# ACID-BASE BALANCE DURING POLYPNEA AND PANTING IN THE UNANESTHETIZED CAT

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This is to certify that the

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IN THE UNANESTHETIZED CAT

presented by

Mary Laurence Morgan

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Physiology

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Date November 2, 1972

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ABSTRACT

ACID-BASE BALANCE DURING POLYPNEA AND PANTING
IN THE UNANESTHETIZED CAT

By

Mary Laurence Morgan

Unanesthetized cats, each equipped with chronically implanted thermocouple guide tubes in the anterior hypothalamus and a cannula in the left carotid artery, were exposed to ambient temperatures between 32 and 42°C. Steady-state values of rectal, hypothalamic, and seven skin temperatures, and respiratory frequency, were recorded at 5-minute intervals during a 30-minute period. Samples of arterial blood, drawn at the beginning and end of the 30-minute measurement period, were analyzed for pH, $P_{CO_2}$, and $P_{O_2}$. Plasma bicarbonate concentration was calculated from pH and $P_{CO_2}$ values using the Henderson-Hasselbalch equation.

Steady-state levels of rectal and average skin temperatures rose linearly with increasing ambient temperature. Hypothalamic temperature was linearly related to rectal temperature at all respiratory frequencies, but the slope of the relationship was altered by panting, so that a change in abdominal temperature was accompanied by a smaller change in diencephalic temperature after panting began than during normothermic exposures.

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$P_{a_{CO_2}}$ declined curvilinearly from 43 to 28 mm Hg as respiratory frequency rose from 18 to 205/min. The decrease was steeper at low respiratory frequencies. pH of arterial blood was not dependent on respiratory frequency, but rose 0.1 unit as $P_{a_{CO_2}}$ was reduced from 43 to 28 mm Hg. Plasma bicarbonate concentration was a direct linear function of $P_{a_{CO_2}}$.

$P_{a_{O_2}}$ rose from 90 to 120 mm Hg as respiratory frequency increased from 20 to 70/min. In resting cats, $P_{a_{O_2}}$ remained at approximately 120 mm Hg as respiratory frequency rose to 250/min. In exercising animals, $P_{a_{O_2}}$ was maintained at lower values, compared to resting cats with the same respiratory frequency, when frequency was greater than 70/min.

"Phase II" breathing, that is, the slow, deep respiratory pattern characteristic of cattle, sheep, and dogs during very severe heat stress, was not observed in this study.

These data are interpreted to indicate that unanesthetized cats exposed to heat stress hyperventilate during panting, but successfully avoid alkalosis. Reduction of plasma bicarbonate concentration is believed to contribute to the retention of normal blood pH in the face of hypocapnia. The oxygen tension of arterial blood in unanesthetized, heat-stressed cats is determined by the thermally driven hyperventilation and the activity level of the animal.

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# ACID-BASE BALANCE DURING POLYPNEA AND PANTING IN THE UNANESTHETIZED CAT

By

Mary Laurence Morgan

A THESIS

Submitted to
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in partial fulfillment of the requirements
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TABLE OF CONTENTS

TABLE OF CONTE

APPENDICES. .

TABLE OF CONTENTS--Continued

TABLE

1. Means and
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2. Means and
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LIST OF TABLES

FIGURE

LIST OF FIGURES

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# INTRODUCTION

A homeotherm subjected to an acute heat stress must dissipate both the heat gained from the environment and that generated by tissue metabolism in order to maintain thermal constancy. When ambient temperature exceeds body surface temperature, evaporation is the sole avenue of heat loss available to the animal. Furred or feathered homeotherms face a further restriction in that most of their external body surface is not suitable as a site for evaporation. These animals must depend on evaporation from the surfaces of the nasal and buccal cavities and upper respiratory passages for maintenance of homeothermy during severe heat stress.

The ancillary use of respiratory passages for thermoregulation may, however, jeopardize the fulfillment of the primary role of the respiratory system--the exchange of oxygen and carbon dioxide. Maintenance of an appropriate rate of gas exchange requires that alveolar ventilation be regulated by the metabolic activity of the body, whereas defense of homeothermy demands that ventilation of the upper respiratory surfaces be governed by the heat load on the animal. Simultaneous achievement of both functions implies a fine matching of respiratory frequency and tidal volume, resulting

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Experiments reported here were designed to elucidate the precision with which the furred homeotherm maintains normal alveolar ventilation during hyperthermally induced panting. The unanesthetized cat was used as a model.

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# REVIEW OF THE LITERATURE

## 1. Definition of terms

Although the respiratory responses of homeotherms to heat stress have been the subject of scientific investigation since the end of the nineteenth century, there has been no standardized terminology to describe the observed phenomena. Richet (1898; quoted in Richards, 1970a) defined "panting" as "a facilitated form of rapid shallow respiration". Some later authors have chosen an arbitrary respiratory frequency and designated all frequencies above this as panting (Lim and Grodins, 1955; Baldwin and Ingram, 1968). Others have reserved the term "panting" for an elevated respiratory frequency accompanied by retraction of the angles of the mouth, relaxation of the lower jaw and protrusion of the tongue (Forster and Ferguson, 1952; Andersson et al., 1956). Those who use this restricted definition often designate a high respiratory frequency without accessory head movements as "polypnea". Other authors treat "polypnea" as a synonym for "panting", regardless of their criteria for "panting". The term "tachypnea" also is used, especially in the older literature, to designate an elevated respiratory frequency. In this review, "panting" will refer to increased respiratory

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The use of anesthetized animals is a further source of difficulty in appraising research on panting. Many studies have shown that anesthesia disrupts the panting response to heat stress both in mammals and in birds (Albers, 1961a; Bligh, 1966). In this review, emphasis will be placed on those observations made on unanesthetized animals.

## 2. Phylogenetic distribution of polypnea and panting

Respiratory evaporative water loss appears to have originated quite early in evolutionary history. It is best developed in the homeotherms (birds and mammals), and is the dominant form of evaporative heat loss in furred mammals and birds.

Lizards are the oldest animal forms in which either polypnea or panting have been reported. Some desert species pant when body temperatures exceed 42°C (Richards, 1970a). Others do not pant, but instead exhibit rhythmic, high-frequency movements of the ventral neck region ("gular pumping"; Bartholomew and Tucker, 1964).

Many birds, except some species native to arctic or mountain regions, include panting among their responses to heat (Salt, 1964). Some birds display gular flutter simultaneously with panting, although it may not be synchronized with the panting rhythm (Calder and Schmidt-Nielsen, 1968).

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Among primitive mammals, prototheres do not pant, although they may elevate respiratory frequency when body temperature approaches the upper lethal limit (Richards, 1970a). Most metatheres exhibit polypnea, and many pant in addition (Richards, 1970a). Among Eutheria, panting is widespread, having been reported in bats (Richards, 1970a), armadillos (Richards, 1970a), rabbits (Hiestand and Randall, 1942), goats (Andersson et al., 1956), sheep (Hales and Webster, 1967), cattle (Bianca, 1955), many African ungulates (Taylor, 1969), pigs (Mount, 1962), and dogs and cats (Hammouda, 1933). Panting has not been observed in rats or guinea pigs, although polypnea occurs at raised body temperatures (Richards, 1968). In sheep (Alexander and Brook, 1960), cattle (McLean, 1963), and some African bovids (Taylor, 1969) sweating and panting occur simultaneously during heat exposure.

3. Control of panting

The control of panting has been studied since the late nineteenth century, but the precise nature of the stimuli which initiate panting, as well as their mode of integration, remain undetermined. Considerable evidence indicates that the hypothalamus is essential for the regulation of body temperature, and also that this region of the brain is thermally sensible (see reviews by Hardy (1961), Bligh (1966), and Hammel (1968)). Early workers were concerned largely with

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the relative importance of central (brain) and peripheral (chiefly skin) stimulation in the initiation of panting. The use of anesthetics and the crudeness of apparatus employed for heating the brain complicate the interpretation of most of these studies. Experiments during the last twenty years using increasingly sophisticated techniques applied to unanesthetized animals demonstrate that in sheep (Bligh, 1959), cattle (Bligh, 1957a,c; Findley and Ingram, 1961), dogs (Hales and Bligh, 1969), and some cats (Forster and Ferguson, 1952) panting can occur as a result of peripheral thermal stimulation without a rise in deep body temperature. In most cats (Forster and Ferguson, 1952; Adams et al., 1970), pigs (Mount, 1962), goats (Andersson et al., 1956) and chickens (Richards, 1970b) panting does not occur unless deep body temperature rises above its thermoneutral range. Direct, localized heating of the thermosensible area of the anterior hypothalamus can initiate polypnea or panting in cattle (Ingram and Whittow, 1962a), cats (Hunter and Adams, 1971), dogs (Hammel et al., 1963), pigs (Baldwin and Ingram, 1968) and rabbits (von Euler, 1964). The response to hypothalamic heating is progressively diminished by decreasing ambient and skin surface temperatures, and enhanced by increases in these temperatures (Randall and Hiestand, 1939; Lim and Grodins, 1955; Ingram and Whittow, 1962a; Baldwin and Ingram, 1968; Hunter and Adams, 1971).

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The influence of evaporative cooling of the upper respiratory surfaces on hypothalamic temperature complicates its consideration as an input to the thermoregulatory controller. Hunter and Adams (1966) have shown that the relationship between hypothalamic and rectal temperatures in the unanesthetized cat is linear, but the slope of the relationship is altered by panting. They demonstrated that evaporative cooling of the upper respiratory tract causes local cooling of the ventral brain, including the hypothalamus. The temperature of the hypothalamus cannot, therefore, be considered representative of the temperatures of other deep body sites. Nevertheless, extrahypothalamic deep body temperatures modify thermoregulatory activity. Evaporative cooling in response to hypothalamic heating lowers deep body temperature (Hammel et al., 1960; von Euler, 1964), which in turn diminishes the response to the central thermal stimulus. The location of the receptors by which extrahypothalamic deep body temperatures are transduced remains unknown. Localized heating of the spinal cord has been reported to initiate panting in dogs (Jessen and Mayer, 1971) and rabbits (Kosaka et al., 1969) and to cause increased cutaneous and respiratory evaporative heat loss in oxen exposed to a hot environment (McLean et al., 1970). Reflex panting has been initiated by heating the scrotum of the ram (Hales and Hutchinson, 1971) and the pig (Ingram and Legge, 1972) and the udder of the goat (Linzell and Bligh, 1961) and the ewe

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(Phillips and Raghavan, 1970b). Bligh (1963) and Phillips and Raghavan (1970a) have suggested the existence of receptors in the upper respiratory tract of sheep which participate in the control of panting. Rawson and Quick (1972) implicated thermosensitive elements in the gut of sheep in thermoregulatory responses to heat stress.

The role of the vagi in controlling panting is species-dependent. Double vagotomy does not affect panting in the anesthetized rabbit, lamb, or pigeon (Richards, 1968), while in the fowl, double but not unilateral vagotomy abolishes panting (Hiestand and Randall, 1942). Double vagotomy has little effect on respiratory frequencies during panting in the anesthetized dog (Albers, 1961b), although it may cause a more abrupt onset and cessation of panting (Anrep and Hammouda, 1933). During the onset of panting, the Hering-Breuer inflation reflex mediated by the vagus disappears gradually in anesthetized dogs (Hammouda, 1933) although it persists at a reduced level in the panting duck and to a larger extent in the rabbit (Hiestand and Randall, 1942).

The role of the cerebral cortex in the panting response also varies with species. Hammouda (1933) described panting as a conditioned reflex in dogs, since after multiple exposures of one animal to 45°C ambient temperature, the latent period before the onset of panting decreased from eight minutes to thirty seconds. In chickens, however, such "learning" did not occur, even after 100 exposures (Richards, 1970b).

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Relatively little work has been done on the integration of thermal with chemical drives to respiration. Anrep and Hammouda (1933) found that hypoxia did not prevent panting in the anesthetized dog until oxygen saturation of the arterial blood fell below 80%. Inhalation of 2% carbon dioxide caused an increase in tidal volume but no change in the frequency of panting. Higher concentrations of carbon dioxide resulted in a decline in frequency and a further rise in tidal volume. Albers (1961c) found in anesthetized dogs that the slope of the minute ventilation--$P_{a_{CO_2}}$ response curve was decreased and the intercept was shifted to a lower $CO_2$ pressure during panting. In contrast, the slope of the alveolar ventilation--$P_{a_{CO_2}}$ response curve was unchanged by either polypnea or panting, although the intercept was shifted to progressively lower $CO_2$ tensions as respiratory frequency rose during panting. Since an increment in body temperature increased minute and alveolar ventilation more when body temperature was high, Albers concluded that the thermal drive is additive to the chemical one, but in a non-linear fashion.

4. Respiratory pattern and site of evaporative cooling

When the unanesthetized dog is initially exposed to heat, respiratory frequency is unchanged or may even decline. As the heat stress continues, respiratory frequency increases, while tidal volume remains unchanged. Consequently, minute ventilation increases, reaching 3.5 times the control value

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before panting is initiated. The dog appears restless during this period of polypnea, but the apparent discomfort disappears as soon as panting begins. The onset of panting is not abrupt; short bursts of panting begin to interrupt the polypnea. The panting bursts consist of rapid thoracic movements superimposed on a tonic abdominal inspiration. During panting bursts the tidal volume declines to about 75% of the control value (Hemingway, 1938).

Albers (1961a) observed that respiratory frequency increases continuously as body temperature rises in anesthetized dogs, while the alternation of polypnea with bursts of panting is confined to the unanesthetized animal. The pattern of discontinuous episodes of panting occurs also in the unanesthetized pig (Ingram and Legge, 1970). In both species, as ambient and skin temperatures rise the polypneic intervals separating the panting bursts become shorter, and respiratory frequency during both polypnea and panting increases.

The decline in tidal volume at the onset of panting occurs in cattle (Bianca and Findlay, 1963; Taylor et al., 1969), sheep (Hales and Webster, 1967), and goats (Heisey et al., 1971). In the pig, tidal volume declines only until frequency reaches 100/min, then stabilizes as frequency continues to rise (Ingram, 1964). The wildebeest departs from this general pattern, since its tidal volume is maintained at control values during polypnea and panting (Taylor et al., 1969). The ostrich responds conversely to the

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mammalian pattern. Its respiratory frequency rises abruptly from 5/min to 45/min when ambient temperature exceeds 25°C. At higher ambient temperatures the evaporative water loss steadily increases despite the constant respiratory frequency, so tidal volume is presumed to increase with elevations in body temperatures (Crawford and Schmidt-Nielsen, 1967). Some birds shift abruptly to a respiratory frequency which approximates the natural resonant frequency of the chest for that species. Other species display a gradual increase in respiratory frequency which is linearly related to body temperature (Richards, 1970a).

The pattern of ventilatory movements during panting is important because borrowing respiratory functions for thermoregulation could interfere with the normal, strict control of alveolar ventilation which maintains blood pH and gas content within physiological limits. The extent to which thermoregulation and blood gas regulation can proceed simultaneously depends to some extent on the portion of the respiratory tract from which evaporative cooling occurs. If evaporation took place in the alveoli, an increase in evaporative water loss would obligate augmented alveolar ventilation and interfere with blood gas regulation. Alternatively, if vaporization of sufficient water occurs as air passes over the upper respiratory tract during respiration, the two functions of evaporation and gas exchange should be separable by matching an increase in frequency with a reduction in tidal

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volume. Bligh (1957b) found the temperature of the blood in the pulmonary artery and in the bicarotid trunk of the panting calf to be the same, suggesting that evaporation does not occur in the alveoli. The temperature of the blood draining into the external jugular vein of the ox decreases markedly during panting (Ingram and Whittow, 1962b). The site of vaporization would consequently appear to be the nasal and buccal cavities, which are drained by the external jugular vein in this species. Similarly in the cat, evaporation from the roof of the mouth resulted in localized cooling of basal brain structures including the hypothalamus (Hunter and Adams, 1966). In the large African ungulates, blood cooled by evaporation in the complex nasal cavities passes through a counter-current heat exchange system in the carotid rete, cooling the arterial blood before it reaches the ventral brain region and enabling these animals to maintain a difference of several degrees C between hypothalamic and rectal temperatures during severe heat stress (Taylor, 1969).

Since evaporative cooling occurs in the upper respiratory tract which constitutes part of the deadspace, the amount of heat lost would be expected to depend upon deadspace ventilation rather than on alveolar ventilation. In cattle, the ratio of alveolar to total ventilation declines as total ventilation rises during panting, and the ratio of deadspace volume to tidal volume increases (Hales and Findlay, 1968a). Such an arrangement would facilitate a desirable separation

of evaporatory and gas exchange functions. Albers (1961a) reported a similar situation in the dog: deadspace volume increased linearly with tidal volume at any given frequency, but the slope of the relationship became steeper the higher the frequency.

The pattern of panting in which tidal volume is diminished as respiratory frequency rises is referred to as "Phase I" breathing, and predominates during mild and moderate heat stress. In very severe heat stress, tidal volume begins to increase as respiratory frequency reaches its peak (Albers, 1961a). Frequency then declines, returning approximately to the control level as tidal volume continues to increase (Bianca and Findley, 1962, cattle; Hales and Webster, 1967, sheep; Hales and Bligh, 1969, dog). In the chicken (Whittow et al., 1964) and the anesthetized cat (Samek et al., 1970), frequency declines at very high body temperatures. In the pig (Ingram and Legge, 1970) and the goat (Heisey et al., 1971) tidal volume increases during very severe heat stress. Respiratory frequency stabilizes when tidal volume increases in the pig, but frequency continues to rise despite the elevated tidal volume in the goat. The pattern common to cattle, sheep, and dogs, i.e., decreased frequency and elevated tidal volume, has been designated "Phase II" breathing (Bianca, 1958). The shift from Phase I to Phase II breathing is not correlated with rectal temperature (Hales and Bligh, 1969). Phase II panting cannot be

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During Phase II panting in both sheep and cattle, alveolar, deadspace and total ventilation increase over values measured at the peak of Phase I breathing, although the increase in alveolar ventilation is more marked than the changes in deadspace and total ventilation (Hales and Findlay, 1968a, cattle; Hales and Webster, 1967, sheep), as expected from the slowing and deepening of the respiratory rhythm. Respiratory evaporative water loss during Phase II panting exceeds that at the peak of Phase I breathing (McLean et al., 1970).

5. Effect of panting on blood gases and pH

Disturbance of alveolar ventilation during panting is minimized by decreasing tidal volume and by maintaining a tonic abdominal inspiration during the high frequency breathing. The success of these compensatory maneuvers will largely determine the animal's ability to maintain normal acid-base balance during heat stress. In the unanesthetized ox exposed to moderate heat stress which evoked Phase I breathing only, Hales and Findlay (1968a) reported that $P_{a_{O_2}}$ rose 5 mm Hg above control, while $P_{a_{CO_2}}$ declined 5 mm Hg and arterial blood pH rose 0.03 units. Albers (1961a) reported that, in the unanesthetized dog, arterial pH, bicarbonate concentration,

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$P_{a_{CO_2}}$, $P_{a_{O_2}}$, and arterial blood oxygen saturation and oxygen capacity are unchanged during moderate heat stress (Phase I), and R (the respiratory exchange ratio) remained at 0.8 before and during panting. In contrast, Shelley and Hemingway (1940) reported that R decreased rapidly in the unanesthetized dog during the first half hour of heat stress, and Flinn and Scott (1923) found that unanesthetized dogs exposed to 40°C ambient temperature had a decrease in venous blood $CO_2$ content, although the venous pH remained within "normal limits" (7.55). Hemingway and Barbour (1938) reported that dogs treated with diathermy so that their heat production rates were one, two, or three times their BMR had lowered $P_{a_{CO_2}}$ but showed no change in arterial blood pH.

At least two factors contribute to the maintenance of normal pH in the face of lowered $P_{CO_2}$. First, during acute heat stress in the Ayrshire calf, the kidneys compensate for the hyperventilation by producing alkaline urine, so that venous pH is unchanged despite a fall of venous $P_{CO_2}$ from 35-40 mm Hg in the control to 27 mm Hg during panting (Bianca, 1955). Fuller and MacLeod (1956) showed that excretion of acid and ammonia fell during hyperventilation in dogs, while bicarbonate excretion increased. Second, excess lactate appears in the blood of panting oxen during exposures to 40°C dry bulb/38°C wet bulb (Hales et al., 1967). Burshtein and Tilis (quoted in Richards, 1970a) have shown that acid

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metabolites accumulate in the blood of heat-stressed dogs. Frankel et al. (1963) observed that excess lactate appeared in the blood of dogs when Phase II breathing began. Plum and Posner (1967) reported that hyperventilation in dogs caused the appearance of excess lactate in blood draining from the brain but not in arterial blood. Anrep and Cannan (1923) demonstrated that the accumulation of lactate in the blood during hyperventilation is not dependent on $P_{O_2}$ or blood oxygen saturation, but is directly related to the extent of over-ventilation. This was confirmed by Frankel (1965) who showed that in artificially respired chickens inhaling $CO_2$, hyperventilation produced no excess lactate unless the $CO_2$ concentration of the inspired gas was less than 5%.

Although several factors act to maintain normal blood pH during panting, as respiratory frequency reaches its peak the compensatory ability of these factors is exceeded, and $P_{a_{O_2}}$ and pH rise while $P_{a_{CO_2}}$ falls substantially below control. In cattle, blood pH begins to rise during the final part of Phase I breathing, and reaches 7.78 during Phase II panting (Bianca and Findlay, 1962). The elevated pH is accompanied by a fall of $P_{a_{CO_2}}$ from 45 mm Hg (control) to 17 mm Hg (Bianca and Findlay, 1962). Tetany was observed in two oxen in which $P_{a_{CO_2}}$ had fallen below 10 mm Hg and pH exceeded 7.8 (Hales and Findlay, 1968a). In sheep also, when respiratory frequency peaks during Phase I panting, venous pH rises from the control value of 7.38 to 7.67, and $Pv_{CO_2}$ falls from 42 mm

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Hg to 24 mm Hg (Hales et al., 1970). In the goat, $P_{a_{CO_2}}$ declines steadily as frequency rises (Heisey et al., 1971). Hales and Bligh (1969) reported a slight decline in $P_{a_{CO_2}}$ with small elevations in $P_{a_{O_2}}$ and pH at maximum respiratory frequency in the unanesthetized dog. Flinn and Scott (1923) found that the venous blood of dogs exposed to 40°C for six hours had normal pH values, whereas the blood of those dogs exposed to 45°C had an average pH of 7.79 at the end of one hour. Dogs exposed to 50°C had venous blood pH values of 7.84 when they were removed from the heat stress to prevent injury. No mention was made of whether these dogs had entered Phase II respiration. Hales and Bligh (1969) observed arterial pH values of 7.77 with $P_{a_{CO_2}}$ at 4 mm Hg in Phase II breathing in one unanesthetized dog. Calder and Schmidt-Nielsen (1968) studied the effects of panting on acid-base balance in a number of avian species. In some, panting was associated with no change in either $P_{a_{CO_2}}$ or pH, whereas in others pH values as high as 7.86 and carbon dioxide tensions as low as 8.6 mm Hg were observed.

The hypocapnia which develops at the end of Phase I panting would be expected to counteract the thermal stimulus for respiration if it led to reduced brain tissue $P_{CO_2}$ or increased brain tissue pH. Brain tissue $P_{CO_2}$ cannot be measured in the unanesthetized animal, but the $P_{CO_2}$ in the vicinity of the medullary chemoreceptors can be estimated if the gas tensions of blood and cerebrospinal fluid (CSF) are known.

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Hales et al. (1970) found, during Phase I breathing in sheep, an increase of CSF pH from 7.32 to 7.47, and a fall of CSF $P_{CO_2}$ from 41 mm Hg to 29 mm Hg. These changes in CSF are in the same direction but are smaller than those in the blood. During Phase II panting, CSF pH peaked at 7.59 before stabilizing at 7.50, and CSF $P_{CO_2}$ declined from 29 to 18 mm Hg. The fall in CSF pH (from 7.59 to 7.50) while CSF carbon dioxide tension was constant or falling reflected a reduction in CSF bicarbonate concentration. That these changes in the CSF are likely to reflect those in brain tissue is suggested by Ponten (1966), who found that changes in brain tissue $CO_2$ content in hyperventilated rats were complete within thirty minutes after a step-change in $P_{a_{CO_2}}$.

Decreased $P_{CO_2}$ and alkalosis would be expected to inhibit respiration, but Chapot (1967) found in cats that lowered arterial $P_{CO_2}$ caused a large increase in phrenic nerve discharge, in a pattern similar to that during thermal panting. Pleschka (1969) observed that, in anesthetized dogs, artificial hypertilation produced polypnea, even if body temperatures were relatively low. The role of this effect in the normal response to heat stress remains to be evaluated.

Hypocapnia resulting from severe panting would be expected to influence brain blood flow, since Hayward (1966) reported that a 2% decrease in end-expired $CO_2$ caused a decrease in blood flow to the brain of the monkey, and Serota

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and Gerard (1938) showed in anesthetized cats that $CO_2$ inhalation increased brain blood flow.

6. Previous studies on cats

Anrep and Hammouda (1933) studied panting in one anesthetized cat and reported that tidal volume declined from 20cc when rectal temperature was 37°C to 9.3cc when rectal temperature reached 39°C, while respiratory frequency rose from 24 to 370/min. Samek et al. (1970) reported a decrease in respiratory frequency in anesthetized cats exposed to severe heat stress. Von Euler et al. (1970) found that tidal volume increased in anesthetized or decerebrate cats which displayed polypnea but not panting when heated to rectal temperatures of 39.6°C.

Blood gas pressures in resting unanesthetized cats have been obtained by two methods. Fink and Schoolman (1962) used chronic intra-arterial cannulae to obtain blood samples, and reported an average blood pH of 7.38 with a $Pa_{CO_2}$ of 28 mm Hg. Sorenson (1967) used samples of gas which had been equilibrated with tissue in subcutaneous gas pockets to obtain a value of 29.9 mm Hg for $P_{a_{CO_2}}$. Herbert and Mitchell (1971), employing intra-arterial cannulae, reported an average pH of 7.426 and a $Pa_{CO_2}$ of 32.5 mm Hg.

7. Summary

Polypnea and panting are common responses to heat stress among mammals and birds. During moderate heat stress, most

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panting species display increased respiratory frequencies and reduced tidal volumes so that hypocapnia and alkalosis are avoided. During severe heat stress, the respiratory pattern is altered and both hypocapnia and alkalosis develop.

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## STATEMENT OF THE PROBLEM

Experiments were designed to determine whether unanesthetized cats exposed to mild, moderate, and severe heat stress become hypocapnic or alkalotic during polypnea and panting, and to quantify the effects of polypnea and panting upon blood oxygen tension. These data will be of value in completing the description of the thermoregulatory responses of a small furred homeotherm, and will also contribute to an understanding of the manner in which the thermoregulatory system interacts with other homeostatic mechanisms in the mammalian body.

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# METHODS

## 1. Animals

All experiments were conducted on adult, short-haired male or non-pregnant, female, domestic cats. The animals were housed in cages in the laboratory, exposed to approximately 14 hours of light per day, and fed "9-Lives" dry cat food (Star-Kist Foods, Inc.). Water was available *ad. lib.*

Five cats were used in the study: cat No. 1, a 4.1 kg male; cat No. 3, 2.3 kg, female; cat No. 5, 2.9 kg, female; cat No. 6, 3.4 kg, male, and cat No. 7, a 3.0 kg female.

## 2. Construction of implanted materials

Blood samples were drawn from a chronically implanted cannula connected to a modified two-way stainless steel stopcock (Figure 1) which was anchored to the skull as shown in Figure 3.

Cannulae were made from two lengths of Silastic tubing (Silastic Medical Grade Tubing, No. 602-151; i.d. .025 inch, o.d. .047 inch; Dow Corning Corp., Midland, Michigan 48640). For cat No. 1 only, the tubing was No. 602-171, i.d. .030 inch, o.d. .065 inch. One end of each Silastic tube was slipped over a 1.5 cm length of Teflon tubing (Teflon Medical

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Grade Tubing, No. 6425, ultra-thin wall; i.d. .018 inch, o.d. .030 inch; Becton, Dickinson, and Co., Rutherford, N. J.). The two Silastic sections were cemented together over the Teflon with Silastic Medical Adhesive (Silicone Type A, Dow Corning; Figure 1). This construction provided a rigid section around which ligatures could be placed. The lumen of each cannula was coated with Siliclad (Clay Adams) to inhibit clot formation.

The upper end of each cannula was fitted over a 5 mm length of 21-gauge needle stock (o.d. .0325 inch) which was soldered into a modified stopcock (Model MSO1 or MSO4, Becton, Dickinson and Co.). For cat No. 1 only, the adaptor was constructed from stainless steel tubing, o.d. .054 inch. A schematic drawing of cannula and stopcock is presented in Figure 1.

Hypothalamic temperature was measured by a 40-gauge, copper-constantan thermocouple inserted into guide tubes which had been surgically implanted, bilaterally, into the brain, and which were secured to the skull surface using a dental acrylic housing and small, stainless steel screws (Figures 2 and 3). Guide tubes for the hypothalamic thermocouples were made by sealing one end of a 35 mm length of 20-gauge needle stock (o.d. .0355 inch) with resin core, silver-lead solder. Two guide tubes were embedded in a disc of dental acrylic (NuWeld, L. D. Caulk Co., Milford, Del., 19963). Twenty-seven mm of guide tube extended below

Figure 1. Schematic drawing of cannula and stopcock.

Sc = stopcock
A = adaptor
Sr = solder
ST = Silastic tubing
SMA = Silastic Medical adhesive
TT = Teflon tubing

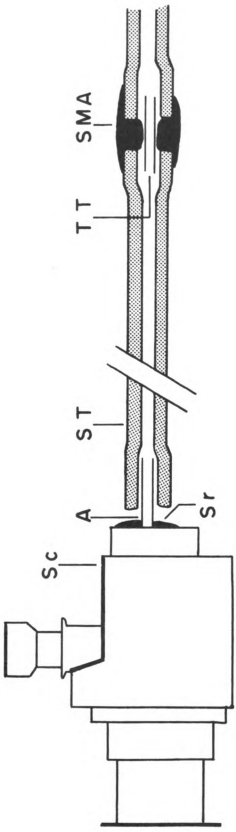


Figure 1

Figure 2. Schematic drawing of thermocouple guide tubes and acrylic disc.

GT = guide tube
SP = solder plug
AD = acrylic disc

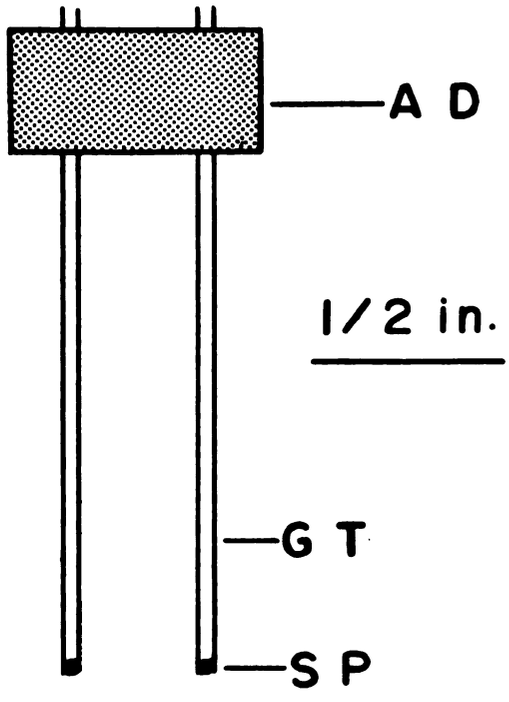


Figure 2

Figure 3. Lateral X-ray view of cat's head showing hypothalamic thermocouple guide tubes, stopcock, and cannula.

The cannula was filled with contrast medium to make it visible in the X-ray.

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the bottom of the disc (Figure 2). Tubes were insulated with Stoner Mudge Protective Coating (S-986-S).

3. Surgery

Arterial cannulation, implantation of guide tubes and attachment of connectors to the animal's skull were performed under a general anesthetic. The initial dose of sodium pentobarbital (Nembutal; Abbott Laboratories, North Chicago, Ill., 60064) was 36 mg/kg, administered ip. Supplements were given as necessary, iv or ip. Aseptic precautions were maintained.

The following procedures were used for the implantation of cannula and guide tubes. The skin and fasciae overlying the skull were incised and, together with the underlying muscles, retracted. The thermocouple guide tubes, fixed in the acrylic disc (Figure 2), were implanted stereotaxically in the preoptic region of the anterior hypothalamus (stereotaxic frame: Model 1204, David Kopf Instruments, Tujunga, Calif., 91402; guide tubes positioned according to Snider and Niemer, 1961; coordinates: 14.5 mm anterior and 6 mm dorsal to the interaural line, 3.5 mm on either side of the midline). Three stainless steel screws (MS 256-6F, Small Parts Inc., Miami, Fla.) were screwed into holes drilled in the skull. The stopcock, with cannula attached, was placed adjacent to the acrylic disc and additional acrylic was poured around screws, stopcock, and disc, as well as over the edges of the

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incised skin. On all cats except No. 1 a protective plastic dome with access holes was cemented with acrylic over the stopcock.

A mid-ventral incision was made in the skin of the neck, the muscles were retracted and the left common carotid artery exposed, care being taken to avoid injuring the vagus nerve. The artery was ligated cranially with silk suture (Ethicon, Inc., size 0, M-404). The cannula was threated subcutaneously from the top of the skull to the neck incision, and the lower section of Silastic was trimmed so that its tip lay over the fourth rib. This insured that when the cannula was in place the tip would lie in the aorta. The lumen of the cannula was filled with 1% heparin solution (Sodium Heparin, 1000 units/ml; Upjohn, Kalamazoo, Mich., 49001) and the exterior was sprayed with a lubricant (Antiform A, Dow Chemical, Midland, Michigan). The carotid artery was cannulated and the cannula threaded down the artery until the small Teflon section lay just inside the vessel. Two ligatures (Ethicon, size 0, M-404) were placed firmly over the artery where it covered the Teflon section. The wound was closed with a non-capillary suture (Vetafil Bengen, Dr. S. Jackson, Washington, D. C., 20014). A long-lasting penicillin preparation (Long-icil, 30,000 units/lb; Fort Dodge Laboratories, Fort Dodge, Iowa) was injected intramuscularly.

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4. Care of animals

At least one week elapsed between surgery and the first experiment. The fluid in the cannula was withdrawn and the cannula flushed with 1% heparin daily. Animals were trained to rest in the restraint device (described below; Figure 4) and were accustomed to the chamber (Figure 4) and the experimental procedures before data collection began.

5. Equipment

a. Restraint device

The restrainer, in which animals were expected to rest quietly during each experiment, consisted of a brass and aluminum frame from which was suspended a plastic mesh sling. The cat's head was held by a plexiglass yoke; the feet extended through holes in the sling to rest on a wide-mesh wire screen (Figure 4).

b. Chamber

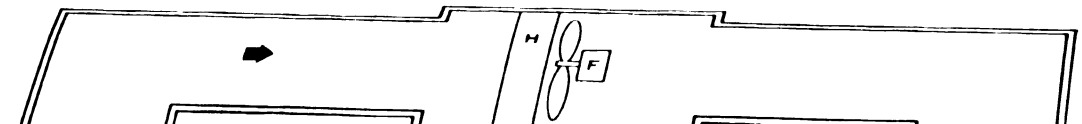
The exposure chamber (Figure 4) was constructed of plexiglass (Polycast Technology Corp., Stamford, Conn.). The walls, floor and ceiling were 1/4 inch thick; the chamber was 28 inches long, 24 inches high and 13 inches wide. One fan drew air from the chamber over a dehumidifier (Sears, Roebuck and Co., Coldspot), then through a duct to the heat exchanger. Chamber temperature was controlled by regulating the flow of hot or cold water to the heat exchanger; water flow was controlled by a YSI Thermistemp temperature controller (Model 71,

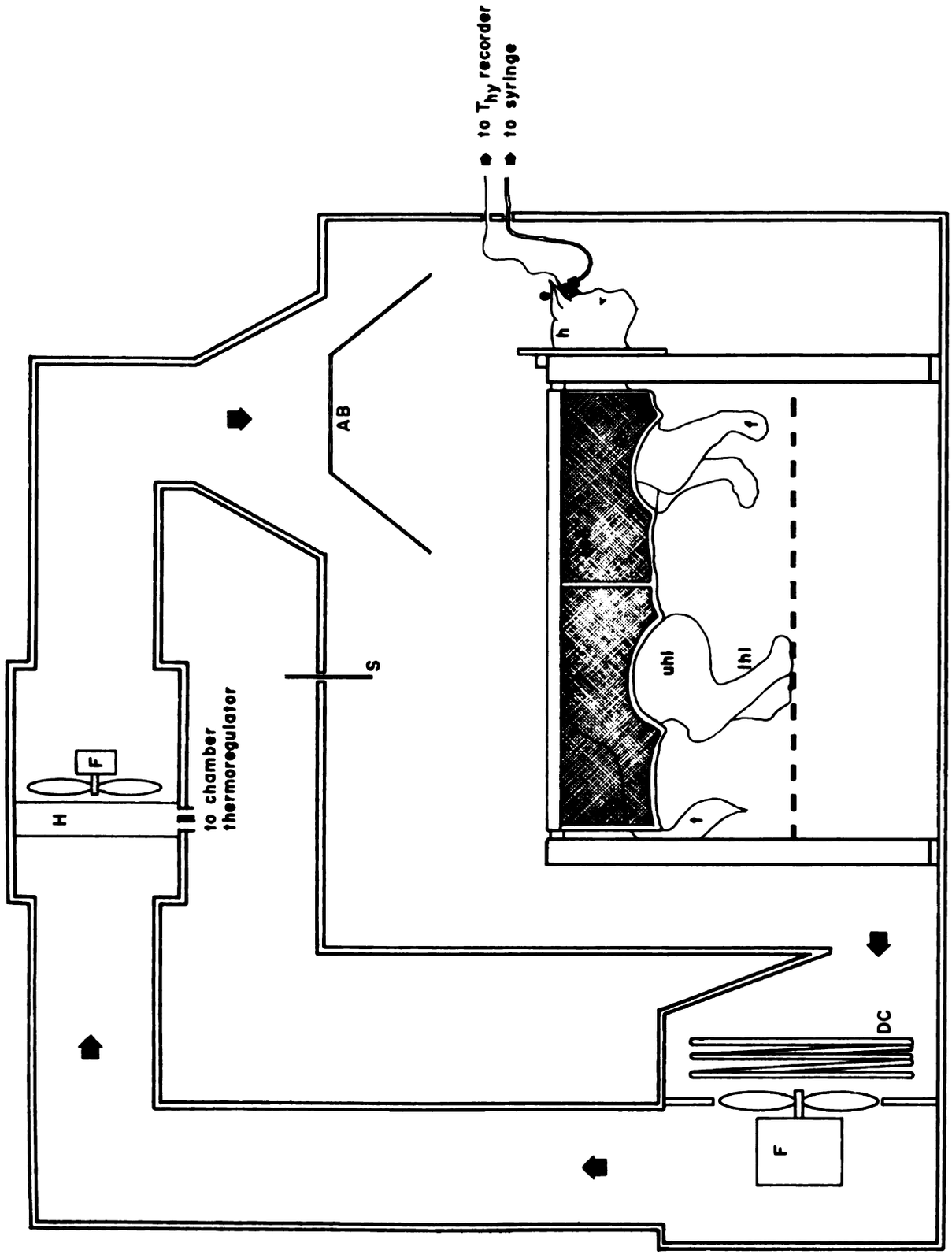
Figure 4. Schematic drawing of cat in exposure chamber and restraint device.

AB = baffle to protect cat's head from direct air currents
DC = dehumidifier coil.
F = fans
H = heat exchanger
S = sensor for chamber temperature controller

Small letters indicate sites of skin temperature measurement:
e = ear
h = head
ch = chest
f = forefoot
uhl = upper hind leg
lhl = lower hind leg
t = tail

Arrows indicate direction of air flow.

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Yellow Springs, Ohio), the sensor of which was located downstream from the heat exchanger. A second fan drew air over the heat exchanger and forced it through a second duct into the chamber. Relative humidity of the air in the chamber was maintained at 35-40% in all exposures and was measured by an Abbeon Certified Hygrometer (Model AB 167, Abbeon, Inc., Jamaica, N. Y., 11432), mounted on the back wall of the chamber. Chamber temperature was continuously monitored with a thermocouple and was regulated to within 0.1°C. The fans provided sufficient air movement within the chamber to prevent thermal layering; maximum temperature difference between points in the chamber was 0.2°C.

Removable ports in the side of the chamber permitted access to its interior without gross disturbance of chamber temperature and relative humidity. A small hole in the front allowed passage of the blood sampling tube.

6. Measurements

Skin temperature was measured at seven sites: ear (center, inner surface of pinna), head (center back of skull), forefoot (dorsal surface), chest (midlateral surface at posterior margin of rib cage), upper hind leg (midlateral surface), lower hind leg (mid-dorsal surface), and tail (midway between base and tip). Skin temperatures were measured with 36-gauge copper-constantan thermocouples referenced to an ice-water bath and attached to small areas of skin which had been

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clipped and freed of hair by a depilatory (Neet, Whitehall Labs., Inc., N. Y., N. Y., 10017). The skin areas were coated lightly with Ace Adherent (Becton, Dickinson and Co.), and the thermocouples were held in place with small squares of thin, plastic surgical tape (Blenderm, 3M Co., St. Paul, Minn.). Rectal temperature was measured with a 36-gauge thermocouple mounted in polyethylene tubing, inserted 10 cm beyond the external anal sphincter and fastened with tape to the base of the tail. Hypothalamic temperature was measured with a 40-gauge thermocouple soldered into a 35 mm length of 24-gauge needle stock and lowered to the bottom of the thermocouple guide tubes implanted in the anterior hypothalamus. Chamber air temperature was measured with a 36-gauge thermocouple suspended from the roof of the chamber. Each temperature was recorded once every 12 seconds on a Speedomax W multipoint recorder (Leeds and Northrup, Model AZAR-H). The calibration curve for the thermocouples is presented in Appendix 1.

Respiratory rate was monitored by a mercury-in-rubber strain gauge stretched around the thorax, and a Model 270 plethysmograph (Parks Electronics Laboratory, Beaverton, Oregon). The output of the plethysmograph was recorded on a Grass polygraph (Model 7WC12PA Ink-Writing Oscillograph).

Blood samples were drawn through a 40-cm length of polyethylene tubing (Intramedic 60: i.d. .030 inch; Clay Adams) connected by an adaptor to the stopcock affixed to the cat's

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skull. The stagnant fluid in cannula, adaptor, and stopcock was withdrawn and discarded, and a 2-3 cc sample of arterial blood was drawn into a 10 cc glass syringe, the deadspace of which was filled with 1% heparin. The back end of the syringe barrel was coated with stopcock grease (Dow Corning) and the syringe was stoppered with a mercury-filled cap. Samples were stored in ice water until analysis, which occurred not more than six hours after the sample was drawn.

Blood pH was determined with a glass electrode (Type e5021a, Radiometer, Copenhagen, Denmark) and pH meter (PHM 27, Radiometer). $P_{CO_2}$ of the blood was determined with a type E5036 $P_{CO_2}$ electrode and a type PHA927b gas monitor (Radiometer). $P_{O_2}$ was determined with a type E5046 electrode and the PHA927b gas monitor (Radiometer). All electrodes were thermostatted to 38-39.5°C (thermostat temperature was recorded during each analysis period). pH values were corrected to the appropriate rectal temperature by the factor of Rosenthal (1948) and gas tensions were corrected to corresponding body temperature using the factors given by Severinghaus (1966). The pH electrode was calibrated with two buffers (pH's 6.84 and 7.384; Instrumentation Lab. Inc., Lexington, Mass., 02173). The $P_{CO_2}$ electrode was calibrated using aliquots from two distilled water reservoirs, each of which had been equilibrated with one of two gases of known $CO_2$ content (analysis performed on a Haldane apparatus). The $P_{O_2}$ electrode was calibrated using an oxygen-free solution (5 ml of

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0.01 M Borax solution and 100 mg sodium sulfite; Radiometer, Copenhagen), and distilled water equilibrated with air. Barometric pressure was read on a mercury barometer (Welch Scientific Co., Skokie, Ill.).

7. Experimental design

Animals were exposed to ambient temperatures of 32.0, 35.0, 36.5, 38.0, 39.5, and 41.0°C. Data collection began after an exposure of not less than 90 minutes, when the cat reached a thermal steady state (skin, hypothalamic, and rectal temperatures and respiratory frequency stable for 30 minutes). A 3 cc blood sample was drawn, and readings of ambient, rectal, skin and hypothalamic temperatures, and respiratory frequency were taken every 5 minutes for a 30 minute period. A second, 2 cc blood sample was then drawn. In some cases readings were continued for another 30 minute period and a third, 2 cc blood sample was drawn.

During the experiments, the cats were observed carefully to determine whether they rested quietly or struggled. Those cats which struggled (violent movements of the legs and trunk) were considered "exercising animals". If the exercise was severe enough to increase rectal temperature the data were discarded. If exercise occurred with no change in rectal temperature, the data were retained but analyzed separately from those obtained from resting animals.

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8. Calculations

Average skin temperature was calculated by weighting the temperature of each skin site according to the proportional contribution of that region to the total body surface area: $\overline{T}_S = T_{ear}\ (0.034) + T_{head}\ (0.110) + T_{forefoot}\ (0.066) + T_{chest}\ (0.405) + T_{upper\ hind\ leg}\ (0.221) + T_{lower\ hind\ leg}\ (0.113) + T_{tail}\ (0.051)$. Proportioning constants for the various skin sites are derived from Vaughan and Adams (1967).

Bicarbonate concentration of arterial blood, in milliequivalents per liter, was calculated from the following equation:

$$\log\ [HCO_3^-] = pH - pK' + \log\ (aP_{CO_2})$$

where pK' and a (the solubility constant for $CO_2$ in plasma) were adjusted according to the appropriate rectal temperature (Severinghaus, 1965).

9. Analysis of data

For all temperatures and respiratory frequency, each point on the graphs (Figures 5-9 and Appendices 2-5) represents the mean of seven measurements taken at 5-minute intervals during a thermal steady state. For blood gas tensions and pH (Figures 10-13 and Appendices 6-16), each point represents the mean of at least 2 determinations on a single blood sample. $P_{aCO_2}$ values from experiments in which the $P_{CO_2}$ of initial and final blood samples differed by more than 3 mm Hg were excluded from all analyses.

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For all graphs in which temperature is the dependent variable, data from exercising animals were included in the statistical analyses. For graphs in which respiratory frequency is the dependent variable, data from exercising cats were excluded. All straight lines were calculated by the method of least squares; the F test was used to detect the presence of significant non-linearity. All non-linear relationships were fitted by eye.

# RESULTS

Data presented in Table 1 and Figures 5 and 6 indicate that the thermoregulatory activity of the cats used in this study conformed to the pattern previously established as characteristic for this species (Adams et al., 1970; see Discussion). The means and standard errors of body temperatures and respiratory frequency in each 30-minute steady-state measurement period are presented in Table 1.

During steady-state adjustments to ambient temperatures between 32 and 42°C, unanesthetized cats maintained rectal temperature at successively higher levels, as shown in Figure 5. An alternative analysis suggests that the rectal temperature increases linearly only at ambient temperatures above 34°C.

Over the ambient temperature range from 32 to 42°C, average skin temperature increased linearly with increasing ambient temperature, as shown in Figure 6. In Appendix 2, average skin temperature is plotted against rectal temperature, of which it appears to be a linear function. The relationship of average skin temperature to hypothalamic temperature, shown in Appendix 3, is less well defined than the relationship to rectal temperature shown in Appendix 2,

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| Cat No. | Run No. | |
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| 1 | 4 | 3 |
| 1 | 5 | 3 |
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| 3 | 1* | 3 |
| 3 | 2 | 3 |
| 3 | 3 | 3 |
| 3 | 4 | 3 |
| 3 | 5 | 3 |
| 3 | 6 | 3 |
| 3 | 7 | 3 |
| 3 | 8* | 4 |
| 3 | 9 | 4 |
| 5 | 1 | 3 |
| 6 | 1 | 3 |
| 6 | 2 | 3 |
| 6 | 3 | 3 |
| 6 | 4* | 3 |

*indicates e

TABLE 1

Means and standard errors of body and ambient temperatures (in °C) and respiratory frequency (in breaths/min) of all cats in all experiments.

| Cat No. | Run No. | $T_a$ | $T_{re}$ | $\overline{T}_S$ | $T_{hy}$ | f |
|---|---|---|---|---|---|---|
| 1 | 2 | 32.0±.10 | 39.1±.08 | 36.6±.04 | 38.6±.08 | 18± 0 |
| 1 | 3 | 35.0±.10 | 39.4±.09 | 37.4±.08 | 38.9±.02 | 21± 1 |
| 1 | 4 | 35.1±.05 | 40.0±.00 | 38.2±.02 | 39.4±.00 | 34± 3 |
| 1 | 5 | 38.0±.01 | 40.4±.00 | 39.0±.09 | 39.4±.10 | 215±10 |
| 1 | 6 | 38.2±.09 | 40.5±.01 | 39.1±.06 | 39.5±.03 | 244± 5 |
| 1 | 7 | 41.2±.06 | 41.0±.04 | 40.5±.02 | 40.1±.01 | 252± 3 |
| 3 | 1* | 32.0±.08 | 39.3±.04 | 37.0±.05 | 39.1±.03 | 41± 1 |
| 3 | 2 | 35.0±.04 | 39.5±.02 | 38.1±.04 | 39.6±.01 | 37± 3 |
| 3 | 3 | 35.1±.07 | 39.3±.02 | 37.4±.01 | 39.1±.04 | 51± 1 |
| 3 | 4 | 36.6±.04 | 39.4±.02 | 38.2±.02 | 39.4±.03 | 58± 2 |
| 3 | 5 | 38.0±.03 | 40.4±.02 | 39.7±.03 | 39.8±.01 | 116± 5 |
| 3 | 6 | 37.9±.03 | 40.0±.00 | 39.5±.01 | 38.9±.09 | 133± 8 |
| 3 | 7 | 39.1±.03 | 40.4±.01 | 39.9±.02 | 39.9±.02 | 134± 4 |
| 3 | 8* | 41.0±.03 | 40.7±.05 | 40.3±.03 | 39.9±.04 | 133± 3 |
| 3 | 9 | 41.0±.10 | 40.8±.01 | 40.4±.02 | 40.1±.04 | 205±13 |
| 5 | 1 | 32.4±.05 | 39.6±.02 | 36.6±.03 | 39.5±.02 | 37± 3 |
| 6 | 1 | 32.0±.03 | 39.4±.03 | 37.0±.03 | 39.5±.05 | 39± 4 |
| 6 | 2 | 33.1±.05 | 39.4±.02 | 37.2±.04 | 39.4±.02 | 61± 5 |
| 6 | 3 | 36.4±.05 | 40.1±.02 | 38.8±.02 | 40.3±.08 | 84± 5 |
| 6 | 4* | 39.8±.01 | 41.1±.08 | 40.1±.01 | 40.2±.06 | 152± 9 |

*indicates exercising animal

Figure 5. Rectal temperature as a function of ambient temperature. Rectal temperature (°C; $T_{re}$; ordinate) is shown as a function of ambient temperature (°C; $T_a$; abscissa). Solid dots indicate resting animals; open circles designate exercising cats. For all resting animals, $T_{re} = 0.182\ T_a + 33.4$; $r = 0.88$. 95% confidence interval on slope = 0.173 - 0.191. The slope is significantly different from 0 (0.01 level).



41.5 E Tre

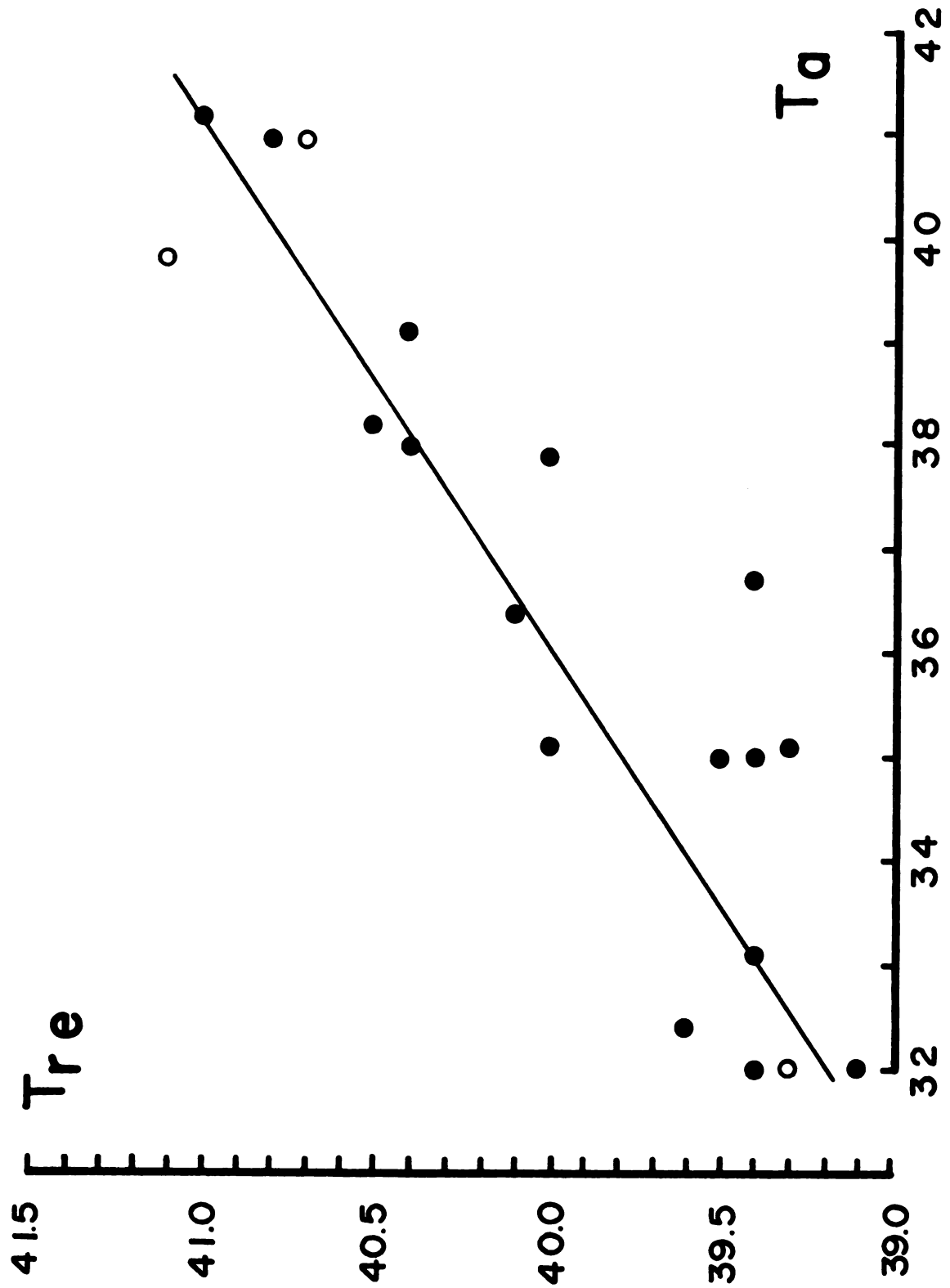
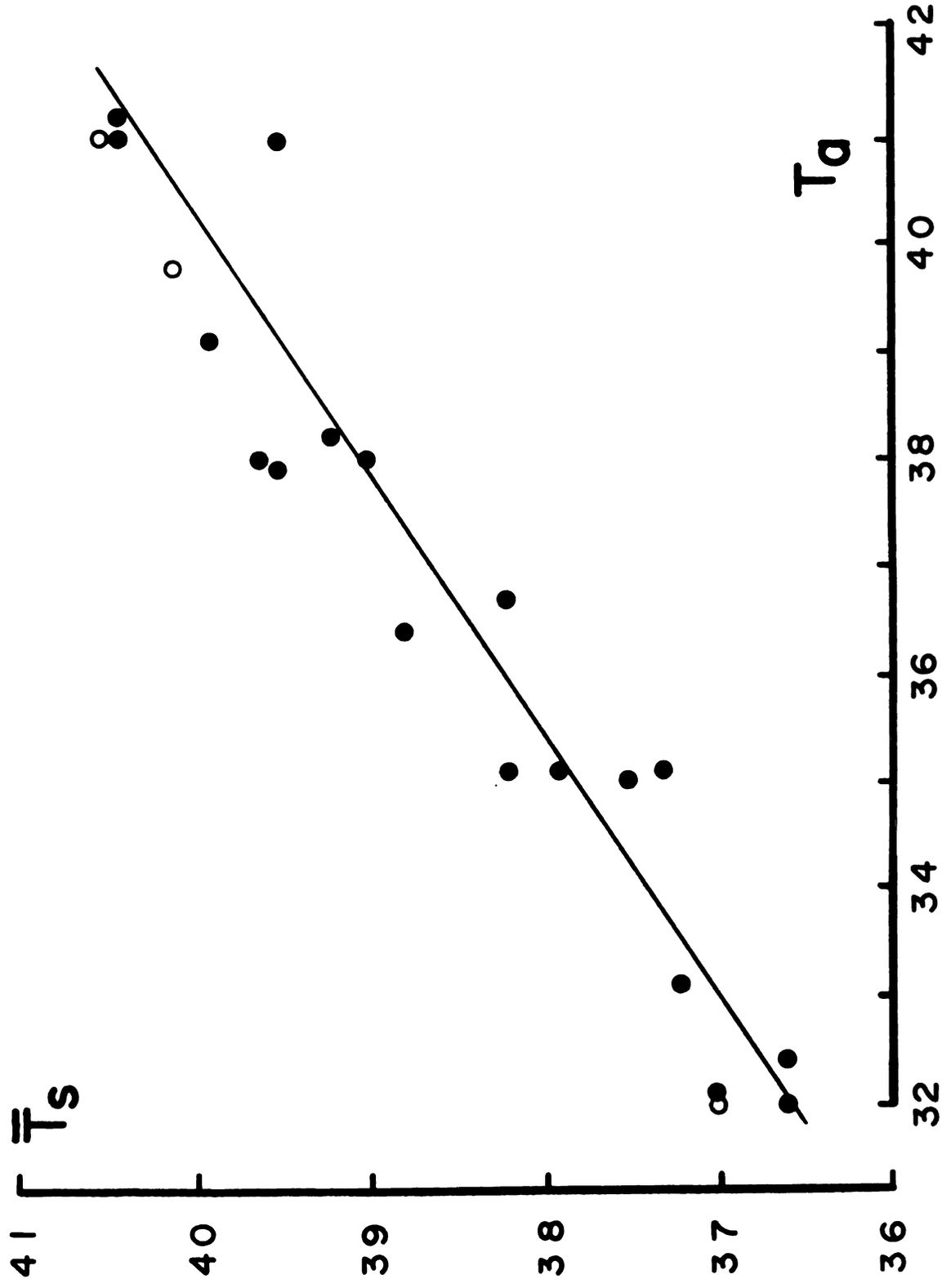



Figure 5

Figure 6. Average skin temperature as a function of ambient temperature. Average skin temperature (°C; $\overline{T}_S$; ordinate) is shown as a function of ambient temperature (°C; $T_a$; abscissa). Solid dots indicate resting animals; open circles designate exercising cats. $\overline{T}_S = 0.422\ T_a + 23.1$; $r = 0.98$. 95% confidence interval on slope: 0.376 - 0.468.

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probably because of the dissociation of hypothalamic temperature from other deep body temperatures in panting animals (see below and Discussion).

The relationships of rectal temperature to hypothelamic temperature during thermal steady states are presented in Figure 7. At low rectal and hypothalamic temperatures (when the cats were not panting) there existed a linear relationship between the two temperatures. When rectal temperature exceeded 39.6°C, and panting occurred, the relationship of rectal to hypothalamic temperature was still linear, but the slope was steeper.

The relationships of respiratory frequency to ambient, rectal, and hypothalamic temperatures, respectively, shown in Figures 8 and 9 and Appendix 4, also conform to the pattern previously established (Adams et al., 1970; Hunter and Adams, 1966). Frequency was relatively independent of ambient temperature when the temperature was below 36°C, but above this threshold value frequency rose with increasing ambient temperature (Figure 8). The existence of a threshold value for rectal temperature is not well established, since the correlation coefficient for frequency as a function of rectal temperature when rectal temperature is greater than 39.5°C is 0.87, compared to r = 0.89 for frequency as a function of rectal temperature when rectal temperature is above 39.0°C (Figure 9). The linear correlation of frequency with hypothalamic temperature was not strong (r = 0.52, Appendix 4). The higher

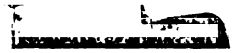


Figure 7. Rectal temperature as a function of hypothalamic temperature.

Rectal temperature (°C; $T_{re}$; ordinate) is shown as a function of hypothalamic temperature (°C; $T_{hy}$; abscissa). Solid dots designate resting animals; open circles indicate exercising cats. For rectal temperatures below 39.7°C, $T_{re} = 0.39\ T_{hy} + 24.1$; $r = 0.83$. 95% confidence interval on slope = 0.16 - 0.62. For rectal temperatures above 39.7°C, $T_{re} = 1.02\ T_{hy} - 0.1$; $r = 0.83$. 95% confidence interval on slope = 0.44 - 1.60.

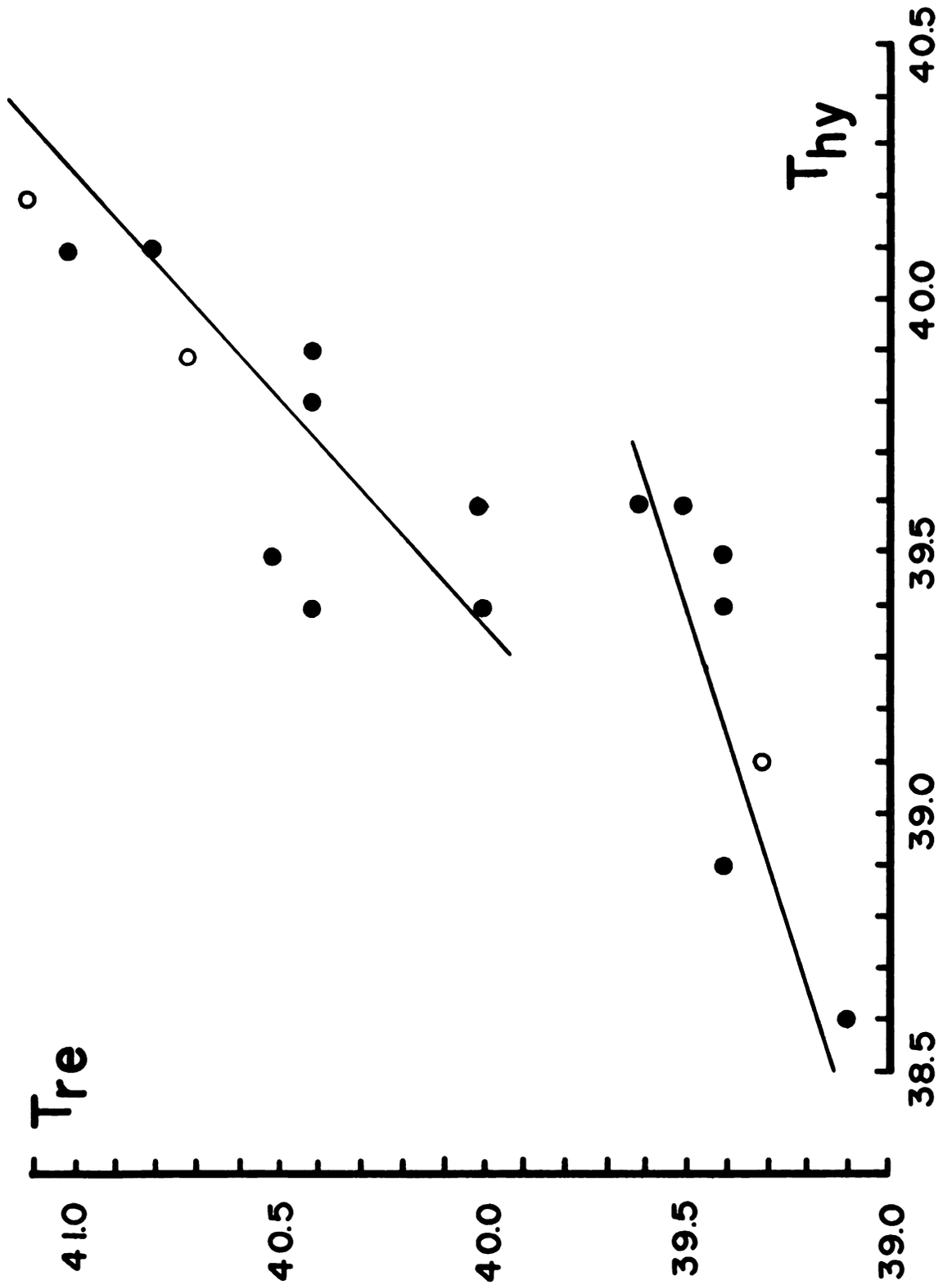



Figure 7

Figure 8. Respiratory frequency as a function of ambient temperature. Respiratory frequency (f; breaths/min; ordinate) is shown as a function of ambient temperature (°C; $T_a$; abscissa). Open circles indicate exercising animals; solid dots designate resting cats. For ambient temperatures above 36°C, $f = 30.0\ T_a - 995$; $r = 0.71$. 95% confidence interval on slope = 3.4 - 56.6.

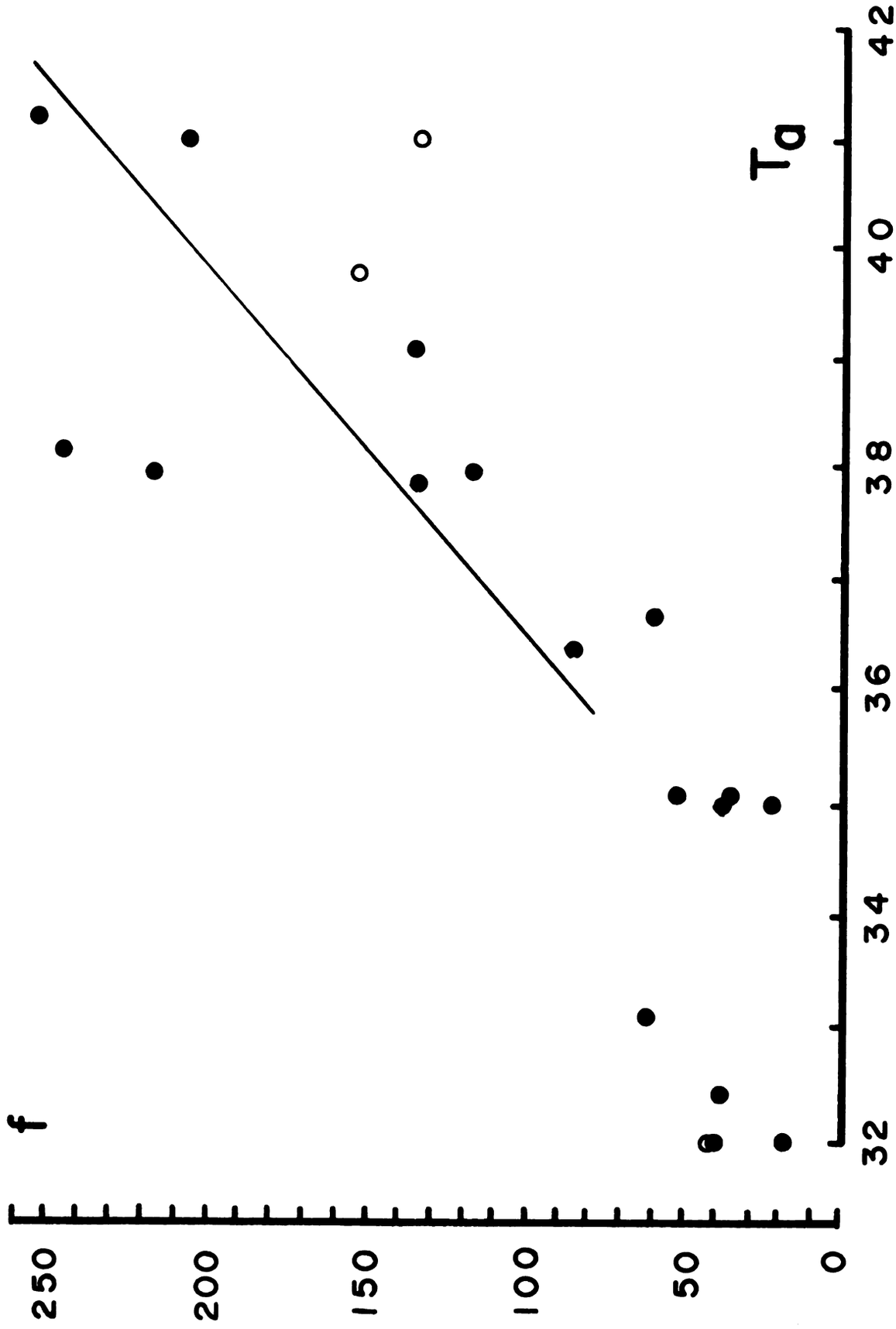



Figure 8

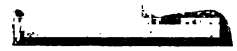


Figure 9. Respiratory frequency as a function of rectal temperature. Respiratory frequency (f; breaths/min; ordinate) is shown as a function of rectal temperature (°C; $T_{re}$; abscissa). Solid dots indicate resting animals; open circles designate exercising cats. For resting animals only, $f = 124.6\ T_{re} - 4870$; $r = 0.89$. 95% confidence interval on slope = 89.8 - 159.4.

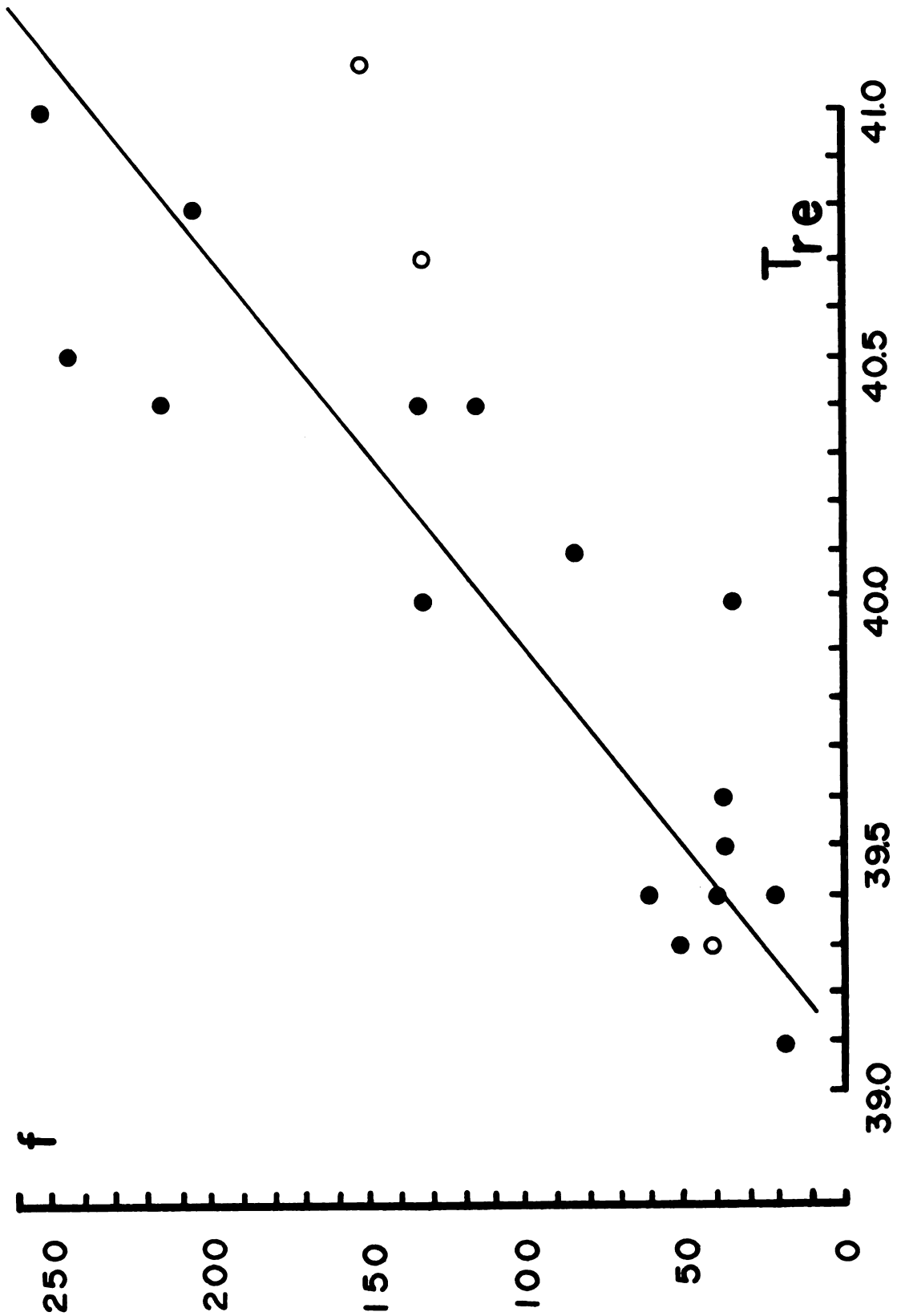



Figure 9

correlation of frequency with rectal temperature than with hypothalamic temperature suggests that hypothalamic temperature is not the primary drive for the respiratory response to heat stress in the unanesthetized cat (see Discussion). The correlation coefficient for respiratory frequency as a function of average skin temperature is 0.38 (Appendix 5).

The effect of polypnea and panting on the pH and gas content of the blood are shown in Table 2 and Figures 10-12. Table 2 contains means and standard errors of pH and blood gas tensions, and means of bicarbonate concentration for all blood samples. All data are derived from steady-state blood samples drawn after a minimum of 90 minutes exposure to a given ambient temperature. The steady-state levels of $Pa_{CO_2}$ during exposure to various ambient temperatures are shown as a function of respiratory frequency in Figure 10. The curve is nonlinear at the 0.01 level, and is not a simple exponential function. $Pa_{CO_2}$ declined most steeply as frequency rose from 20/min to 50/min. Above this frequency (ca. 50/min) $Pa_{CO_2}$ continued to decrease as frequency rose, although less steeply than at low frequencies. The relationships of arterial blood carbon dioxide tension to ambient and body temperatures are shown in Appendices 6-9. All of these relationships of $Pa_{CO_2}$ to temperature are believed to be a consequence of the relationship of $Pa_{CO_2}$ to frequency and the dependence of frequency on the various temperatures (Figures 8 and 9 and Appendices 4-5).

TABLE 2

Mean values and standard errors of blood gas tensions, and pH and means of bicarbonate concentration for all cats in all experiments.

| Cat No. | Run No. | Sample | $Pa_{CO_2}$ (mmHg) | pH | $Pa_{O_2}$ (mmHg) | $[HCO_3^-]$ (mEg/10 |
|---|---|---|---|---|---|---|
| 1 | 2 | 1 | 42.4± .2 | 7.386± .003 | ---- | 24.5 |
| | | 2 | 43.6± .4 | 7.358± .003 | ---- | 23.6 |
| 1 | 3 | 1 | ---- | 7.370± .000 | ---- | ---- |
| | | 2 | ---- | 7.338± .004 | ---- | ---- |
| 1 | 4 | 1 | 41.0± .0 | 7.338± .009 | ---- | 21.3 |
| | | 2 | 40.1±1.4 | 7.338± .008 | ---- | 20.6 |
| 1 | 5 | 1 | ---- | 7.377± .006 | ---- | ---- |
| | | 2 | ---- | 7.374± .002 | ---- | ---- |
| 1 | 6 | 1 | 39.2± .4 | 7.334± .002 | ---- | 19.8 |
| | | 2 | 32.0± .7 | 7.384± .002 | ---- | 18.4 |
| 1 | 7 | 1 | 29.4± .0 | 7.419± .001 | 116.2±0.8 | 18.1 |
| | | 2 | 25.6± .4 | 7.436± .002 | 113.8±0.0 | 16.6 |
| 3 | 1* | 1 | 33.9± .7 | 7.365± .003 | 108.3±0.4 | 18.6 |
| | | 2 | 37.5± .6 | 7.228± .010 | 116.0±0.4 | 14.9 |
| 3 | 2 | 1 | 36.7± .0 | 7.384± .004 | 115.8±0.0 | 21.0 |
| 3 | 3 | 1 | 33.2± .4 | 7.418± .001 | 109.4±0.1 | 20.8 |
| | | 2 | 31.6± .2 | 7.414± .002 | 117.4±0.5 | 19.5 |
| 3 | 4 | 1 | 33.0± .4 | 7.435± .001 | 115.0±0.7 | 21.4 |
| | | 2 | 34.0± .6 | 7.414± .005 | 116.0±0.0 | 21.0 |
| 3 | 5 | 1 | 31.3± .6 | 7.415± .005 | 116.4±0.5 | 19.3 |
| | | 2 | 27.4± .3 | 7.316± .004 | 122.6±0.9 | 13.4 |
| 3 | 6 | 1 | 34.0± .2 | 7.380± .000 | 111.8±0.4 | 19.2 |
| | | 2 | 33.9± .5 | 7.376± .004 | 112.0±1.4 | 19.0 |
| 3 | 7 | 1 | 35.5± .5 | 7.409± .003 | 116.8±1.5 | 21.6 |
| | | 2 | 34.2± .2 | 7.415± .000 | 116.7±0.6 | 21.0 |
| | | 3 | 35.8± .2 | 7.386± .006 | 110.1±0.5 | 20.6 |
| 3 | 8* | 1 | 32.0± .3 | 7.335± .007 | 91.7±1.7 | 16.2 |
| | | 2 | 30.2± .6 | 7.391± .004 | 96.0±0.2 | 17.5 |
| 3 | 9 | 1 | 29.2± .0 | 7.420± .002 | 115.1±1.0 | 18.1 |
| | | 2 | 28.1± .1 | 7.405± .004 | 123.7±0.6 | 16.8 |
| 5 | 1 | 1 | 34.9± .6 | 7.388± .005 | 98.0±0.5 | 20.2 |
| | | 2 | 30.4± .2 | 7.398± .005 | 101.6±0.9 | 18.0 |
| 6 | 1 | 1 | 36.8± .0 | 7.360± .000 | 90.1±1.5 | 19.9 |
| 6 | 2 | 1 | 38.8± .0 | 7.329± .008 | 99.8±0.8 | 19.6 |
| 6 | 3 | 1 | 32.8± .2 | 7.364± .005 | 121.8±1.2 | 18.0 |
| | | 2 | 36.5± .4 | 7.354± .000 | 126.2±1.4 | 19.4 |
| 6 | 4* | 1 | 39.5± .9 | 7.310± .000 | 90.7±1.4 | 18.8 |
| | | 2 | 37.1± .1 | 7.318± .006 | 102.8±0.2 | 18.0 |

*indicates exercising animal

Figure 10. $P_{a_{CO_2}}$ as a function of respiratory frequency.
Arterial blood carbon dioxide tension ($P_{a_{CO_2}}$; mm Hg; ordinate) is shown as a function of respiratory frequency (f; breaths/min; abscissa).

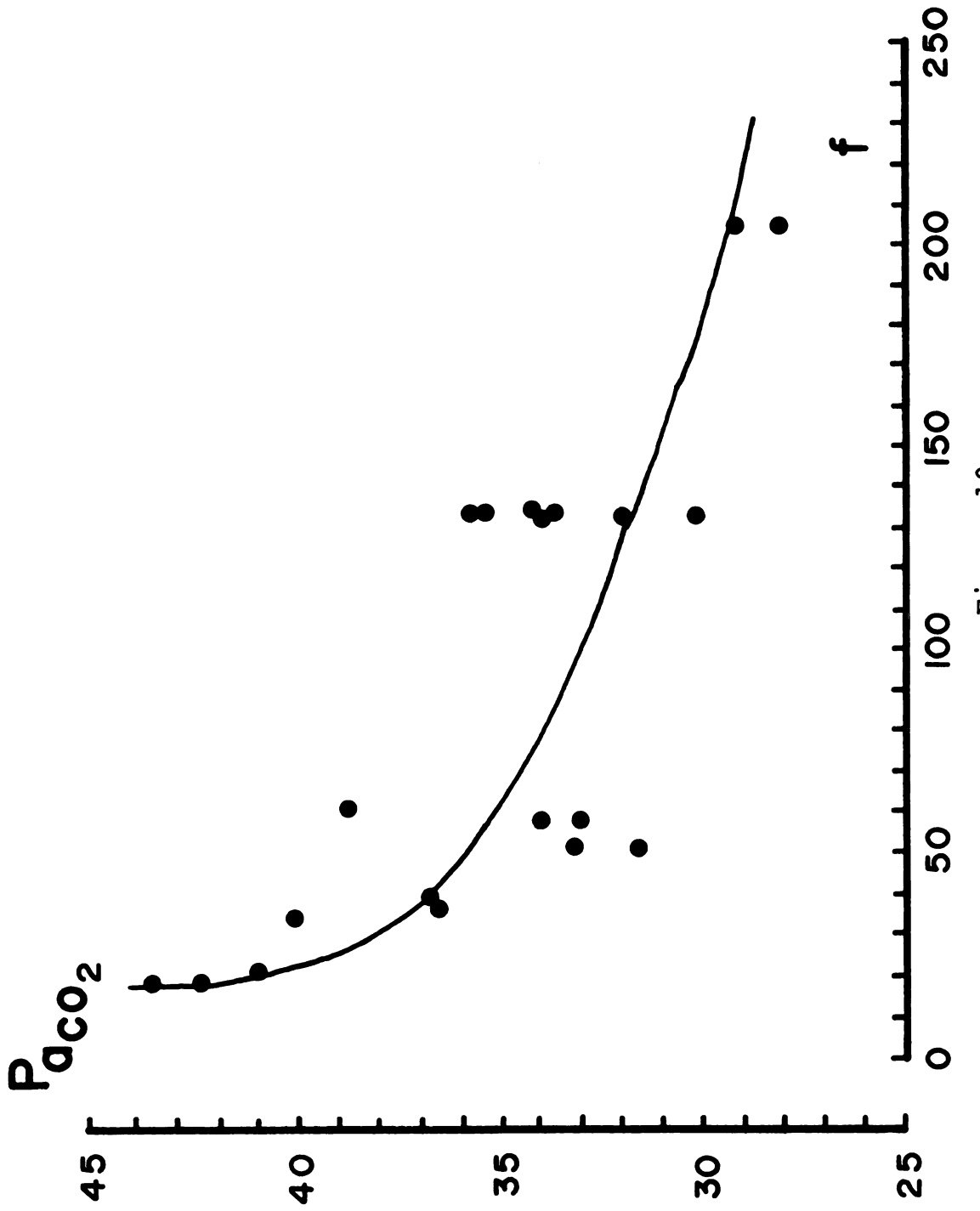



Figure 10

The development of hypocapnia produced no severe alkalosis, as shown in Figures 11 and 12. There was no dependence of arterial blood pH on respiratory frequency (Figure 11), nor on ambient or body temperatures (Appendices 10-12). Nevertheless, there was a linear increase of pH with decreasing $Pa_{CO_2}$ (Figure 12), although the correlation coefficient was not high ($r = -0.72$). As shown also in Figure 12, the calculated bicarbonate concentration of the blood fell with decreasing $Pa_{CO_2}$. Although the correlation coefficient for a linear dependence of bicarbonate concentration on $Pa_{CO_2}$ is -0.78, the distribution of the data also suggests a sigmoid curve, with bicarbonate concentration stable when $Pa_{CO_2}$ is between 32 and 40 mm Hg.

The changes in $Pa_{O_2}$ during heat stress in the unanesthetized cat are shown in Figure 13. At low respiratory frequencies, $Pa_{O_2}$ rose steeply as a function of increasing frequency. When frequency exceeded 50/min, $Pa_{O_2}$ was stable and maximum in resting cats. Exercising animals consistently maintained lower arterial blood oxygen tensions at high respiratory frequencies. Relationships of $Pa_{O_2}$ to ambient and body temperatures are presented in Appendices 13-16.

Figure 14 is a record of respiratory movements from one cat (No. 7) exposed to 38°C. The animal was panting steadily; the mouth was always open. Cyclic variations in frequency are evident, and oscillations in the amplitude of the excursions are also present.

Figure 11. pH as a function of respiratory frequency.
Arterial blood pH (ordinate) is shown as a function of respiratory frequency (f; breaths/min; abscissa).

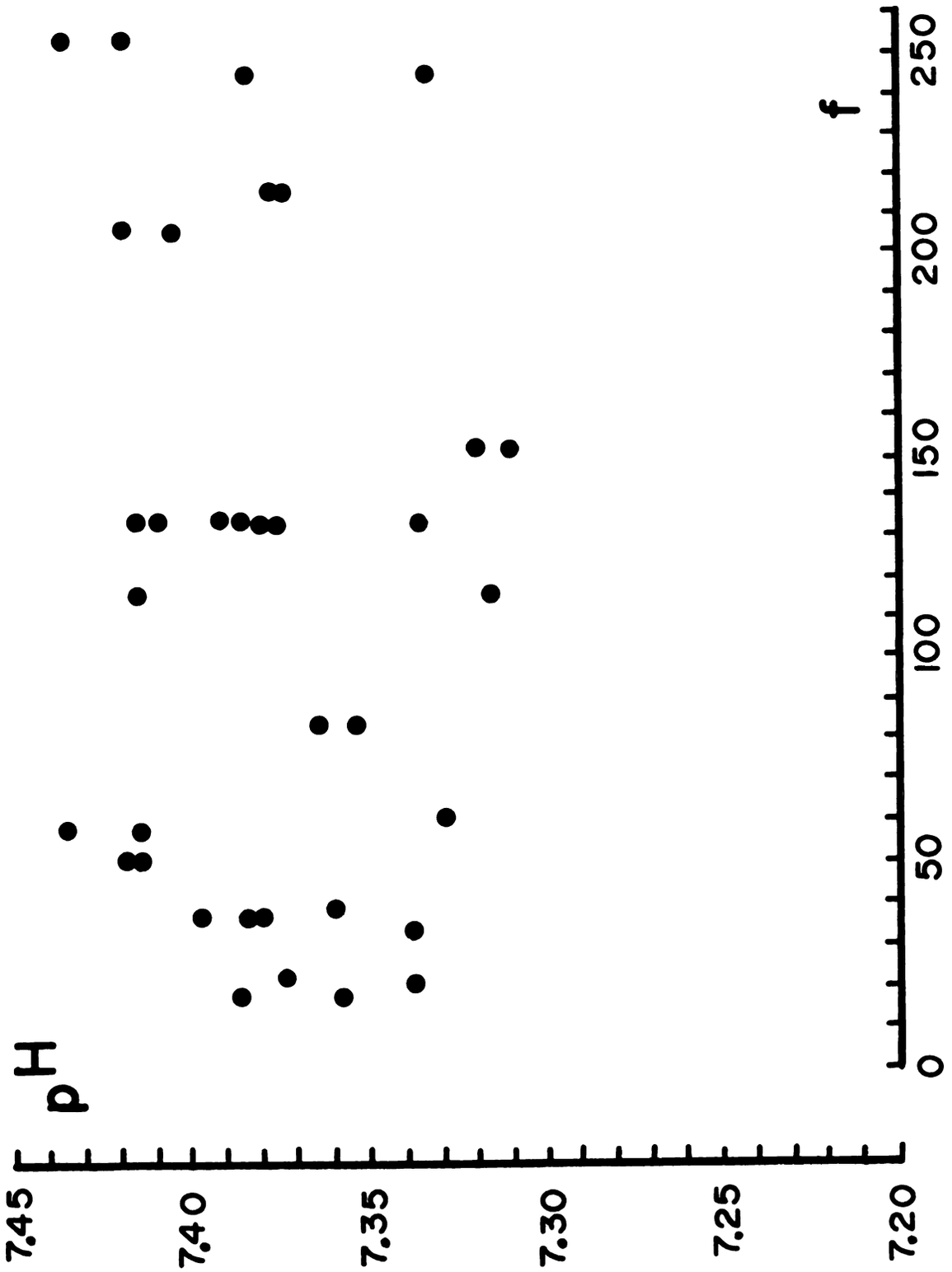
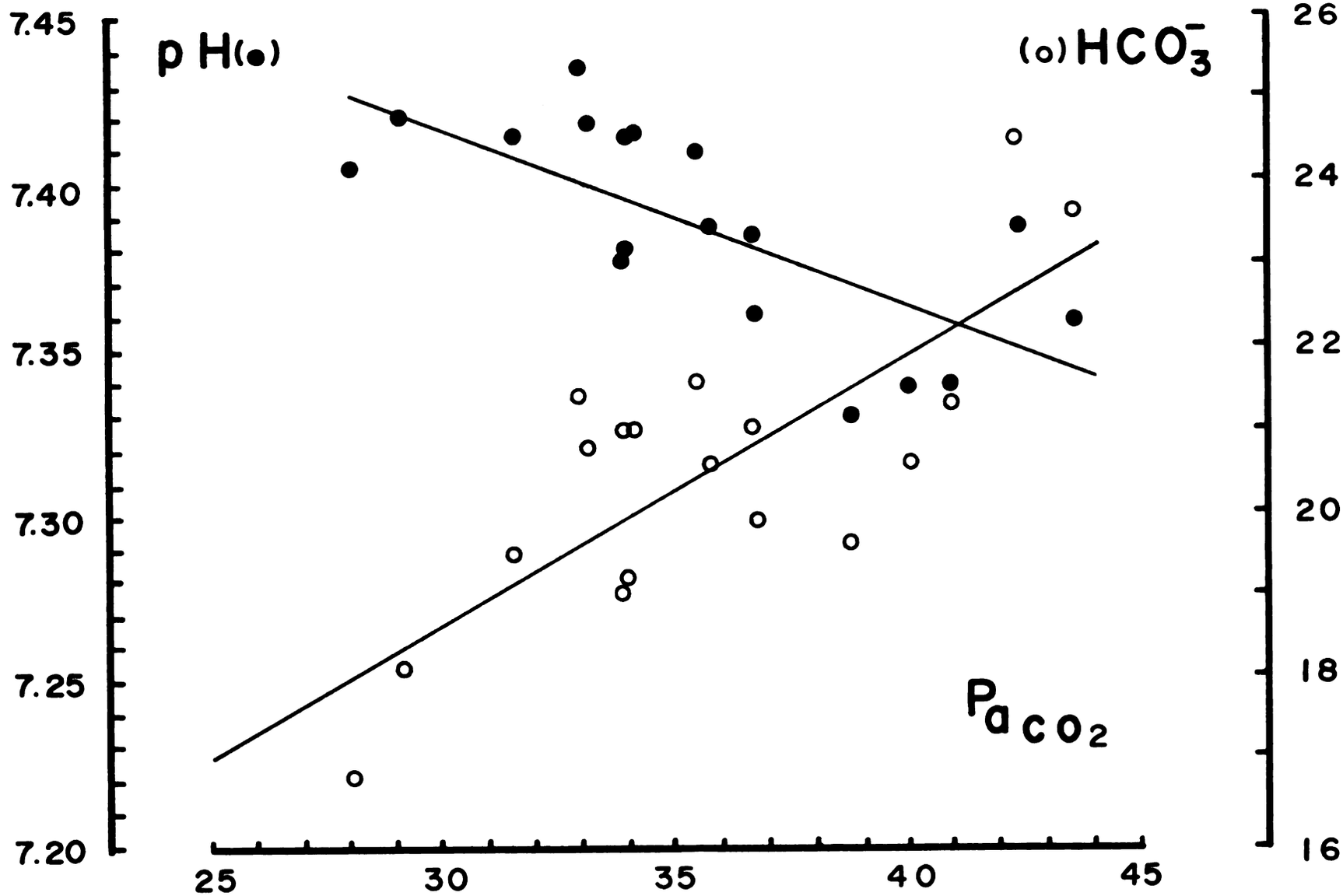



Figure 11

Figure 12. pH and plasma bicarbonate concentrations as functions of $Pa_{CO_2}$ in resting cats.

Arterial blood pH (solid dots; left ordinate) and bicarbonate concentration (mEq/l; open circles; right ordinate) are shown as functions of arterial blood carbon dioxide tension ($Pa_{CO_2}$; mm Hg; abscissa). pH = -0.0054 $Pa_{CO_2}$ + 7.579; r = -0.72. 95% confidence interval on slope = -0.0027 - -0.0081. Bicarbonate concentration = 0.328 $Pa_{CO_2}$ + 8.8; r = 0.78. 95% confidence interval on slope = 0.187 - 0.469.


7.45
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7.35
7.30
7.25
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(○)HCO$_3^-$
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45
$P_{aCO_2}$

Figure 12

Figure 13. $P_{a_{O_2}}$ as a function of respiratory frequency.
Oxygen tension of arterial blood ($P_{a_{O_2}}$; mm Hg; ordinate) is shown as a function of respiratory frequency (f; breaths/min; abscissa). Solid dots indicate resting cats; open circles designate exercising animals.

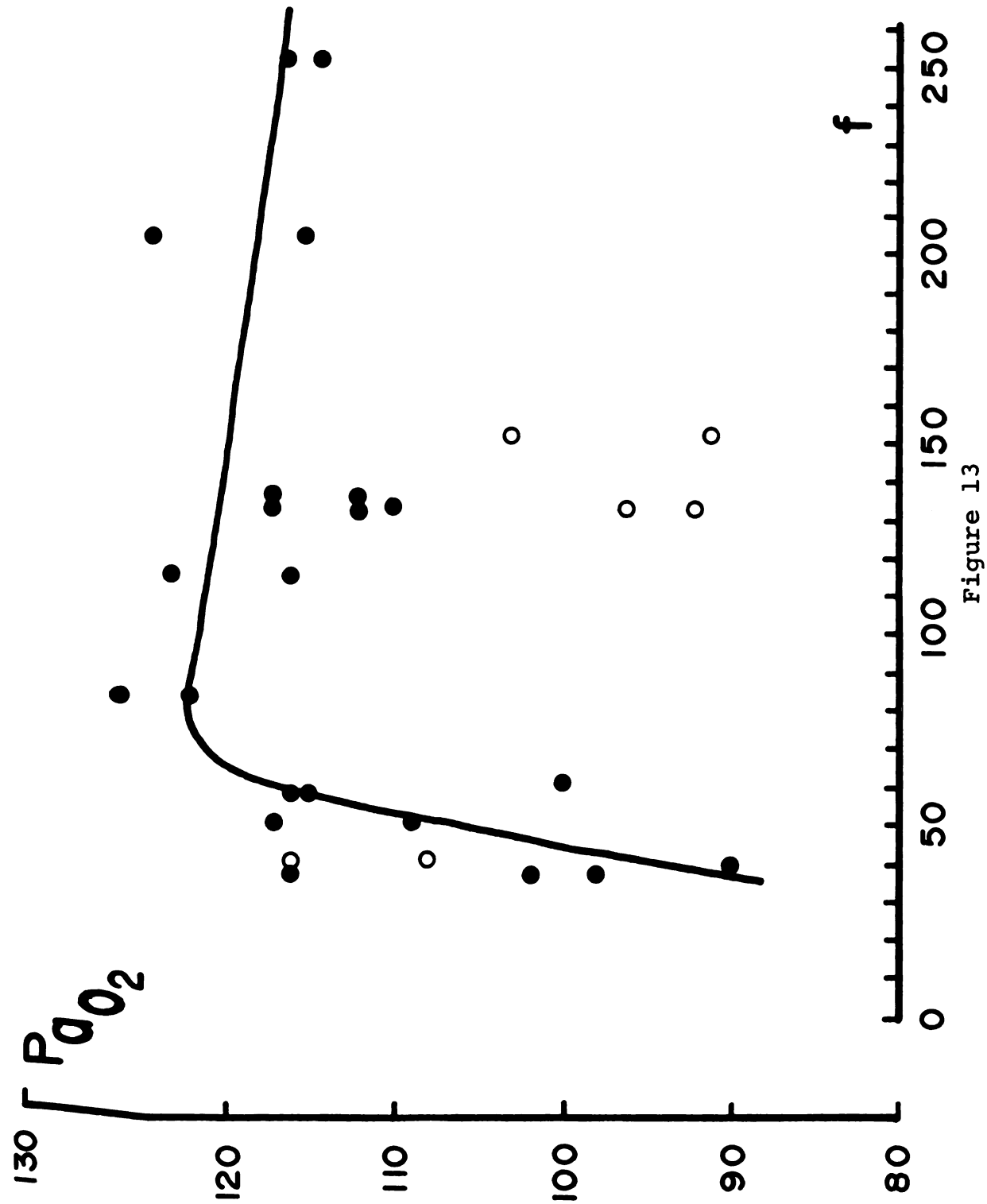


Figure 13

Figure 14. Record of respiratory movements from a single cat.
Record of respiratory movements from a single unanesthetized cat exposed to an ambient temperature of 38°C.

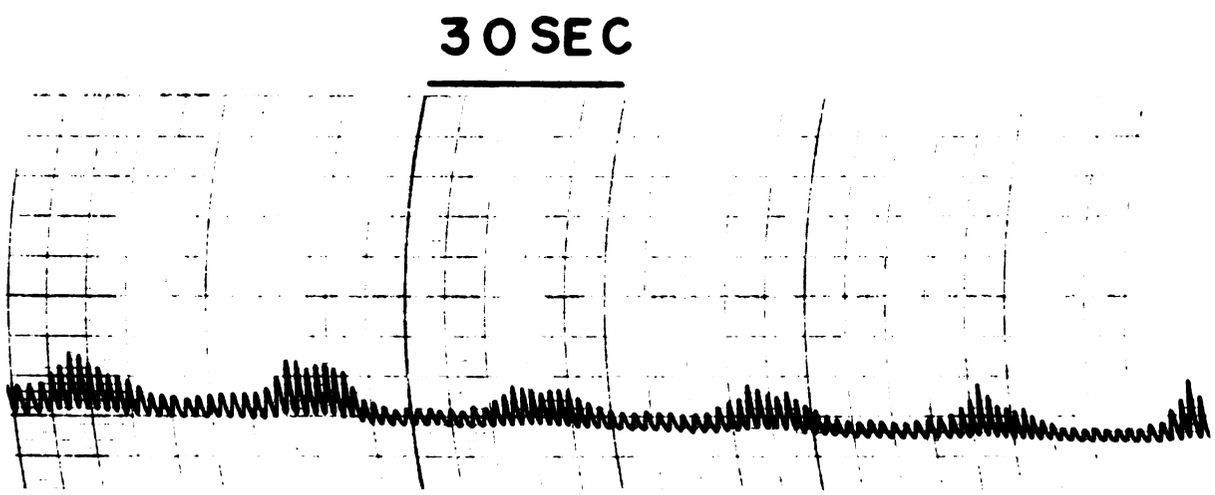


Figure 14

# DISCUSSION

A homeotherm, by definition, is capable of maintaining a relatively constant deep body temperature despite moderate changes in the thermal properties of its environment. When exposed to a mild heat stress, the animal may employ conductive, convective, and radiant heat transfer (collectively referred to as "dry" heat exchange) as well as evaporative heat loss to dissipate the heat produced by metabolism in its tissues. Since each of these three forms of dry heat exchange depends upon the temperature gradient from the animal's body surface to the environment, and upon the body surface area available for heat exchange, a homeotherm can modulate its dry heat exchange by controlling the temperature of those portions of its body which have large surface area-to-volume ratios. Such alterations in body surface temperature are due primarily to changes in cutaneous blood flow. Selective cutaneous vasomotion in response to mild and moderate heat stress has been demonstrated in the unanesthetized cat (Adams et al., 1970) and is confirmed by the data presented here (Figure 6). Average skin temperature increased linearly as ambient temperature rose from 32°C to 42°C, and therefore the increase in dry heat loss begins at ambient

temperatures just above the thermoneutral zone (26-32°C; Adams et al., 1970). The linear relationship also suggests that dry heat loss can be graded for a response proportional to the levels of thermal stress.

In addition to augmenting heat loss by increasing skin temperature, the homeotherm may store heat, thereby changing the temperature of its tissues and its total body heat content. The storage must be limited if the animal is to remain homeothermic, but such retention of heat may result in a considerable saving of water. Data presented in Figure 5 confirm the previous report (Adams et al., 1970) that unanesthetized cats tolerate a substantial increase in deep body temperature during severe heat stress, and Figure 9 presents evidence that maximum respiratory frequency is not evoked unless deep body temperature is raised.

As ambient temperature rises, dry heat loss declines due to the reduction in the temperature gradient between body surface and environment. Evaporative heat loss must rise to compensate for the reduced dry heat loss if homeothermy is to be maintained. Evaporative cooling in a furred homeotherm is essentially restricted to the upper respiratory tract, and an increase in evaporative heat loss without a large rise in body temperature implies augmented air movement over these evaporative surfaces. Such an increase in total air movement can be brought about by elevating either respiratory frequency or tidal volume, or both. Figures 8 and 9 and Appendices 4

and 5 present evidence that respiratory frequency of the unanesthetized cat rose as ambient and body temperatures increased. The rise in frequency began when ambient temperature exceeded 35.5°C, and respiratory frequency rose linearly with ambient temperatures above 35.5°C (Figure 8). Mild exercise resulted in a lower respiratory frequency at a given ambient (Figure 8) or rectal temperature (Figure 9).

The evaporative heat loss from the upper respiratory tract results in cooling of the epithelial linings of the upper pharynx and roof of the buccal cavity. These membranes are only a few millimeters from the base of the brain in the cat (Figure 3), and the localized cooling of the upper respiratory tract strongly influences the relationship of hypothalamic temperature to other deep body temperatures (Figure 7). The onset of polypnea shifted the linear relationship of rectal to hypothalamic temperature from one line to another with a steeper slope. The presumed increase in heat loss from the upper respiratory passages as a consequence of panting tended to maintain hypothalamic temperature even further below rectal temperature than it is in thermoneutral or warm exposures, when panting does not occur. This selective cooling of the lower brain areas implies that during heat stress the cat can reduce its thermoregulatory effort, increase heat storage and allow deep body temperatures to rise without developing high brain temperatures. This effect is even more strikingly demonstrated by some desert-dwelling antelopes (Taylor, 1969).

Mild exercise, which resulted in a lower respiratory frequency at a given ambient temperature (Figure 8) did not appear to affect the relationship of hypothalamic to rectal temperature during heat stress (Figure 7). This suggests that the decreased respiratory frequency during exercise was accompanied by an increased tidal volume so that total air movement over the upper respiratory surfaces, and total heat loss from those surfaces, was similar to that of the resting animal under analogous exposure conditions.

Respiratory frequency was better predicted by rectal and ambient temperatures than by hypothalamic temperature or average skin temperature (Figures 8 and 9, and Appendices 4 and 5). This suggests that the temperature of the thermosensible cells in the anterior hypothalamus (where hypothalamic temperature was measured in this study) is not the primary input driving the respiratory response to heat stress. This hypothesis is further supported by observations on cats during the transition from polypnea to panting as the animal approached the steady state. Rectal and hypothalamic temperatures rose in parallel during polypnea (Figure 7). When panting began, hypothalamic temperature stabilized or sometimes fell, while rectal temperature continued to rise, later to stabilize at a higher value. Respiratory frequency never declined when hypothalamic temperature fell if rectal temperature was still rising.

Forster and Ferguson (1952) reported two separate patterns for the initiation of panting in unanesthetized cats. One group of cats began to pant when ambient and skin temperatures rose, with no rise in rectal temperature ("reflex panters"); the other group began to pant only when deep body temperature rose ("central panters"). Data points at f = 215 and f = 244, which lie to the left of the data grouping in Figures 8 and 9, were recorded from a single cat (No. 1). This animal increased its respiratory frequency more steeply with increasing temperature than did the other cats. It is possible that this animal was a "reflex panter"; the other cats would then have been "central panters". Alternatively, at the initiation of panting the one cat (No. 1) may have shifted abruptly to a respiratory frequency near the resonant frequency of its thorax, as reported in dogs (Crawford, 1962), while the other cats showed a more gradual increase in frequency. Further, the unevaluated influence of the animal's previous experience with high ambient temperatures may play a role. Possibly cat No. 1 had experienced severe heat stress before this exposure and its response patterns were better established than those of the other cats.

The onset of panting in all cats conformed to the pattern described by Hemingway (1938) and Albers (1961a) for dogs and by Ingram and Legge (1970) for pigs; that is, short bouts of panting interrupted the polypnea at gradually decreasing intervals. Also, the animals became increasingly restless as

respiratory frequency rose during the period of polypnea, and the animals' apparent discomfort disappeared when panting began (see Hemingway, 1938, regarding similar responses by dogs). Shortly before the initiation of panting the cats began to lick their noses frequently, and also licked the restraining frame.

"Phase II" breathing, defined as a decrease in respiratory frequency with a concomitant increase in tidal volume during very severe heat stress (Bianca, 1958), was never observed in this study. In preliminary experiments, cats which were exposed to 41°C ambient temperature developed rectal temperatures as high as 41.8°C without exhibiting the Phase II pattern. The failure to observe Phase II breathing in these experiments is judged not to be due to an insufficiently high rectal temperature and Phase II breathing does not appear to be a characteristic hyperthermic response of unanesthetized cats.

The increase in respiratory frequency in response to heat stress in the unanesthetized cat serves to increase the total air flow over the upper respiratory passages and facilitates heat loss by evaporation (Adams et al., 1970). However, were air movement over alveolar surfaces also increased, hypocapnia and alkalosis would ensue, adding the threat of acid-base disturbances to that of the thermal stress. Elevation in respiratory frequency might, of course, be countered by decreased tidal volume, as has been reported in

the unanesthetized ox, sheep, goat, pig, and dog (see Review of the Literature). In the ox (Hales and Findlay, 1968a), sheep (Hales et al., 1970), and dog (Albers, 1961a) such compensation is sufficient to prevent hypocapnia and alkalosis until respiratory frequency reaches its maximum value. In the goat, hypocapnia and alkalosis develop despite the reduced tidal volume (Heisey et al., 1971).

The responses of the unanesthetized cat do not conform to either the pattern reported for the dog (no alkalosis or hypocapnia) or that observed in the goat (severe hypocapnia with alkalosis), since cats developed hypocapnia ($P_{a_{CO_2}}$ falling from 43 mm Hg to 33 mm Hg) at low respiratory frequencies (below 50/min), but failed to exhibit severe alkalosis even at respiratory frequencies up to 200/min (Figures 11 and 12). The decrease in $P_{a_{CO_2}}$ with rising respiratory frequency is quite steep at frequencies below 50/min (10 mm Hg drop in $P_{a_{CO_2}}$ as frequency rises from 18 to 50/min), which suggests that at respiratory frequencies below 50/min the unanesthetized cat fails to compensate for the increased respiratory frequency with a decrease in tidal volume, and hyperventilation results. At respiratory frequencies above 50/min, the decline of $P_{a_{CO_2}}$ continued, but was considerably less steep (5 mm Hg decline with an increase of 150/min in frequency), suggesting that the cat compensates relatively more effectively for large increases in respiratory frequency.

These data are consistent with those of von Euler et al. (1970), who reported that, as body temperature of decerebrate cats increased from thermoneutral levels to values just below the threshold for panting, minute ventilation increased due to elevations in both tidal volume and frequency. The greater the increase in temperature, the larger was the contribution of respiratory frequency to the total increase in ventilation. Albers (1961a) also observed that the ratio of deadspace to tidal volume rose as frequency increased during panting in the dog.

In a resting animal at thermoneutral ambient temperature, alveolar ventilation is strictly regulated by the $P_{CO_2}$ of the interstitial fluid (and inferentially the intracellular pH) in the region of the medullary respiratory control centers (Leusen, 1972). The hypocapnia exhibited by the cats in this study ($Pa_{CO_2}$ decreasing from 43 mm Hg to 29 mm Hg; Figure 10) should be a potent inhibitor of ventilation if present under thermoneutral conditions. Not only would the decreased $P_{CO_2}$ of the blood perfusing the carotid and aortic bodies be inhibitory to ventilation (Gray, 1968), but systemic hypocapnia results in a loss of $CO_2$ from the cerebrospinal fluid and a rise in CSF pH (Kazemi et al., 1967). Since the interstitial fluid bathing the chemosensitive areas of the medulla oblongata is in contact with both blood and CSF, carbon dioxide tension near the medullary chemoreceptors should fall, and intracellular pH should rise. That the

reduced chemoreceptor drive from both central and peripheral receptors fails to inhibit respiration during thermal panting in the cat implies that fundamental modifications of the respiratory control system have occurred.

Albers (1961c) found that the threshold for increased ventilation in response to $CO_2$ inhalation was decreased during panting, although the slope of the alveolar ventilation--$P_{a_{CO_2}}$ response curve was unchanged. The patterns of the response to $CO_2$ during normothermia and hyperthermia differed significantly. If respiratory frequency was initially low, it rose when $P_{a_{CO_2}}$ increased. If frequency was initially high due to a thermal drive, it fell when $CO_2$ inhalation began, and the increased ventilation in response to $CO_2$ was brought about by an elevated tidal volume. It appears, therefore, that a compromise is reached during panting so that increased respiratory evaporative heat loss and regulation against hypercapnia coexist. The decreased threshold for the $CO_2$ response curve permits panting to continue despite a degree of hypocapnia which would otherwise be inhibitory to respiratory frequency. If hypercapnia (induced, for example, by $CO_2$ inhalation) becomes a threat to homeostasis, the shallow respiratory pattern of panting is modified by decreasing the respiratory rate and increasing tidal volume. This hypothesis also explains the lower respiratory frequencies seen during exercise in this study (Figure 8). The contracting muscles provide an internal source of $CO_2$, and the response

is a slowing and, probably, a deepening of the respiratory pattern (see above).

Chapot (1967) suggested that hypocapnia is actually a prerequisite for panting. Using the anesthetized cat, he found that hypocapnia produced phrenic nerve discharge patterns very similar to those associated with thermal panting. Chapot proposed that panting is normally initiated by increased body temperature which enhances alveolar ventilation, and the resultant decrease in $P_{a_{CO_2}}$ then triggers panting. The increased alveolar ventilation could result from a rise in the temperature of the carotid bodies, since Bernthal and Weeks (1939) showed that warming the blood perfusing this tissue causes an increase either in respiratory frequency or in tidal volume, or in both.

Chapot's hypothesis that hypocapnia induces panting is supported by Pleschka's observations on dogs (Pleschka, 1969), in which hypocapnia induced polypnea even when body temperature was low. Von Euler et al., (1970) also found that, irrespective of the cause of polypnea (decortication, electrical stimulation of dorsal hypothalamus, thermal stimulation of ventral hypothalamus), an inverse respiratory frequency--$P_{a_{CO_2}}$ relationship resulted, paralleling the responses reported in Figure 10.

A pronounced oscillation in respiratory frequency and tidal volume in decorticate polypneic cats breathing pure oxygen has been reported (von Euler et al., 1970). Similar

oscillations in respiratory frequency, and presumably in tidal volume, were observed in one panting cat in the present study (Figure 14). The $Pa_{O_2}$ of panting cats is high (see below, and Figure 13), and the oxygen-sensitive chemoreceptors should have been "functionally denervated" in this animal, although perhaps not as completely as they were in the cat breathing oxygen.

$Pa_{CO_2}$ values in cats resting at 32°C ambient temperature (36.9-43.6 mm Hg), with respiratory frequency below 40/min (Figure 10 and Table 2) are higher than those reported earlier for unanesthetized cats (28-32 mm Hg; Fink and Schoolman, 1962; Sorensen, 1967; Herbert and Mitchell, 1971). Cats in this study were resting quietly in the restraining hammock, and frequently became drowsy when exposed to 32-35°C environments. The lower $Pa_{CO_2}$ values reported previously might have resulted from emotional hyperventilation during blood sampling in the earlier studies, and from failure of the authors to adjust measured values for the effect of body temperature.

In several species of homeotherms which rely on panting to combat heat stress, the hypocapnia which becomes marked at the peak of Phase I breathing is accompanied by alkalosis (ox, Bianca and Findlay, 1962; sheep, Hales et al., 1970; goat, Heisey et al., 1971). However, data reported in Figure 11 reveal that no severe alkalosis occurred in the panting cat despite the existence of substantial hypocapnia. The mean

pH (7.384) for all cats at all ambient temperatures agrees with that (7.38) reported by Fink and Schoolman (1962) for unanesthetized cats at thermoneutral temperatures. Data reported in Figure 12, in which pH is shown as a function of $P_{a_{CO_2}}$, indicate that pH increased by less than 0.1 unit as $P_{a_{CO_2}}$ fell from 43 to 28 mm Hg. Data reported in Figures 11 and 12, taken together, suggest that tidal volumes in panting cats are variable, since were they constant, the inverse relationship of $P_{a_{CO_2}}$ to respiratory frequency should cause pH to rise as frequency increases.

The rise of pH with decreasing $P_{a_{CO_2}}$ is not large (0.1 unit with a 15 mm Hg change in $P_{a_{CO_2}}$; Figure 12). Several factors act to minimize alkalosis despite the hypocapnia: first, the buffering capacities of the plasma proteins and hemoglobin, and second, the decrease in plasma bicarbonate concentration (Figure 12). The reduction in bicarbonate concentration is larger than can be accounted for by loss of bicarbonate as $CO_2$, even if all the $CO_2$ which is lost (as $P_{a_{CO_2}}$ falls from control to the stable hypocapnic level) is assumed to come from plasma bicarbonate stores. It is probable that some of the bicarbonate is excreted by the kidneys, since Fuller and MacLeod (1956) demonstrated that renal bicarbonate excretion increases during respiratory alkalosis. Studies by Sullivan and McVaugh (1963) indicate that the effect of changes in $P_{CO_2}$ on renal $H^+$ excretion, and inferentially on $HCO_3^-$ reabsorption, is rapid. Also, Bianca (1955)

reported that acutely heat-stressed calves excrete alkaline urine while maintaining a normal venous blood pH. Finally, lactic acid has been shown to accumulate in the blood of dogs (Frankel et al., 1962), cattle (Hales et al., 1967), and chickens (Frankel, 1965) during thermal panting. This accumulation is independent of $P_{O_2}$ and oxygen saturation (Anrep and Cannan, 1923; Frankel et al., 1963) and increases with decreasing $P_{aCO_2}$ (Anrep and Cannan, 1923; Takano, 1968, 1970). Lactate has also been shown to increase in CSF (Granholm and Siesjo, 1969), probably as a consequence of decreased brain blood flow caused by the hypocapnia (Smith et al., 1971).

The effect of thermal panting on $P_{a_{O_2}}$ is shown by data reported in Figure 13. $P_{a_{O_2}}$ rose steeply as respiratory frequency was elevated from 20/min to 70/min. The increase in arterial oxygen tension is due to hyperventilation, as indicated by data reported in Figure 10, and also possibly to a decrease in oxygen consumption. Hales and Findley (1968b) reported a decreased oxygen consumption during moderate heat stress in the ox. At ambient temperatures of 32 and 35°C (f = 20-70/min) cats appeared relaxed and drowsy, and reduced whole body metabolic rate could be reasonably presumed.

At respiratory frequencies above 70/min, the arterial oxygen tension of resting cats declined slightly as frequency rose (Figure 13). This reduction is attributed to increased oxygen extraction from arterial blood with an insufficient

increase in alveolar ventilation. The increased oxygen consumption is presumed to be due to the increase in body temperature (Van't Hoff-Arrhenius effect), and to increased work by the respiratory muscles (Hildebrandt, 1969) and the heart (Whittow, 1965).

At low respiratory frequencies (below 70/min; Figure 13) the $Pa_{O_2}$ of resting and exercising cats appears to be the same. At respiratory frequencies exceeding 70/min, exercising animals maintained arterial oxygen tensions consistently lower than those of resting cats with the same respiratory frequency. The lower oxygen tensions in the exercising cats are believed to be due to a considerable increase in oxygen extraction from arterial blood by the somatic musculature, and possibly also the heart, without a sufficient increase in alveolar ventilation. During acute heat stress in the unanesthetized cat, oxygen tension of arterial blood does not appear to be regulated, but appears to be the passive result of variable amounts of oxygen extraction superimposed upon thermally driven hyperentilation, at least when $Pa_{O_2}$ exceeds 90 mm Hg.

# CONCLUSIONS

1. The increase in respiratory frequency displayed by unanesthetized cats during heat stress results in hyperventilation, with a decline in $P_{a_{CO_2}}$ from 43 mm Hg when respiratory frequency is 18/min to 28 mm Hg at a frequency of 205/min.

2. pH of arterial blood is not dependent on respiratory frequency, but rises 0.1 unit as $P_{a_{CO_2}}$ falls from 43 to 28 mm Hg.

3. The decline of plasma bicarbonate concentration as $P_{a_{CO_2}}$ falls helps to minimize the alkalosis in the face of hypocapnia.

4. At respiratory frequencies below 70/min, $P_{a_{O_2}}$ rises steeply due to the thermally induced hyperventilation. At frequencies above 70/min, the steady-state $P_{a_{O_2}}$ level results from varying amounts of oxygen extraction by peripheral tissues superimposed upon the thermally driven hyperventilation.

5. "Phase II" breathing is not a characteristic response of the unanesthetized cat to severe heat stress.

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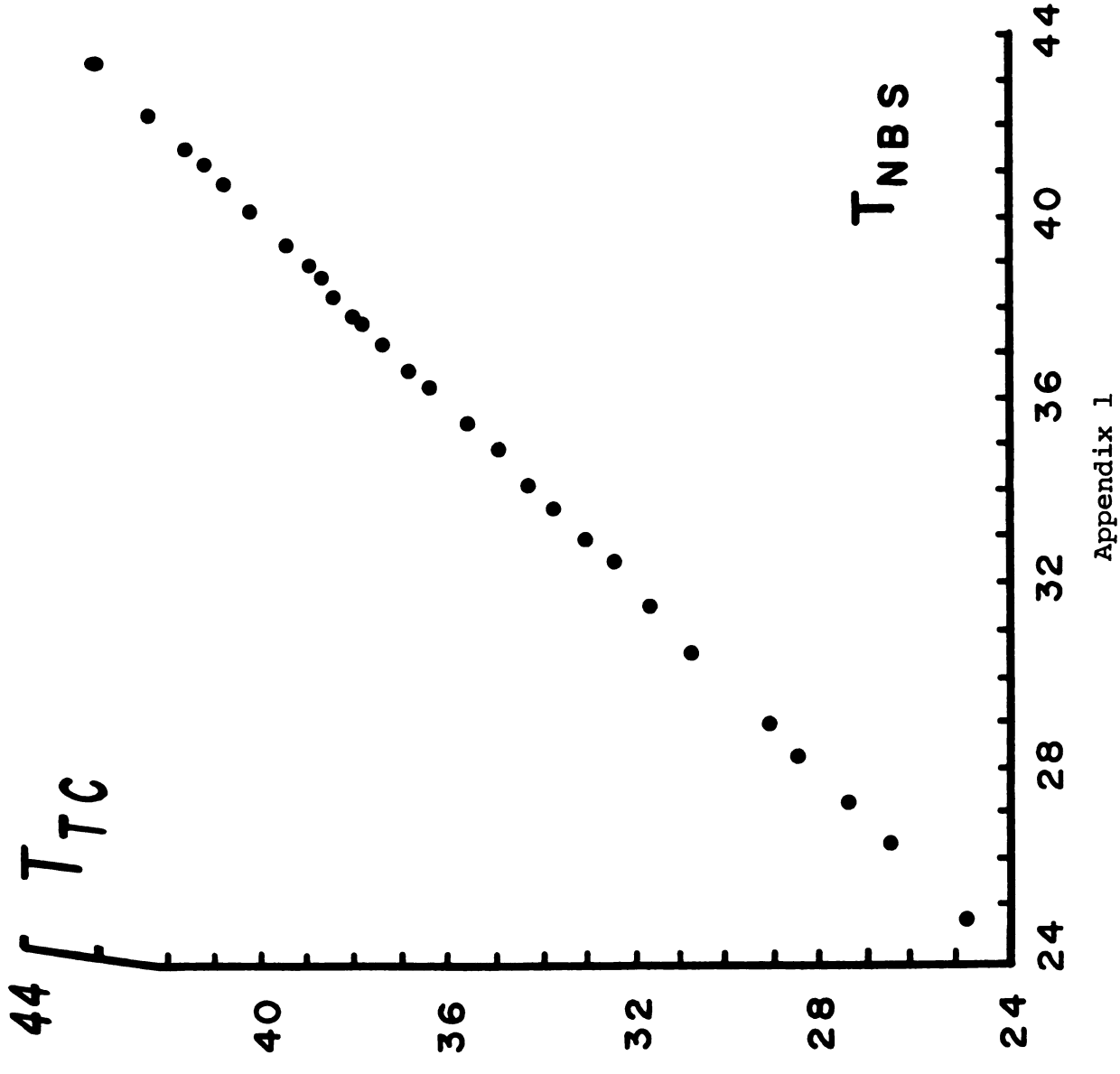
# APPENDICES

Appendix 1. Calibration curve for thermocouples.

$T_{TC}$ (°C; ordinate) = thermocouple temperature

$T_{NBS}$ (°C; abscissa) = temperature of National Bureau of Standards thermometer



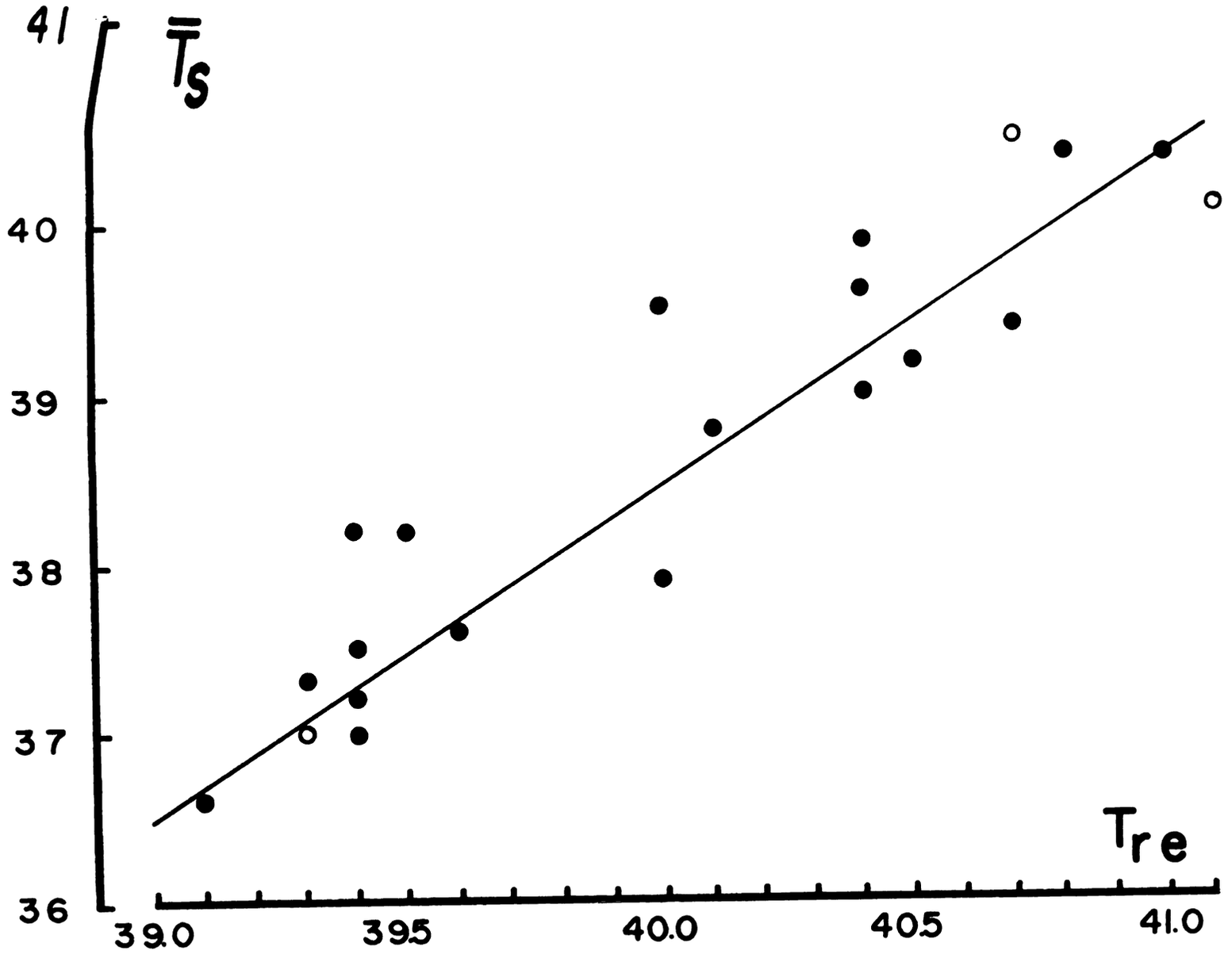

Appendix 1

Appendix 2. Average skin temperature as a function of rectal temperature. Average skin temperature (°C; $\bar{T}_S$; ordinate) is shown as a function of rectal temperature (°C; $T_{re}$; abscissa). Solid dots designate resting cats; open circles indicate exercising animals.

$\bar{T}_S = 1.89\ T_{re} - 37.2$

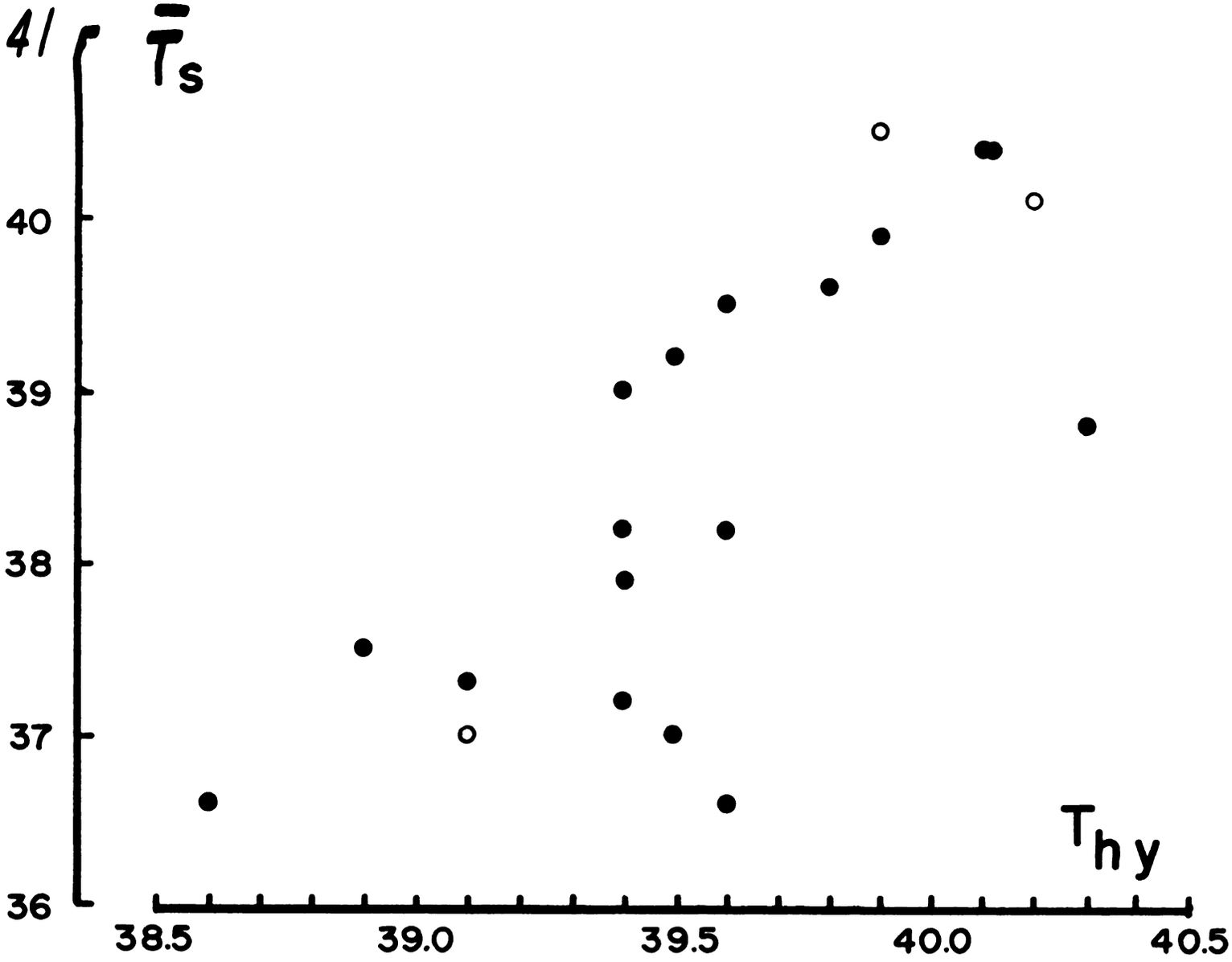
$r = 0.90$

95% confidence interval on slope = 1.45 - 2.33.




Appendix 2

Appendix 3. Average skin temperature (°C; $\bar{T}_S$; ordinate) as a function of hypothalamic temperature (°C; $T_{hy}$; abscissa). Open circles indicate exercising animals; solid dots represent resting cats.



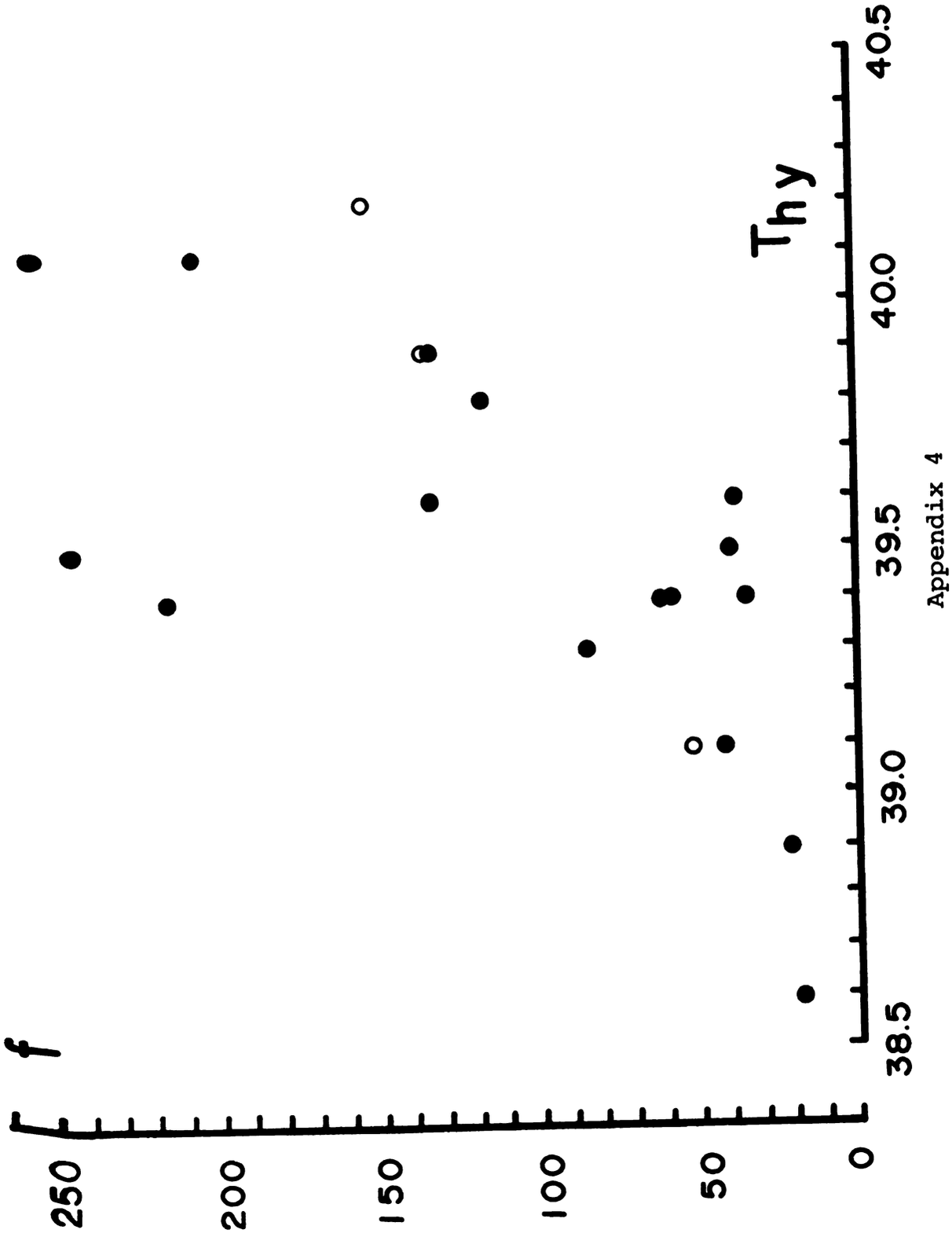

Appendix 3

Appendix 4. Respiratory frequency as a function of hypothalamic temperature. Respiratory frequency (f; breaths/min; ordinate) is shown as a function of hypothalamic temperature (°C; $T_{hy}$; abscissa). Solid dots designate resting animals; open circles indicate exercising cats.

$f = 98.3\ T_{hy} - 3769$

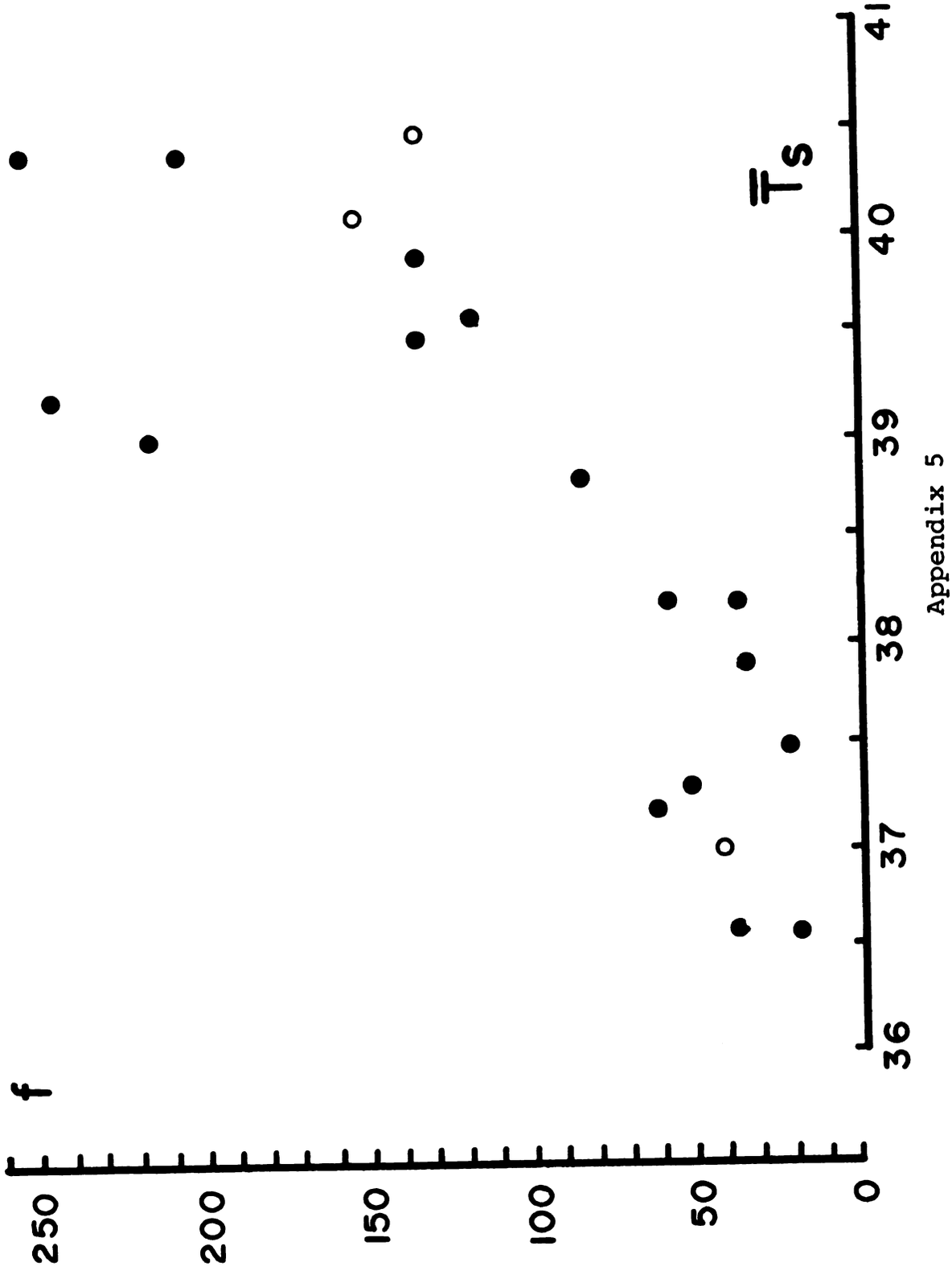
$r = 0.52$

95% confidence interval on slope = 10.1 - 186.5.



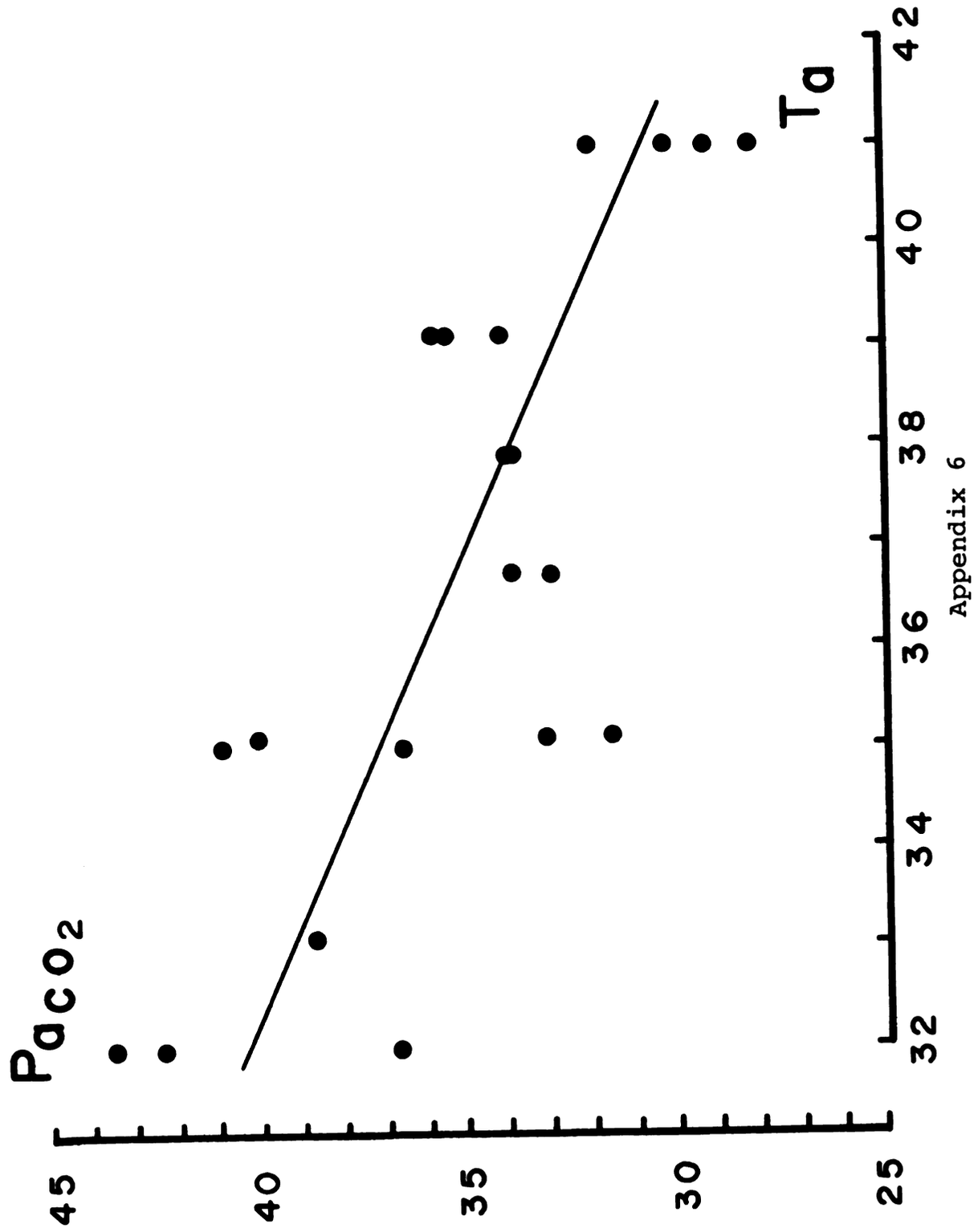

Appendix 4

Appendix 5. Respiratory frequency (f; breaths/min; ordinate) as a function of average skin temperature (°C; $\overline{T}_S$; abscissa). Open circles represent exercising animals; solid dots designate resting cats.



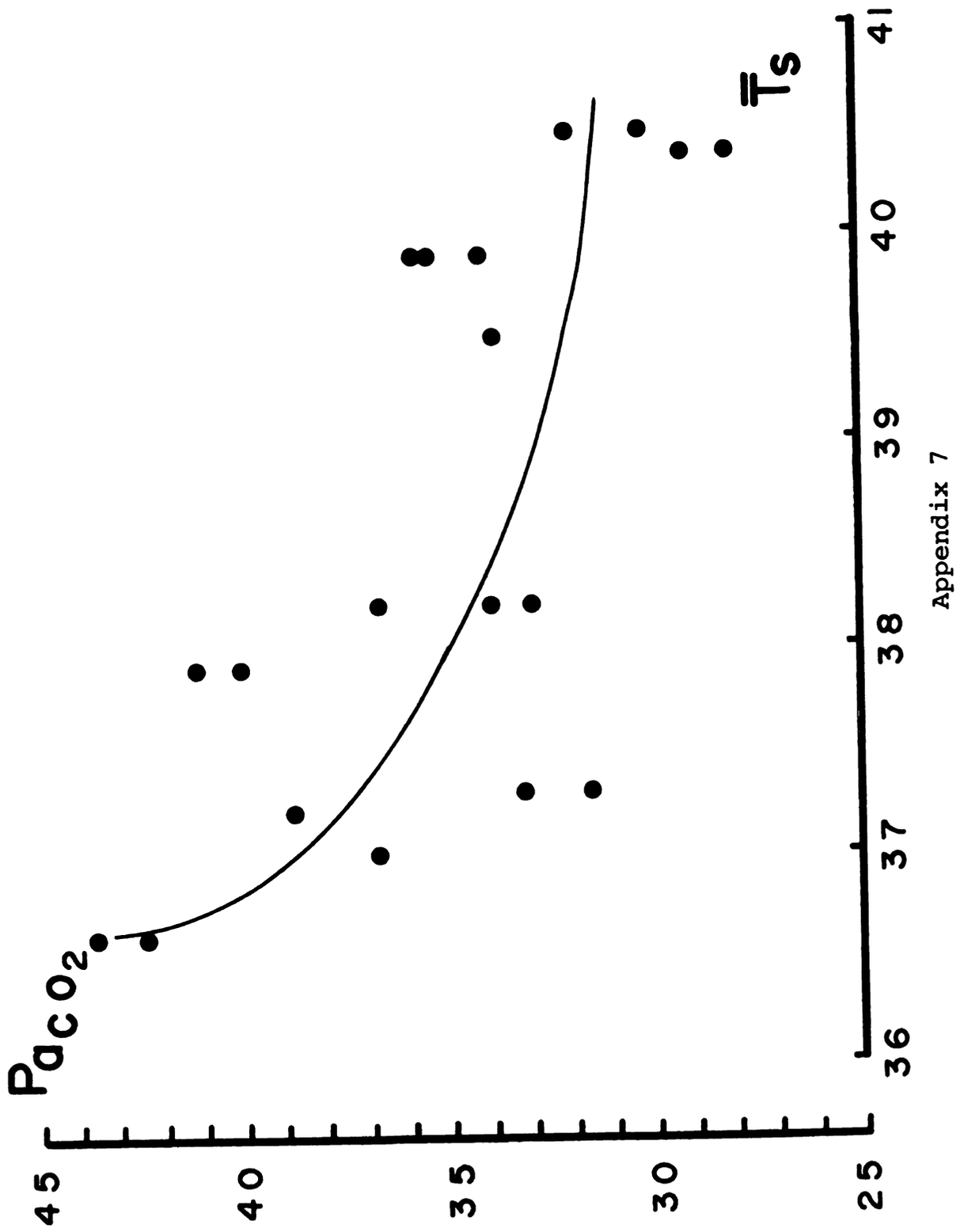

Appendix 5

Appendix 6. $Pa_{CO_2}$ as a function of ambient temperature.
Carbon dioxide tension of arterial blood ($Pa_{CO_2}$; mm Hg; ordinate) is shown as a function of ambient temperature (°C; $T_a$; abscissa).
$Pa_{CO_2} = -1.07\ T_a + 74.5$;
$r = \pm 0.78$
95% confidence interval on slope = -0.65 - -1.49.



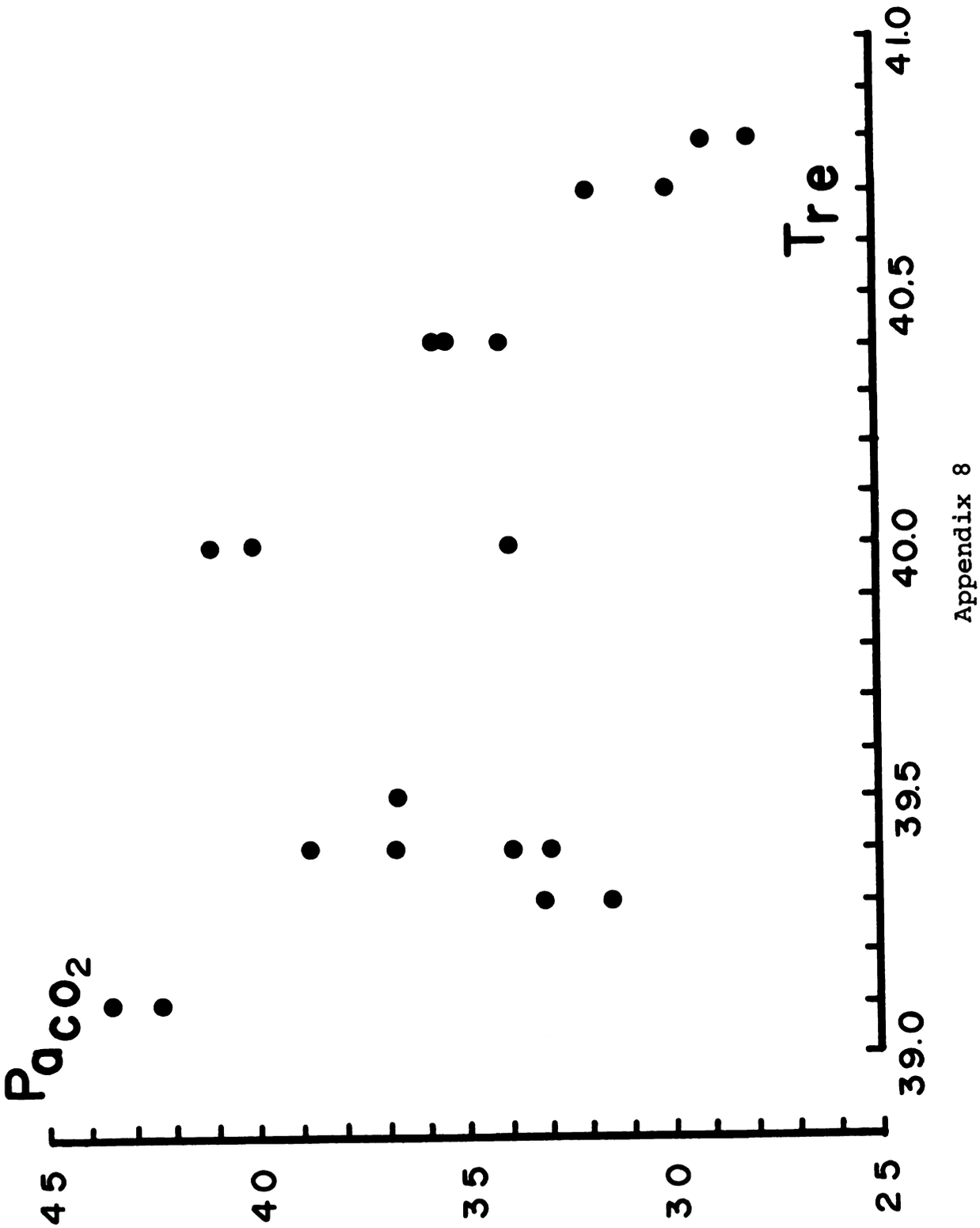

Appendix 6

Appendix 7. $P_{a_{CO_2}}$ as a function of average skin temperature.
Carbon dioxide tension of whole arterial blood ($P_{a_{CO_2}}$; mm Hg; ordinate) is shown as a function of average skin temperature (°C; $\overline{T}_S$; abscissa). The curve is significantly non-linear at the 0.01 level.



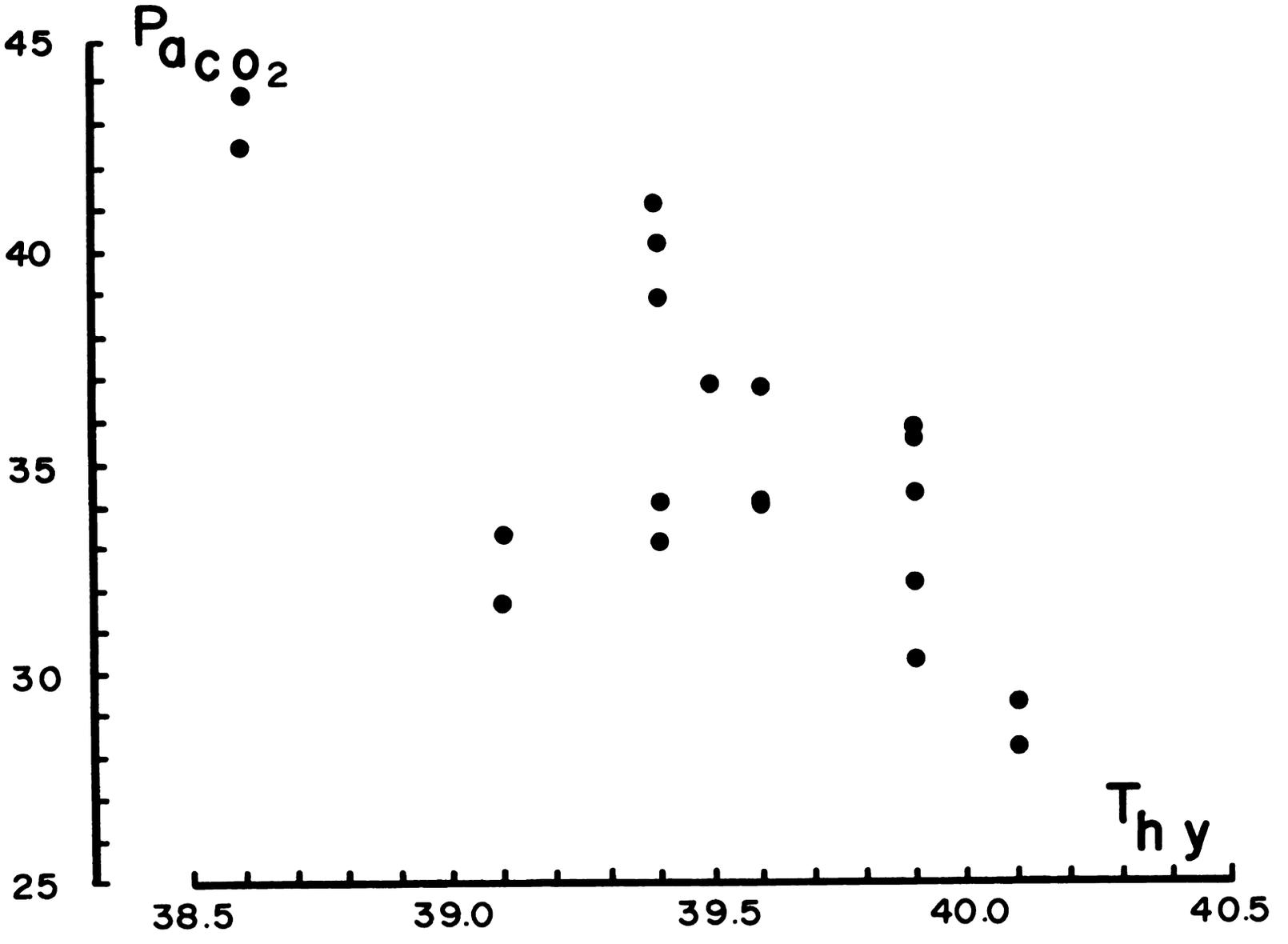

Appendix 7

Appendix 8. $P_{a_{CO_2}}$ (mm Hg; ordinate) as a function of rectal temperature (°C; $^2T_{re}$; abscissa).



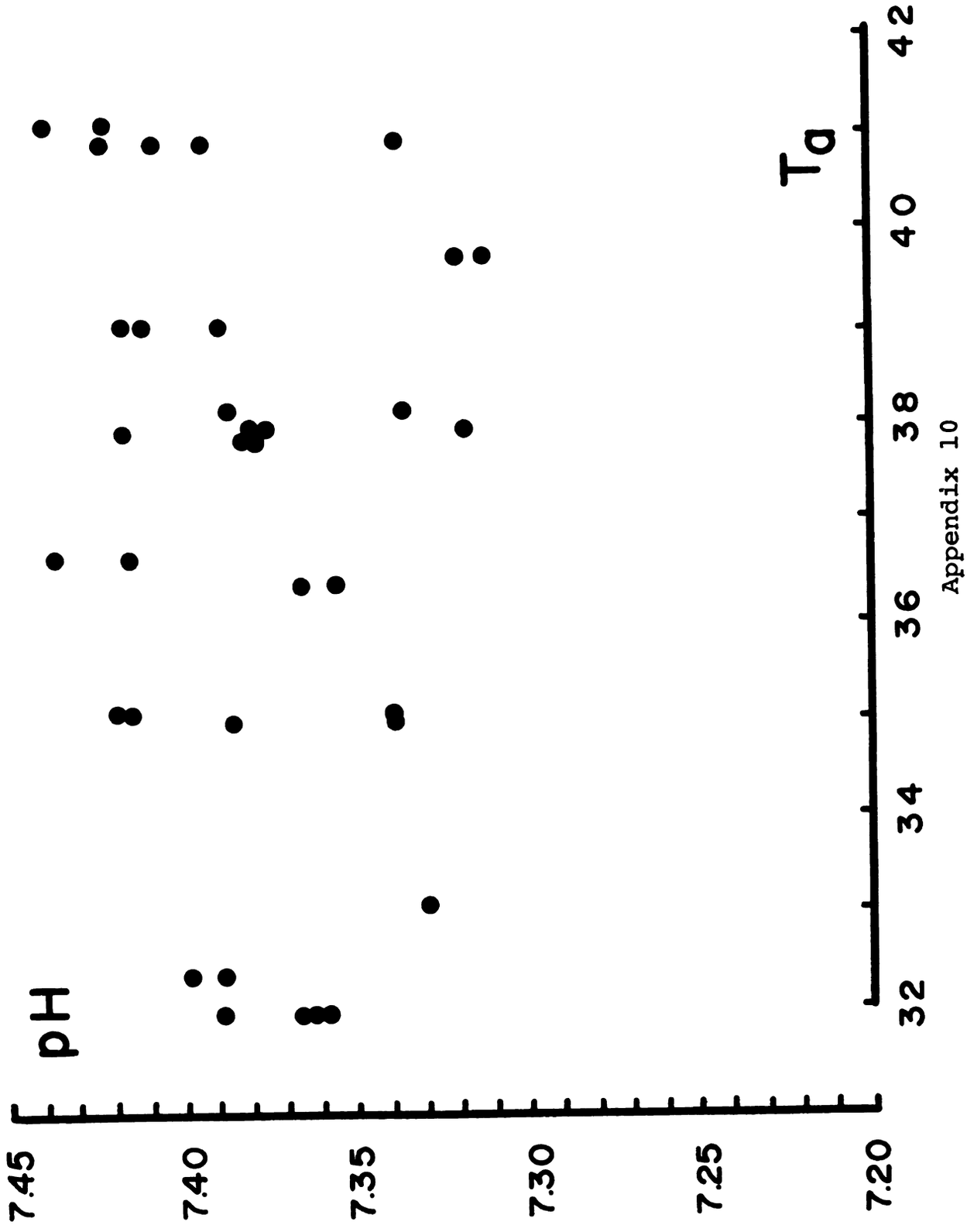

Appendix 8

Appendix 9. $P_{a_{CO_2}}$ (mm Hg; ordinate) as a function of hypothalamic temperature (°C; $T_{hy}$; abscissa).



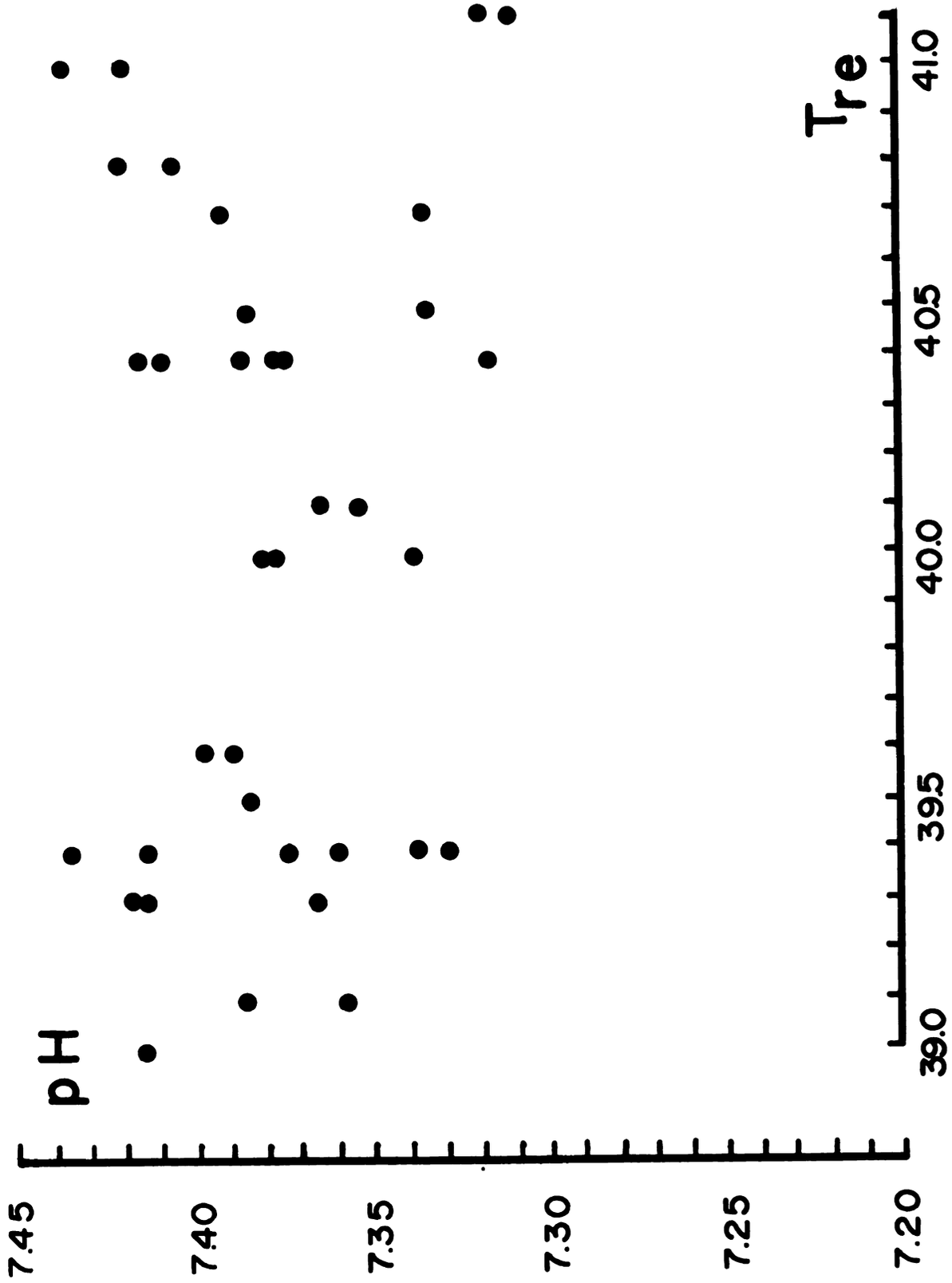

Appendix 9

Appendix 10. pH (ordinate) as a function of ambient temperature (°C; $T_a$; abscissa).



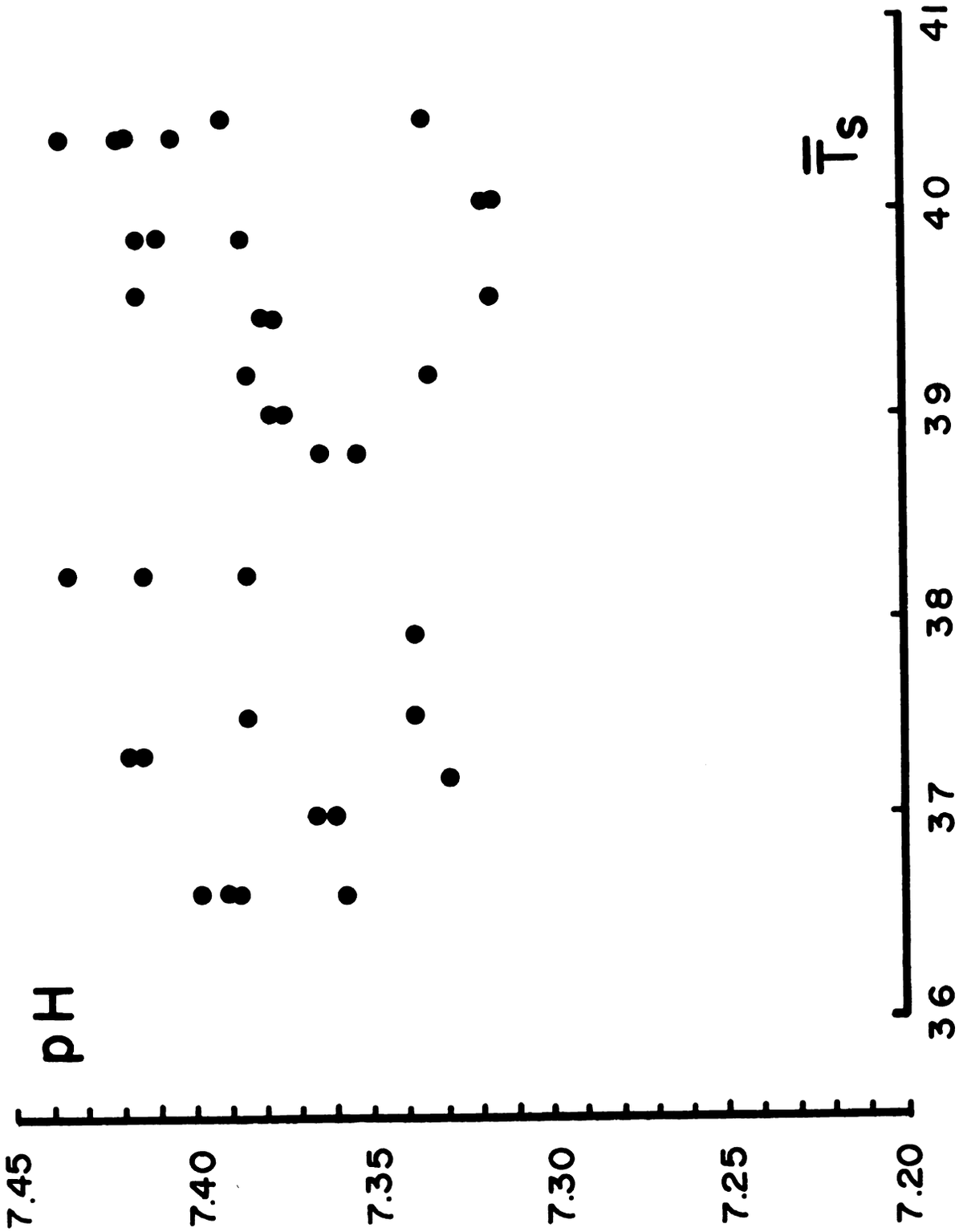

Appendix 10

Appendix 11. pH (ordinate) as a function of rectal temperature (°C; $T_{re}$; abscissa).



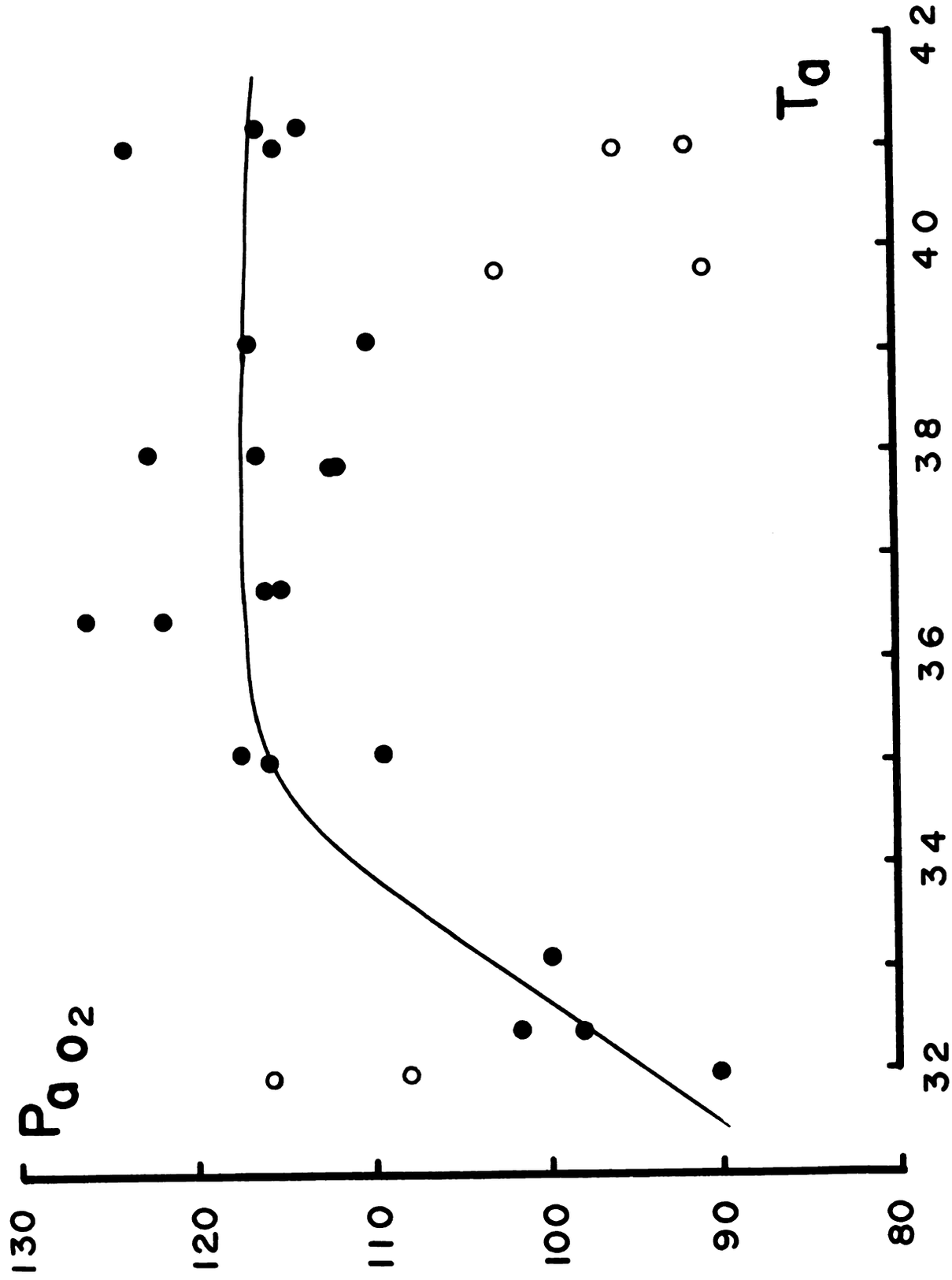

Appendix 11

Appendix 12. pH (ordinate) as a function of average skin temperature (°C; $\overline{T}_S$; abscissa).



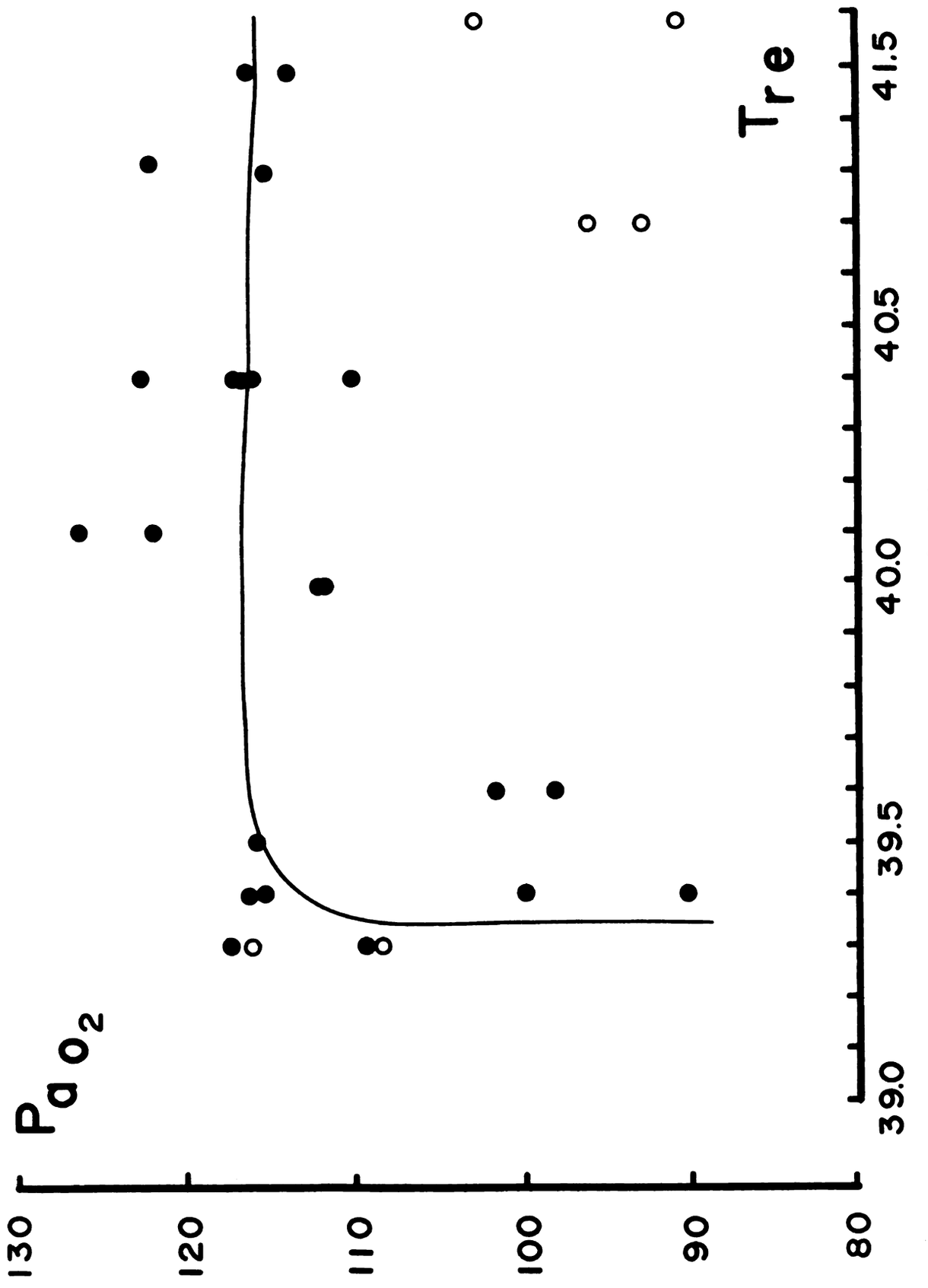

Appendix 12

Appendix 13. $P_{a_{O_2}}$ (mm Hg; ordinate) as a function of ambient temperature (°C; $T_a$; abscissa). Open circles designate exercising cats; solid dots represent resting animals.



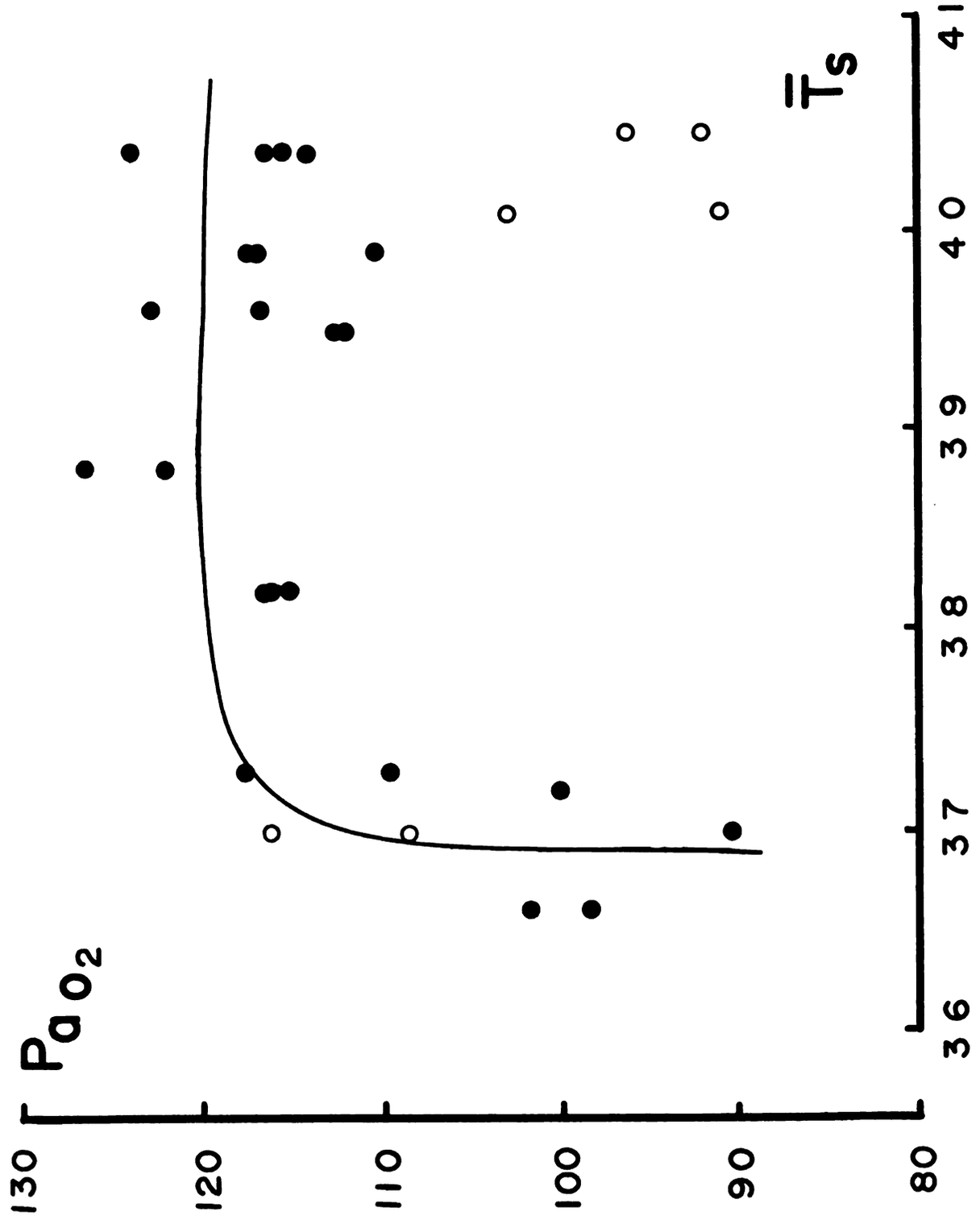

Appendix 13

Appendix 14. $P_{a_{O_2}}$ (mm Hg; ordinate) as a function of rectal temperature (°C; $T_{re}$; abscissa). Solid dots designate resting animals; open circles indicate exercising cats.



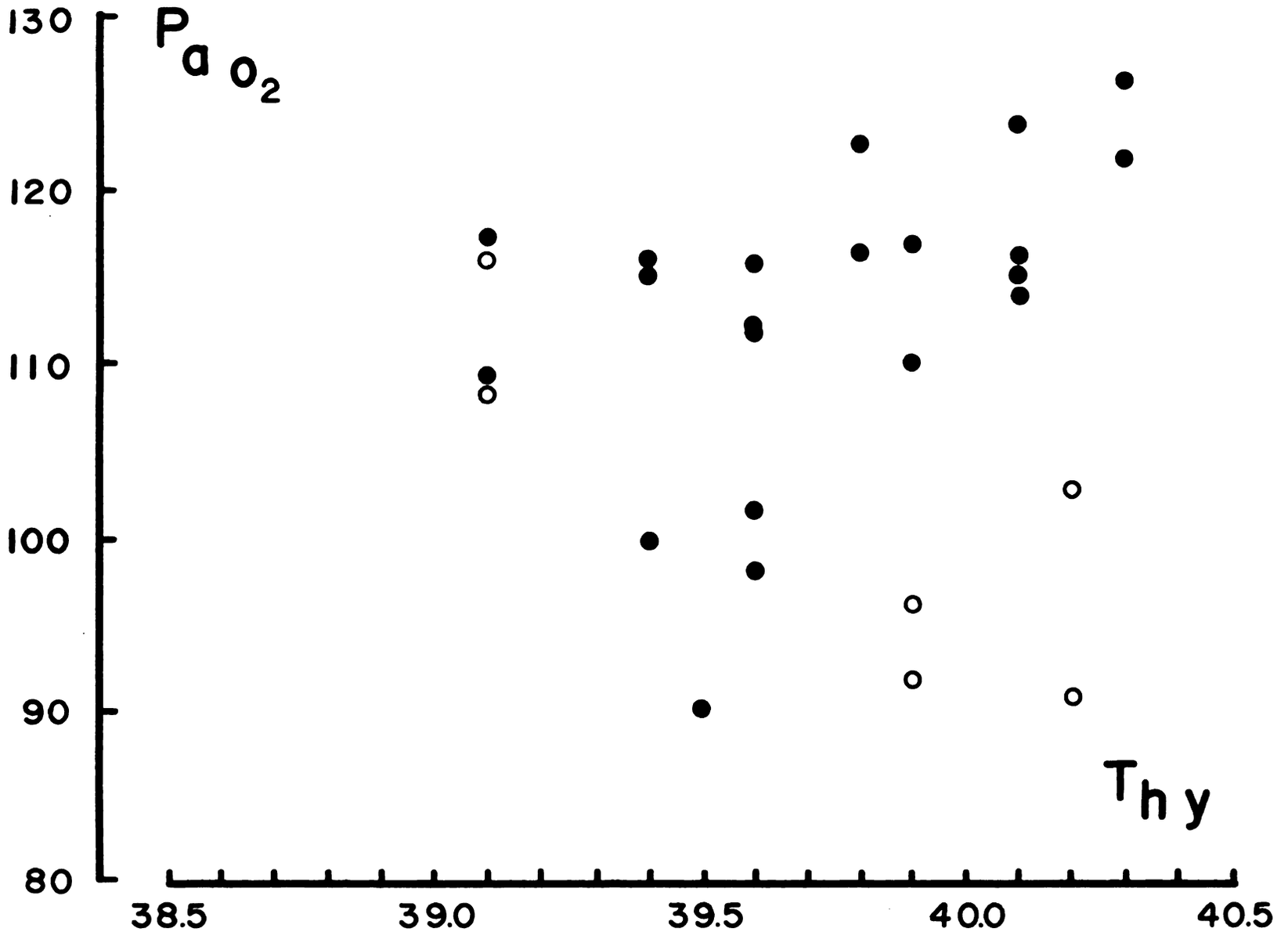

Appendix 14

Appendix 15. $Pa_{O_2}$ (mm Hg; ordinate) as a function of average skin temperature (°C; $\bar{T}_S$; abscissa). Solid dots indicate resting cats; open circles represent exercising animals.




Appendix 15

Appendix 16. $P_{a_{O_2}}$ (mm Hg; ordinate) as a function of hypothalamic temperature ($T_{hy}$; °C; abscissa). Solid dots represent resting cats; open circles indicate exercising animals.




Appendix 16