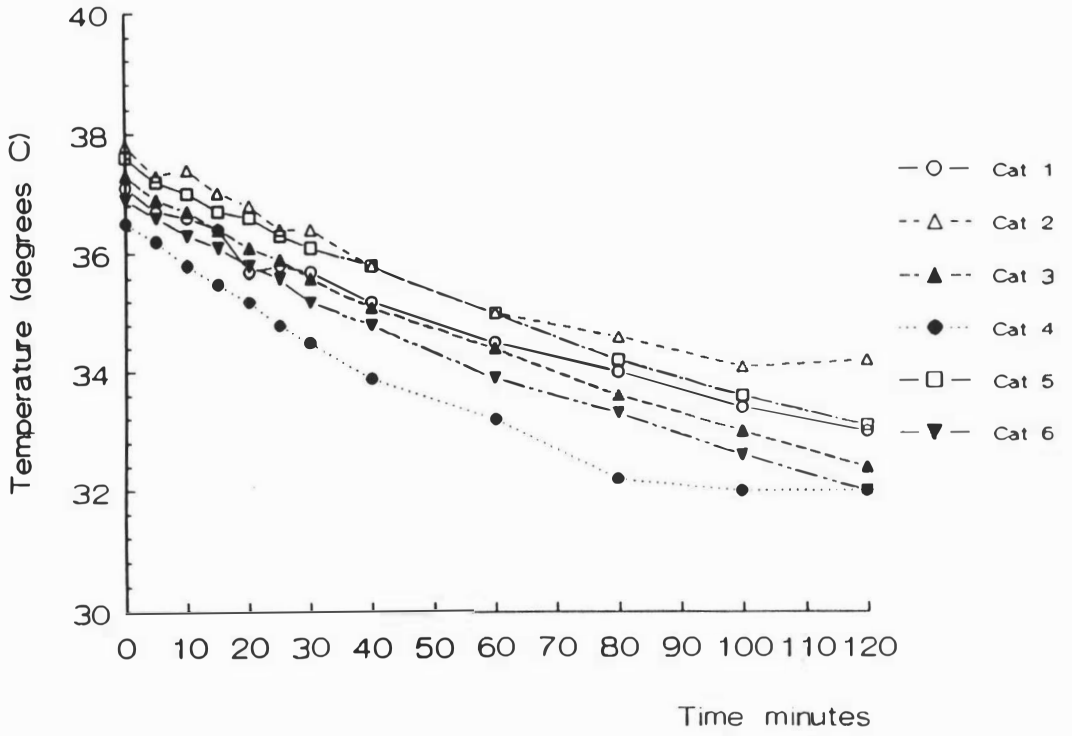


Figure 14.

Trial I Rectal Temperature (degrees celsius)

Table VIII.

Trial II **Rectal Temperature °C**

Time (mins)

	-60	0	5	10	15	20	25	30	40	50	60	70	80	90	100	110	120	Fall in Temperature °C
Cat 1(a)	38.4	37.5	37.0	36.6	37.0	36.7	36.6	36.4	36.2		35.8		35.2		34.5		34.2	4.2
Cat 2	38.4	36.9	36.5	36.1	35.9	35.7	35.5	35.2	34.8		33.8		33.1		32.4		32.0	6.4
Cat 3	37.9	37.3	36.9	36.5	36.2	35.8	35.5	35.2	34.7		33.6		32.8		<32		<32	>5.9
Cat 4	38.7	37.5	37.3	37.1	36.8	36.6	36.4	36.3	35.9		35.3		34.7		34.1		33.6	5.1
Cat 5	38.0	36.6	36.5	36.2	35.9	35.7	35.5	35.3	34.9		34.1		33.5		33.0		32.5	5.5
Cat 1(b)		37.0	36.8	36.6	36.4	36.2	35.9	35.7	35.3		34.5		33.7		33.0		32.3	4.7
Mean	38.3	37.1	36.8	36.5	36.4	36.1	35.9	35.7	35.3		34.5		33.8		33.4		32.9	

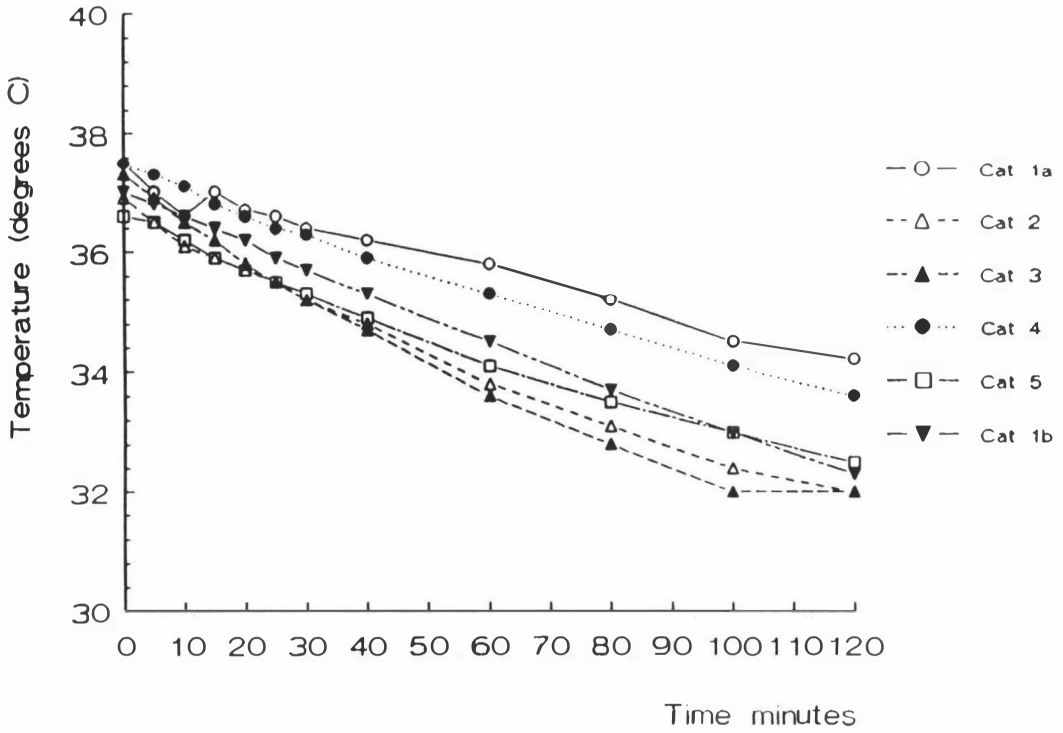


Figure 15.

Trial II Rectal Temperature (degrees celsius)

Table IX.

Trial III **Rectal Temperature ^{0}C**

Time (mins)

	-60	0	5	10	15	20	25	30	40	50	60	70	80	90	100	110	120	Fall in Temperature ^{0}C
Cat 1	38.6	37.1	37.0	36.5		36.2	36.1	35.9	35.5		35.0		34.4		33.7		33.2	5.4
Cat 2	37.2	36.9	36.7	36.3	36.0	35.6	35.5	35.1	34.7		33.7		32.8		32.1		<32	>5.2
Cat 3	38.4	38.8	38.4	38.1	37.8	37.7	37.5	37.2	36.8		36.1		35.3		34.6		34.1	4.3
Cat 4	38.0	36.8	36.4	36.3	36.1	35.9	35.7	35.4	35.1		34.4		33.8		33.2		32.7	5.3
Cat 5	37.6	36.7	36.6	36.1	35.8	35.6	35.3	35.1	34.6		33.6		32.8		32.2		<32	>5.6
Cat 6	37.9	36.3	36.1	35.7	35.5	35.2	35.1	34.9	34.5		33.9		33.2		32.6		32	5.9
Mean	38.0	37.1	36.9	36.5	36.2	36.0	35.9	35.6	35.2		34.5		33.7		33.1		33	

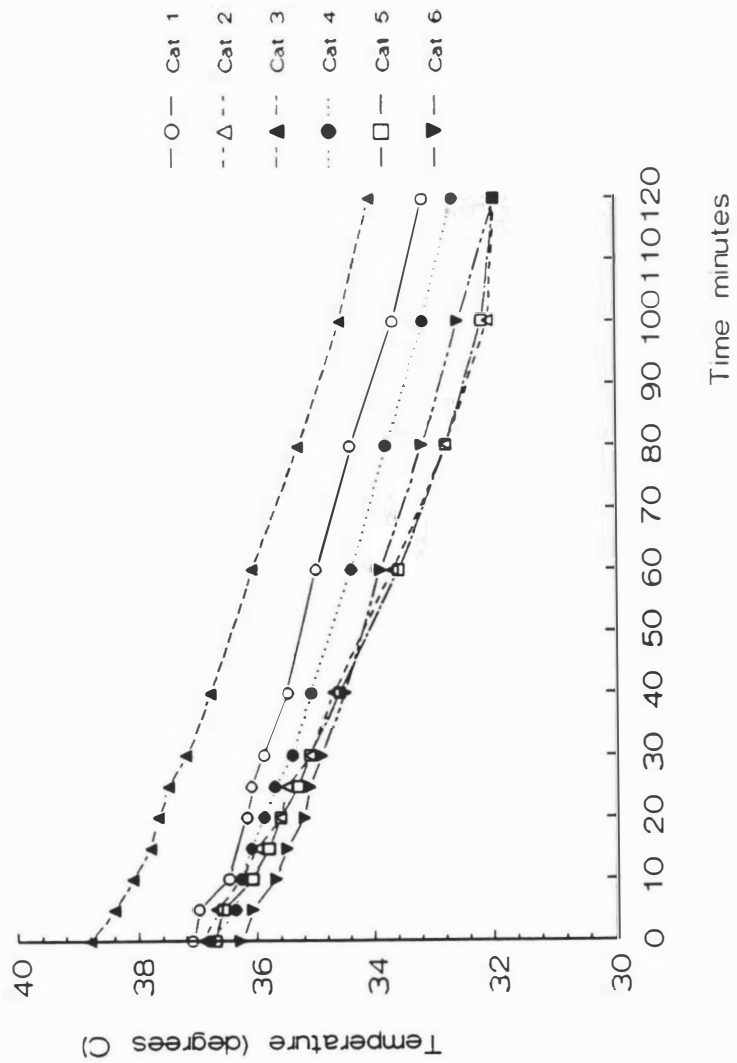


Figure 16.

Trial III Rectal Temperature (degrees celsius)

Table X.

Trial I **Respiratory Rate (breaths per min)**

	Time (mins)													
	-60	**0**	**10**	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**	**120**
Cat 1	48	12	12	12	12	12	12	12	12	12	12	12	12	9
Cat 2		28	24	25	25	20	20	20	24	24	24	24	24	24
Cat 3	27	20	16	16	16	16	16	16	16	12	12	12	20	21
Cat 4	48	12	12	12	12	12	12	12	16	12	12	12	12	12
Cat 5	60	20	36	36	32	28	36	36	24	24	24	30	28	24
Cat 6	48	28	24	28	28	28	28	24	24	24	24	24	24	24
Mean	46	20	21	22	21	19	21	20	19	18	18	19	20	19
Standard Error	±5	±3	±4	±4	±4	±3	±4	±4	±2	±3	±3	±3	±3	±3

Table XI.

Trial I **Heart Rate (beats per minute)**

	Time (mins)													
	-60	0	10	20	30	40	50	60	70	80	90	100	110	120
Cat 1	180	126	126	116	112	104	112	112	104	104	100	112	104	100
Cat 2		120	120	104	108	108	104	88	100	104	152	128	120	112
Cat 3	192	104	96	88	84	76	76	80	80	80	76	76	132	128
Cat 4	200	104	96	96	88	84	88	84	76	64	78	72	66	60
Cat 5	168	176	168	138	144	162	120	132	120	120	120	126	108	120
Cat 6	148	96	96	96	102	100	92	102	96	88	84	84	84	78
Mean	178	121	117	106	106	106	99	100	96	93	102	100	102	100
Standard Error	±9	±12	±12	±7	±9	±12	±7	±8	±7	±8	±12	±10	±10	±11

Table XII.

Trial II **Respiratory Rate (breaths per min)**

Time (mins)

	-60	0	10	20	30	40	50	60	70	80	90	100	110	120
Cat 1 (a)		16	12	12	16	16	16	16	16	16	16	25	16	16
Cat 2	72	18	16	18	16	16	16	16	16	16	16	16	16	16
Cat 3	52	20	18	16	16	16	16	14	12	16	16	16	16	14
Cat 4	28	40	24	28	28	28	32	36	32	36	32	40	40	44
Cat 5	45	16	16	16	12	12	12	12	12	12	16	12	12	12
Cat 1 (b)	40	16	12	12	12	16	16	12	12	12	16	12	12	12
Mean	47	21	16	17	17	17	18	18	17	18	19	20	19	19
Standard Error	±7	±4	±2	±2	±2	±2	±3	±4	±3	±4	±3	±4	±4	±5

Table XIII.

Trial II **Heart Rate (beats per min)**

Time (mins)

	-60	0	10	20	30	40	50	60	70	80	90	100	110	120
Cat 1 (a)		146	132	124	132	120	116	128	120	116	120	124	120	116
Cat 2	132	102	104	96	88	88	84	78	80	76	68	64	64	68
Cat 3	140	96	88	84	84	80	80	76	76	78	72	72	66	64
Cat 4	184	200	120	112	108	102	100	90	92	92	96	90	84	84
Cat 5	176	88	84	76	112	128	120	148	100	104	100	96	88	96
Cat 1 (b)	172	140	128	132	132	128	120	120	124	116	114	116	116	116
Mean	161	129	109	104	109	108	103	107	99	97	95	94	90	91
Standard Error	±10	±17	±8	±9	±8	±8	±7	±12	±8	±7	±9	±10	±10	±9

Table XIV.

Trial III **Respiratory Rate (breaths per min)**

Time (mins)

	-60	0	10	20	30	40	50	60	70	80	90	100	110	120
Cat 1		16	16	16	16	16	16	16	16	16	16	16	12	12
Cat 2	68	16	16	16	16	12	16	16	16	16	12	12	12	12
Cat 3	60	20	20	16	16	20	24	20	20	20	24	20	24	20
Cat 4	42	12	16	16	12	16	12	12	16	16	12	12	15	16
Cat 5	48	18	18	16	18	16	16	16	16	20	16	16	16	12
Cat 6	48	20	20	16	16	20	20	20	16	16	20	16	16	16
Mean	53	17	18	16	16	17	17	17	17	17	17	15	16	15
Standard Error	±5	±1	±1	±0	±1	±1	±2	±1	±1	±1	±2	±1	±2	±1

Table XV.

Trial III **Heart Rate (beats per min)**

Time (mins)

	-60	0	10	20	30	40	50	60	70	80	90	100	110	120
Cat 1	160	144	140	148	120	136	124	124	120	148	116	112	108	96
Cat 2	132	120	112	102	96	96	96	78	76	78	76	72	72	68
Cat 3	168	124	108	104	102	104	96	92	96	90	96	88	92	88
Cat 4	186	116	104	100	88	92	92	84	84	84	80	76	80	76
Cat 5	116	114	108	104	96	92	92	84	88	88	80	80	76	76
Cat 6	240	96	100	100	96	96	88	92	88	88	84	84	80	80
Mean	167	119	112	110	100	103	98	92	92	96	89	85	85	81
Standard Error	±18	±6	±6	±8	±4	±7	±5	±7	±6	±11	±6	±6	±5	±4

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