THE USE OF MIXED VENOUS BLOOD IN DETERMINING ACID-BASE STATUS OF SYSTEMIC TISSUES WHEN METABOLIC INPUT IS MANIPULATED

by

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CHAPTER I

INTRODUCTION

Arterial blood has historically been analyzed to determine acid-base status. To classify acid-base disturbances, the values of pH, pCO_2 and HCO_3^- in arterial blood must be known. Blood-gas analysis is the procedure used to determine pH, pCO_2 and pO_2 of the blood. When the values of arterial pH and pCO_2 have been determined through blood-gas analysis, the HCO_3^- concentration can be calculated using the Henderson-Hasselbalch equation or determined from a nomogram. The arterial pO_2 though not essential for classifying acid-base disturbances is important for assessing cardiopulmonary function. (Keyes, 1976.)

Two reasons are usually given for using arterial rather than capillary or venous blood for blood-gas analysis. They are:

1. Arterial blood reflects cardiopulmonary function more directly than does capillary or venous blood.
2. Arterial blood has uniform composition throughout the body whereas capillary and venous blood fluctuate in response to changing metabolic rates in various tissues (Slonim & Hamilton,

1976; Samet, Linhart, Barlod & Hildner, 1969).

For these reasons, investigators have stated that no satisfactory substitute exists for the use of arterial blood for blood-gas analysis (Slonim & Hamilton, 1976; Samet, Linhart, Barlod & Hildner, 1969). Evidence is accumulating, however, indicating that arterial blood does not provide all the information needed to accurately assess acid-base status, especially at the systemic tissue level (Long, 1977; Austin, 1970).

The analysis of venous blood drawn simultaneously with arterial blood should provide additional information for the assessment of acid-base status. This assertion is based on the following argument.

Theoretical Framework

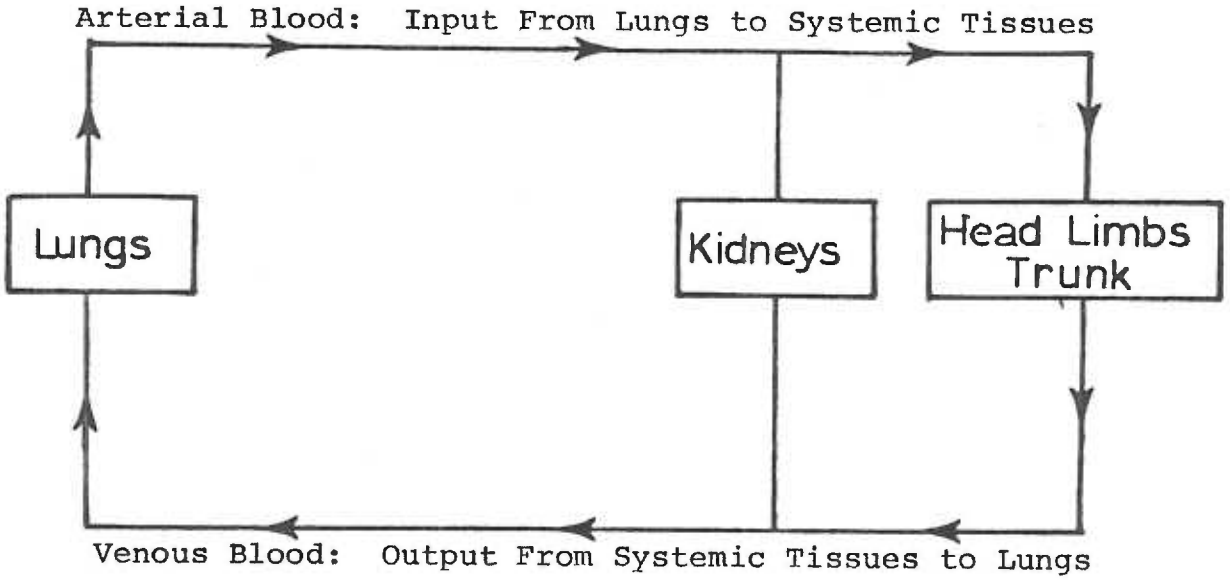
Arteries contain blood which is oxygenated in the lungs. The gas composition of arterial blood reflects the balance between ventilation and blood flow.

Veins on the other hand, contain blood flowing from the systemic tissues. Acids such as carbonic acid (from hydration of CO_2) and lactic acid are added to the blood as it flows through the tissues. Therefore, venous blood-gas composition should reflect the acid-base status of systemic cells. (Figure 1.)

In general, because of the uniform composition of arterial blood, almost any peripheral artery can be used to obtain an

Figure 1

Model: Arterial versus Venous Blood



Arterial blood-gas composition represents the input to systemic tissues. Venous blood-gas composition reflects the output from the tissues. In the model, arterial blood differs from venous blood by what the lungs add and remove; i.e., O_2 and CO_2, respectively. Thus, arterial blood gives a modified picture of the acid-base status of systemic tissues. The kidneys are shown for emphasis as a separate parallel circuit in the systemic circulation because they are one of the prime regulators of acid-base status.

arterial blood sample. However, the site for sampling venous blood is more critical. It is apparent from the model that there are several different sites from which a venous blood sample may be obtained. Blood flow to tissues and metabolic rates of tissues vary throughout the body. Therefore, venous blood-gas composition lacks uniformity. A venous sample drawn from one of the parallel circuits may have a blood-gas composition that is not representative of the entire systemic flow. A true average of all blood returned to the heart via the superior vena cava, inferior vena cava and coronary veins is found in the pulmonary artery (Wilson, 1978). Thus, blood from the pulmonary artery (mixed venous blood) would seem to be the best source for obtaining venous blood samples that will reflect the overall acid-base status of systemic tissues.

Since the development of the flow-directed catheter, samples of mixed venous blood from the pulmonary artery may be obtained with relative ease. Many patients in the acute care setting have flow-directed catheters introduced into the pulmonary artery to assess left ventricular end-diastolic pressure, and to determine cardiac output. The flow-directed catheter can serve as a conduit for obtaining mixed venous blood samples.

The value of obtaining arterial blood-gas composition is recognized. Information about input to tissues (indicative of cardiopulmonary function) is obtained by analyzing

arterial blood. If arterial blood alone is analyzed, however, the acid-base status of systemic tissues may not be accurately assessed. Additional information about systemic input into the circulation is also needed and may be obtained from mixed venous blood. Therefore, it seems reasonable to suggest that to accurately assess acid-base status of the body, both arterial and mixed venous blood-gas analysis must be done simultaneously.

Problem Statement

In the following study, arterial and mixed venous blood-gas composition were analyzed when metabolic components were manipulated. The following questions were answered:

1. Is there a predictable pattern to the way mixed venous blood-gas composition changes in states of metabolic acid-base disturbance?
2. In what way does mixed venous blood-gas composition differ from arterial blood-gas composition in states of metabolic acid-base disturbance?

Review of the Literature

Research on the use of mixed venous blood for blood-gas analysis seems to be directed towards answering three major questions:

1. Is there uniformity of blood-gas composition in samples taken from the great veins, the

right heart chambers and the pulmonary artery?

2. Can central or mixed venous blood be used as a substitute for measuring arterial blood gases?
3. What knowledge can be gained from knowing both arterial and mixed venous blood-gas composition?

A review of the literature pertaining to each of these questions will be presented.

1. Is there uniformity of blood-gas composition in samples taken from the great veins, the right heart chambers and the pulmonary artery?

Oxygen is the parameter most frequently used to determine the uniformity of blood-gas composition between various central venous sites. A probable reason for this is that venous oxygen content (along with arterial oxygen content) is essential for determining the presence of pulmonary shunts and for determining cardiac output using the Fick principle (Slonim & Hamilton, 1976).

Dexter, Haynes, Burwell, Eppinger, Sagerson and Evans (1947) studied 44 patients with evidence of heart failure, anemia and pulmonary disease. For 13 of these patients, they compared the oxygen content of blood from the right ventricle with that from the right atrium. They noted that blood from the right ventricle had a higher oxygen content (concentration in vol%) than blood from the right atrium by a maximal amount of 0.9 vol%. Blood from the pulmonary

artery had a higher oxygen content than blood from the right ventricle. The maximal amount by which the oxygen content of blood from the pulmonary artery exceeded the oxygen content of blood from the right ventricle was 0.5 vol%.

For 15 patients from the group, blood from the right atrium had a higher oxygen content than blood from the superior vena cava by a maximal amount of 1.9 vol%.

Samples of blood from the inferior vena cava had uniformly higher oxygen content than blood from the right atrium. Maximal variation of oxygen content of blood from various sites within the right atrium was 11.4 vol%. Maximal variation of samples from various sites in the right ventricle was 0.8 vol%. Samples taken from the trunk and one of the main branches of the pulmonary artery showed maximal variation of 0.4 vol%. The authors concluded that because of the more uniform composition of blood in the pulmonary artery, this site should serve as the source from which to obtain samples of mixed venous blood.

Barrett-Boyes and Wood (1957) analyzed the oxygen saturation of venous blood in 26 healthy unanesthetized adults undergoing heart catheterization. (Fifteen of the subjects were healthy male physicians who were volunteers, and 11 were patients in whom cardiac catheterization ruled out the presence of cardiac abnormalities.) Multiple oxygen saturation determinations were made on samples drawn from various central venous sites in rapid succession.

Oxygen saturation of blood samples from the superior vena cava was significantly less than inferior vena cava saturation. Mean and range values for superior vena cava were 76.8% (64-84%), and for the inferior vena cava was 83% (76-88%). Oxygen saturation of blood in the right atrium was between those values found in the superior and inferior vena cava.

Samples were drawn from various sites in the right ventricle. Blood from the main ventricular chamber and adjacent to the tricuspid valve was described as being (anatomically) low. Blood taken from near the ventricular outflow tract was termed (anatomically) high.

Samples withdrawn from various sites within the right ventricle showed a mean oxygen saturation of 78.5% (64-84%). This mean was 1% less than the mean value of right atrial oxygen saturation. The mean value for oxygen saturation of blood from the pulmonary artery was 78% (73-85%). With the catheter in wedge position, mean and range oxygen saturations were 98.2% and 90-100%, respectively. From these data it is apparent that inferior vena cava blood has a higher oxygen saturation than blood in the superior vena cava. Right atrial blood is less saturated than inferior vena cava blood but more saturated than superior vena cava blood. These investigators found no systematic differences in 0_2 saturation of blood obtained from the right atrium, from low in the right ventricle and from the pulmonary

artery. Furthermore, no systematic differences could be demonstrated in oxygen saturation of blood samples obtained from high and low in the right ventricle compared to the pulmonary artery. Range of differences in oxygen saturation of individual pairs of samples from the pulmonary artery and right ventricle was less than between other sites.

When the effects of laminar flow and changes in cardiac output were accounted for, the investigators indicated that mixing of systemic venous blood is relatively complete only when blood reaches the right ventricular outflow tract and the pulmonary artery, and not in sites proximal to these points.

Scheinman, Brown and Rapaport (1969) analyzed the oxygen saturations of blood obtained from 24 critically ill patients. The purpose of the study was to determine if oxygen saturation of blood taken from catheters used to measure central venous pressure accurately reflected the oxygen saturation of blood in the pulmonary artery. A central venous catheter was placed in either the right atrium, superior vena cava, the innominate or subclavian veins. Blood from the latter three sites was termed central venous blood. Another catheter was floated into the pulmonary artery or right ventricle. Blood from these two sites was referred to as mixed venous blood. Fifty-two simultaneous measurements of mixed venous and central venous oxygen saturations were made on 18 patients. In seven patients, right atrial and pulmonary artery oxygen

saturations were compared. For the group as a whole, mean central venous oxygen saturation was greater than mean mixed venous oxygen saturation ($p<.001$). However, no significant difference between means was noted in oxygen saturation of blood from the right atrium and pulmonary artery. In 34 determinations, there was no significant difference in means between central venous and pulmonary artery oxygen saturations. Changes in saturation correlated highly between these two sites ($r=+.90$). In 12 simultaneous determinations, there was no significant difference in means and correlation was strong between changes in right atrial and mixed venous oxygen saturations ($r=+.96$). Weak correlation between central venous and mixed venous oxygen saturation was found in patients with shock or heart failure. Under these conditions, central venous oxygen saturation was significantly higher than mixed venous oxygen saturation. During shock, individual values for central venous and mixed venous oxygen saturation showed less correlation ($r=+.53$). Based on these results the researchers concluded that central venous oxygen saturation accurately reflects mixed venous oxygen saturation in seriously ill patients as long as these patients do not have evidence of heart failure or shock.

Goldman, Branif, Harrison and Spavick (1968) compared the oxygen saturations of samples drawn simultaneously from the superior vena cava and the pulmonary artery.

Their 28 subjects had all been diagnosed as having myocardial infarction. Mean oxygen saturation for blood from the superior vena cava was 66.2%, and from the pulmonary artery was 64.9%. The difference between the superior vena cava and pulmonary artery samples averaged 1.3% saturation with a range of 0.3-10.5%. Because of this close relationship, the authors felt that the superior vena cava samples provide a "reasonable approximation" of oxygen saturation of mixed venous blood in patients with myocardial infarction.

Wilson (1978) likewise compared the oxygen content of 107 simultaneously drawn samples from the central veins and the pulmonary artery. (He did not indicate the exact source from which the central venous samples were taken.) His subjects were 45 critically ill patients in intensive care units (ICU). He noted that as long as the difference between systemic arterial and central venous oxygen content was 3.5 vol% or greater, then central venous blood closely resembled mixed venous blood in terms of oxygen content ($r=.85$). If the oxygen content difference was less than 3.5 vol% the coefficient of correlation was reduced ($r=.35$). Cardiac indices were calculated for the group of patients as a whole, for those with an oxygen content difference between systemic arterial and central venous blood greater than 3.5 vol%, and for those with an oxygen content difference less than 3.5 vol%. For

each group, Wilson compared the indices computed when central venous blood was used and when pulmonary artery blood was used. He found that when central venous blood was used, the cardiac indices computed were higher than those for pulmonary artery blood by 0.5L/min/m^2, .07L/min/m^2 and 1.0L/min/m^2, respectively.

From this study, he concluded that central venous blood does resemble mixed venous blood. Therefore, data obtained from central venous blood can be used to calculate clinically important data such as cardiac indices, particularly in patients whose oxygen content difference between arterial and central venous blood is 3.5 vol% or greater.

Dongre, McAslan and Shin (1977) studied samples of superior vena cava blood and pulmonary artery blood in 51 ICU patients without evidence of shock. In 171 determinations, the parameters compared were pH, pCO_2, pO_2 and oxygen saturation. The pH of superior vena cava blood correlated highly with the pH of mixed venous blood ($r=.95$, slope=.93). Similarly, correlation of pCO_2 between the two sites was high ($r=.87$, slope=.85). The pO_2 of superior vena cava blood was significantly higher than the pO_2 of mixed venous blood ($p<.05$). Neither a close nor predictable relationship could be demonstrated in oxygen content of samples compared from the two sites. When physiologic shunt calculations and cardiac outputs were computed using superior vena cava blood rather than

pulmonary artery blood, large errors were encountered. These authors concluded that the assessment of mixed venous oxygen content can only be done accurately on samples of blood from the pulmonary artery.

Suter, Lindauer, Fairley and Schlobohm (1975) compared the pO_2 and pCO_2 of blood from various sites within the pulmonary artery. They also determined how rate of withdrawal of blood affected the pO_2. The subjects were 25 critically ill patients with acute respiratory failure necessitating mechanical ventilation. They noted that rate of withdrawal did not alter O_2 content when samples were obtained from the first 5cm of the pulmonary artery, but significantly affected those taken from beyond this point. Mean oxygen content of all samples showed a significant increase in the distal position (flow directed catheter in wedge position, with balloon deflated) compared to the proximal pulmonary artery, and as withdrawal rate increased, oxygen content of samples increased directly.

Values for pCO_2 were shown to be higher in samples from the main trunk of the pulmonary artery than samples taken from the wedge position with the balloon deflated.

These researchers noted that large errors may result when calculating cardiac outputs and pulmonary shunting if lack of consideration is given to determining accurate placement of the flow directed catheter and to rate of

withdrawal of samples.

It is apparent that there is little information reported regarding uniformity of blood-gas composition from the central veins, the right heart chambers and the pulmonary artery in terms of pH and pCO_2. Most of the investigative work deals with uniformity of oxygen composition. Results obtained are not always in agreement. Apart from the report of Dexter, et al. (1947) the research seems to indicate that mixed venous blood has the lowest pO_2 and the highest pCO_2 concentrations. As blood returns to the heart, the highest pO_2 is seen in the inferior vena cava blood. This is interpreted as being due to the high blood flow through the kidneys. Blood returning to the heart from the kidneys passes through the inferior vena cava (Scheinman, 1969). Blood from the coronary sinuses and Thebesian system for the most part drain into the right atrium. Therefore, points proximal to the right atrium cannot be considered as representing total systemic tissue input. As indicated by Barrett-Boyes, et al. (1957) laminar flow and changing cardiac output result in blood not being totally mixed until it has reached a point of entry into the ventricular outflow tract and the pulmonary artery. As indicated in the introductory model, there are numerous sites from which samples of venous blood may be drawn. However, the site which would seem to give the best reflection of the acid-base status of

systemic tissues is the pulmonary artery.

2. Can central venous or mixed venous blood be used as a substitute for measuring arterial blood-gases?

Zahn and Weil (1966) simultaneously collected 101 paired arterial and central venous blood samples from 32 critically ill patients. Central venous samples were withdrawn from the superior vena cava or the right atrium. Arterial blood pH values ranged from 6.86-7.70 with a mean of 7.45. Venous pH values ranged from 6.85-7.64 with a mean value of 7.439. Arterial pCO_2 ranged from 22-100 mmHg with a mean of 44.85 mmHg. The pCO_2 of venous blood ranged from 16-100 mmHg with a mean of 47.01 mmHg. When cardiac output, venous oxygen saturation, hemoglobin content and venous hematocrit were accounted for, the coefficient of correlation between arterial and central venous pH was .978 (slope=.976), and for pCO_2 was .962 (slope=.885). Based on these results, Zahn and Weil concluded that central venous blood reliably mirrors arterial blood in the parameters of pH and pCO_2 and can be used to assess the acid-base status of critically ill patients.

Similar results were reported by Phillips and Peretz (1969). They compared the pH and pCO_2 of blood drawn simultaneously from a peripheral artery and from the superior vena cava in 41 critically ill patients. (The

central venous blood was drawn from a catheter with the tip placed in the low superior vena cava.) The arterial pH values ranged from 6.970 to 7.560 with an average value of 7.409. Venous pH values ranged from 6.964 to 7.501 with an average value of 7.365. From a cumulative probability curve, Phillips and Peretz showed that in more than 90% of cases, the arterial pH could be estimated from the venous pH with an absolute error of .04 pH units.

The range for arterial pCO_2 varied from 20-60 mmHg with a mean value of 34 mmHg. The range for venous pCO_2 was 22 to 73 mmHg with a mean value of 42 mmHg. From a linear approximation graph, 80% of arterial pCO_2 values could be estimated within 4 mmHg from the venous pCO_2. They concluded that if central venous blood-gases are normal, then arterial blood-gases are invariably normal. Thus, the need to draw arterial blood-gases can be obviated. They stated that for assessing metabolic acid-base disturbances, "venous samples are a reliable practical substitute for arterial sampling . . . however, central venous blood is at best a rough screening procedure in the assessment of respiratory acid-base abnormalities" (p. 745). Evidence in support of this conclusion, however, is not presented in their research paper.

Marty, Barsamian and Smith (1970) analyzed the pH, pCO_2 and pO_2 of samples of arterial and central venous (superior vena cava) blood which were drawn simultaneously.

Their subjects were 36 patients who had undergone cardiopulmonary bypass for aortic and/or mitral valve replacement. Paired arterial and central venous values for pH and pCO_2 were found to correlate highly as long as central venous pO_2 was greater than 25 mmHg. Correlations were poor when central venous pO_2 was less than 25 mmHg. They concluded that if central venous pO_2 is greater than 25 mmHg, then central venous blood samples can be used to estimate arterial values for pH and pCO_2.

Sutton, Wilson and Walt (1967) determined the difference in pH, pCO_2, HCO_3^- concentration and O_2 saturation between central venous and arterial blood. Central venous samples were obtained from the innominate veins, superior vena cava and right atrium. A total of 133 determinations were made on 55 seriously ill patients. When central venous pH values were plotted graphically against pH differences (arterial minus central venous), arterial pH could not be accurately predicted from central venous pH values. When central venous pCO_2 values were plotted against the % change between central venous and arterial pCO_2 values, arterial pCO_2 values could not predictably be determined from the venous values. Thus, they concluded, contrary to findings presented this far, that when blood-gas values for central venous blood are abnormal, then the differences between arterial and central venous blood-gas composition will be too random to allow accurate prediction of

arterial blood-gas values from central venous blood. Thus, arterial blood must be used for the accurate assessment of acid-base status.

Samet, et al. (1969) compared blood-gas parameters of mixed venous blood with simultaneously drawn samples of arterial blood. His subjects consisted of 50 patients with a variety of cardiac problems. When the difference between mixed venous and arterial pCO_2 values were plotted against the mixed venous pCO_2, the coefficient of correlation was +.29 ($p=.05$). Similarly, when the difference between mixed venous and arterial pO_2 was plotted against the mixed venous pO_2, the coefficient of correlation was -.26 ($p > .05$).

A plot of the difference in pH values between the systemic arterial and pulmonary artery sites and the mixed venous pH gave a coefficient of correlation of -.20 ($p > .05$). Values for mixed venous and arterial base excess treated in the same manner gave a coefficient of correlation of -0.65 ($p < .01$).

They concluded that while there may be general trends in the relationship between measurements of pH, pCO_2, pO_2 and base excess from the pulmonary artery and systemic arteries, mixed venous blood cannot be substituted for arterial blood for the determination of acid-base status.

Apart from the conclusions of Samet, et al. (1969) and Sutton, et al. (1967) researchers seem to be in

agreement that central venous blood can be used to assess the acid-base status of critically ill patients.

3. What knowledge can be gained from knowing both arterial and venous blood-gas composition?

Goldman, et al. (1968) studied the value of measuring the oxygen saturation of serial samples of central venous blood in 27 patients with myocardial infarction.

The authors reasoned that the delivery of oxygen to the tissues and extraction of oxygen by the tissues (indicative of the adequacy of circulation) should be reflected in the central venous oxygen saturation. Assuming that oxygen consumption is constant in patients at rest, a decrease in venous oxygen saturation without a fall in arterial oxygen saturation would imply greater extraction of oxygen by the tissues which could result from a decrease in cardiac output. Thus, they noted that under basal conditions, changes in central venous oxygen saturation could be used to determine whether cardiac output was changing, and in what direction the change was taking place.

Valentine, Fluck, Moursey, Reid, Shillingford and Steiner (1966) analyzed serial samples of mixed venous and arterial blood in 19 patients with recent myocardial infarction. They found that the more severe the myocardial dysfunction after myocardial infarction, the greater the arterial-venous oxygen content difference,

and the greater the unsaturation of arterial blood. Mixed venous oxygen saturation was reduced to an average of 53% in patients with pulmonary edema and to 59% in those without pulmonary edema. Normal mixed venous oxygen saturation was reported to be 70%. However, individual baseline values for the subjects were not determined. In 18 of 19 patients, mixed venous oxygen saturation was found to be reduced "even when circulation was judged adequate on clinical grounds".

Marty, et al. (1970) studied 36 patients who had surgery for aortic and/or mitral valve replacement. They also conducted studies on five dogs with induced hemorrhage and subsequent volume replacement. They noted that disturbances in tissue perfusion could be identified when differences between central venous and arterial values for pCO_2 and pH increased. Confirmation of inadequate perfusion was provided when there was concomitant reduction in central venous pO_2.

Wilson, Wilson, Gibson and Lucas (1974) conducted a retrospective study on 501 critically ill patients, all of whom had physiologic shunting in the lungs. The purpose of the study was to determine the uniformity of differences between arterial and central venous blood-gas values and the clinical significance of knowing these differences. The exact site from which central venous blood samples were drawn was not indicated. They noted that arterial

and central venous differences averaged 0.04 units for pH, 7.5 mmHg for pCO_2 and 3.5 vol% for oxygen content. The arterial and central venous values for standard bicarbonate were almost identical in most patients. They reported that low differences in oxygen content between arterial and central venous blood, or high venous oxygen saturation was indicative either of peripheral shunting, or of poor utilization of oxygen by systemic tissues.

Austin (1970) analyzed the difference in arterial and peripheral venous pCO_2 when respiratory input was manipulated. His subjects were eight mongrel dogs that were tracheally cannulated and maintained on Harvard respirators. After allowing the pCO_2 values to stabilize at about 60 mmHg, the minute volume was doubled. Simultaneous arterial and venous samples were drawn and analyzed for pCO_2. Arterial pCO_2 dropped rapidly during the first few minutes. This was attributed to hyperventilation. Decreases in venous pCO_2 on the other hand were much slower. Decreases in pCO_2 due to hyperventilation are not represented in venous blood as readily as in arterial blood. Furthermore, venous blood has been in contact with CO_2 stores in the tissues. Austin indicated that decreases in pCO_2 of venous blood probably result from the depletion of the CO_2 stores of the body rather than being simply the effects of hyperventilation. He concludes that venous blood reflects the steady-state of

the body and hence the acid-base status of the body more accurately than arterial blood.

Most of the research concerning central venous or mixed venous blood-gas analysis has been conducted to determine cardiac output and peripheral and pulmonary shunting. Little research seems to be available about the value of determining mixed venous blood-gas composition in terms of systemic tissues input. The study by Austin (1970) is one example. While he determines the effect of respiratory manipulation on blood-gas parameters of arterial and venous blood, manipulation of metabolic input is not researched.

Implications for Nursing

Acid-base disturbances are frequently found in the critically ill patient. Such disturbances must be corrected in order for the body to return to optimal function. Intervention is frequently required to correct these disturbances.

This research proposes that data obtained from mixed venous blood, drawn simultaneously with arterial blood will provide additional information for the determination of acid-base status. Drawing and analyzing two samples of blood to determine acid-base status may seem to violate principles of cost containment. If the additional information from analyzing two samples allows for more

accurate assessment and initiation of treatment prior to the onset of complications then cost reduction could, in fact, result.

Nurses draw blood samples in order to obtain data to assess acid-base status. They participate in interpreting results of blood-gas samples and in rendering treatments to alter or maintain acid-base status.

Nursing practice and judgments must be based on sound scientific knowledge. Nurses must participate in developing this scientific knowledge base for the purpose of improving nursing practice and consequently improving patient care.

CHAPTER II

METHODS

Part I - Statement of Variables

The independent variable in this study is the amount of fixed acid or base infused at the time of sampling.

The dependent variables are pH, pCO_2, pO_2 and HCO_3^- concentrations of arterial and mixed venous blood. The arterial blood-gas determinations serve as controls for each kind of acid-base disturbance. The mixed venous blood samples provide the experimental blood-gas values. The dependent variables were measured at baseline conditions.

Changes in each variable were measured in relation to the amount of acid or base infused at the time of sampling.

Since normal healthy dogs were used for this experiment, it is assumed that the amount and concentration of chemical buffers in their bodies were normal. See Appendix (A) for definitions of terms.

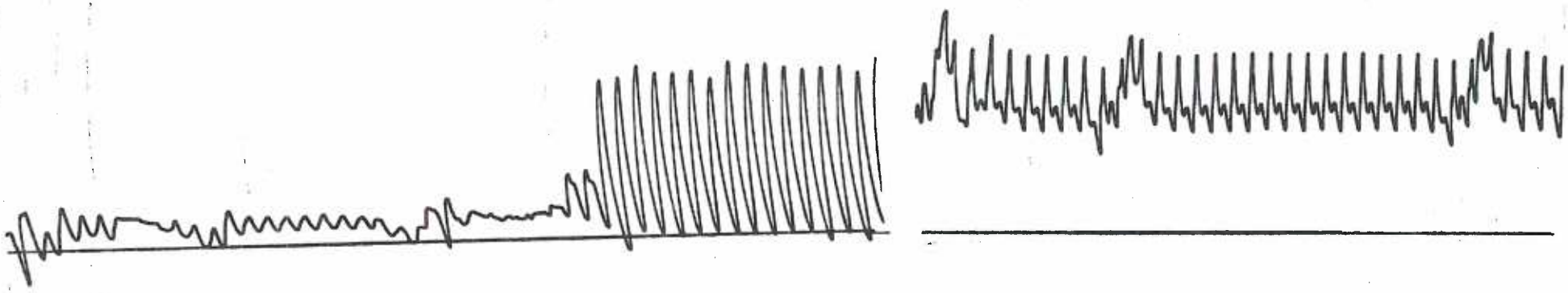
Part II - Procedure

Nine healthy mongrel dogs of both sexes were anesthetized with Sodium Pentobarbital. (30mg/Kg body weight.) Each animal's treachea was cannulated. Sodium Pentobarbital was given in 30 mg doses as needed to maintain anesthesia.

The right femoral artery was cannulated to permit withdrawal of samples of arterial blood. The femoral vein was catheterized to permit infusion of needed solutions.

A Swan-Ganz flow-directed catheter was passed into the pulmonary artery via the right jugular vein to permit withdrawal of mixed venous blood samples. Progression of the catheter was monitored and position of the catheter determined by pressure and wave form changes recorded on a polygraph. (Figure 2.) Position of the catheter was confirmed by direct visualization and palpation on post-mortem examination. Patency of the catheter was maintained with periodic infusions of heparinized normal saline (concentration 1 ml 1:1000 heparin per 100 ml normal saline).

Figure 2



Right Atrium Right Ventricle Pulmonary Artery

Tracing of Polygraph Record Showing Pressure Wave Forms from the Right Atrium, Right Ventricle and Pulmonary Artery. This Tracing (from Dog 9, May 6) is Typical of the Patterns Observed for the Nine Experimental Dogs.

To establish baseline values for blood-gas parameters, 1ml blood samples were drawn from the femoral and pulmonary arteries as soon as the catheters were in place. Five to six analyses were made on these samples.

All samples throughout the study were drawn simultaneously and anaerobically in heparinized glass syringes. The plunger and barrel were lubricated with stopcock grease to reduce the likelihood of air entry or exit along the plunger and barrel. The syringes contained elemental mercury to facilitate mixing of samples within the syringe.

A volume equal to the deadspace of the catheter was withdrawn and discarded prior to drawing the samples. When each sample had been obtained, the syringe was stoppered and placed in an ice bath to reduce oxygen consumption and metabolic rate of the blood cells. Thus, the sample reflected conditions existing in the blood at the time of sampling with minimal contribution of cell metabolism. All catheters were flushed with heparinized normal saline following the withdrawal of samples.

To develop progressing metabolic acidosis, 0.3M NH_4Cl (Bakers analyzed reagent) in 5% Dextrose and water was infused at a rate of 5-7mEq/Kgm.two hour time period through the femoral vein in a continuous infusion (Russell, Illickal, Mahoney, Roeher & DeLand, 1972). Duplicate arterial and mixed venous blood samples were drawn at approximately 30 minute intervals during

the infusion. The quantity of acid infused at the time of sampling was recorded. All samples were analyzed immediately. Sequence of analysis of the samples (arterial and venous) was randomized. The infusion was maintained until the arterial pH decreased to approximately 7.0.

Sodium Bicarbonate 1 molar solution was infused at a rate of 7-10mEq/Kg·hour to develop progressing metabolic alkalosis until a pH of approximately 7.7 was reached (Russell, et al., 1972). Methods for infusion, obtaining and analyzing the samples were the same as previously stated for acidosis.

Since body temperature may affect acid-base status, rectal temperature was measured and recorded throughout the experiment

With each sample, pH, pCO_2 and pO_2 were measured using the Radiometer blood-gas analyzer (Model, BGA 3 Mark 2). The machine was calibrated prior to analyzing baseline samples. Calibration of the pH, pCO_2 and pO_2 electrodes was checked prior to analyzing each set of samples. See Appendix (B).

HCO_3^- concentration was calculated using the Hendersen-Hasselbalch equation.

A reliability study was done to familiarize the investigator with the equipment and techniques necessary for blood-gas analyses.

CHAPTER III

RESULTS

The results of this project are discussed under three broad categories:

1. General descriptive data.
2. Results obtained when arterial and mixed venous blood-gas parameters are viewed as a function of the amount of acid or base infused per kilogram of body weight.
3. Results obtained when arterial blood is compared to mixed venous blood during metabolic acidotic and alkalotic states.

Within the two latter categories, the blood-gas parameters of pH, pCO_2, pO_2 and HCO_3^- are discussed.

A summary of the raw data from each experiment is found in Appendix (C).

General Descriptive Data

These experiments were performed on five male and four female mongrel dogs. The animals' weights ranged from 10 to 22.3 kilograms.

During the experiments, the animals' temperature, heart rate and respiratory rates were monitored. A

summary of these measurements is found in Table 1.

Table 1

Mean of Means and Standard Error of the Mean for Temperature, Heart Rate and Respiratory Rate

	T	H R	R
Mean of Mean	37.9	145	22
S.E.M.	±0.34	±6.5	±2.0

Five dogs were infused with acid solution at a rate of 5-7 mEq/Kg body wt/2hr time period as outlined by Russell, et al. (1972). The range of alkaline infusion rates for the four dogs in which alkalosis was induced was 6-18 mEq/Kg body wt/hr.

A record of the amount of acid infused per kilogram of body weight is not available on the first experimental dog. (Appendix C, Dog 1 - December 15, 1978.) Therefore, his arterial and mixed venous blood values cannot be included in the second category of analysis. Values from this dog, however, are included in the third category of analysis.

Dog 9 (March 9) after reaching a pH of 7.61 and 7.59 for arterial and mixed venous blood, respectively, developed severe hypoventilation. His arterial pH decreased to 7.46 and mixed venous pH to 7.45 pH units.

Limits of reproducability in this study were found to be within ±0.005 units for pH measurements. Excepting

for one arterial pCO_2 and one mixed venous pCO_2, all pCO_2 measurements were within ±1mmHg. With the exception of two arterial pO_2 values, all pO_2 measurements were within ±1mmHg.

1. Analysis of blood-gas parameters as a function of the amount of acid or base infused per kilogram of body weight.

Correlation coefficients (Pearson Product Moment, r) slopes and intercepts were computed for all blood-gas parameters in arterial and mixed venous blood as a function of the amount of acid or base infused per kilogram of body weight. A summary of these results may be found in Table 2. The original data from which this summary was derived may be found in Appendix (D).

As can be seen in Table 2, there is a strong correlation between amount of acid or base infused and a given blood-gas parameter. This is also apparent in Figures 3 through 10.

The mean values for slope, intercept and correlation between arterial and mixed venous blood do not differ significantly for pH, pCO_2 and HCO_3^- ($p > 0.05$). (See Table 3.)

The difference between mean values (arterial minus mixed venous) for the intercept of pO_2 versus the amount of acid or base infused is significant in both acidotic

and alkalotic animals ($p < 0.001$). The results from the t-tests may be found in Table 3.

As the quantity of acid infused per kilogram of body weight increased, both arterial and mixed venous pH decreased. Graphically they appeared to mirror each other with mixed venous pH being consistently lower than arterial pH.

As the alkaline infusion began, pH of both arterial and mixed venous blood rose sharply. Once a pH of approximately 7.6 was reached, however, (in spite of increments in the rate of Sodium Bicarbonate infusion) a pH of greater than 7.67 for arterial blood and 7.63 for mixed venous blood could not be attained.

The dog that reached these pH values was receiving approximately 4.7 times more alkaline solution per kilogram body weight as he received when his arterial pH was 7.55 and his mixed venous pH was 7.54. (Appendix C, Dog 8 - February 27, 1979.)

A graph showing the relationship between pH and HCO_3^- concentration is found in Figures 11 and 12.

2. Comparison of arterial versus mixed venous blood during metabolic acidotic and alkalotic states.

A summary of the mean values obtained for all parameters when arterial blood is compared to mixed venous blood during metabolic acidotic and alkalotic states

is presented in Table 4. Raw data from which these results were obtained may be found in Appendix (E).

pH - The range of arterial pH values obtained during the experiments to induce acidosis was 7.39-6.88. The mixed venous pH values ranged from 7.40-6.86. During the acid infusion, the difference between arterial and mixed venous pH ranged from 0.001-0.03 pH units (mean = 0.026 ± 0.02; unless stated, values of all means are followed by standard deviations).

During the alkaline infusion, arterial and mixed venous pH values ranged from 7.43-7.67 and from 7.41-7.63, respectively. The difference between arterial and mixed venous pH ranged from 0.005-0.039 (mean = 0.02 ± 0.01).

A t-test was computed to determine the significance of the differences between means, slope, correlation coefficient and intercept in acidotic and alkalotic states. No significant difference was found between mean correlation coefficients for acidotic and alkalotic dogs ($p > 0.4$). Significant differences were found between mean slopes and intercepts from acidotic and alkalotic dogs ($p < 0.01$). The results of the t-test are presented in Table 5. Figure 13 shows the identity relationship for pH.

pCO_2 - During acid infusions, the pCO_2 ranged from 44.8 to 18.1 mmHg for arterial blood and from 48.4 to 25.9

mmHg for mixed venous blood. Arterial pCO_2 values were always less than mixed venous values. The range of difference between arterial and mixed venous pCO_2 was from -1.83 to -12.7 mmHg (mean = 6.0 $\pm$ 2.8).

During the alkaline infusions, the ranges of arterial and mixed venous pCO_2 were from 37.8 to 95.4 mmHg and from 38.6 to 98.1 mmHg, respectively. The range of differences between arterial and mixed venous pCO_2 values was from -9.0 to +1.0 mmHg (mean = -4 $\pm$ 2.3). In all but one sample, arterial pCO_2 was lower than mixed venous pCO_2. In this instance values for arterial and mixed venous pCO_2 were essentially equal.

Arterial and mixed venous pCO_2 decreased during the acid infusions and increased during the alkaline infusions.

No significant difference was found between mean correlation coefficients for pCO_2 in acidotic and alkalotic dogs. However, mean slopes were significantly different ($p < 0.05$) as was the difference between mean values of intercepts ($p < 0.005$). (See Table 5 and Figure 14.)

$\underline{pO_2}$ - During the acid infusions, arterial and mixed venous pO_2 ranged from 82.6 to 125.6 and 49.3 to 85.6, respectively. Arterial blood differed from mixed venous blood by a mean value of 33.7 $\pm$ 9.0 mmHg (range 17.6 to 50.9 mmHg). Mixed venous pO_2 was always less than arterial pO_2.

Both arterial and mixed venous pO_2 values rose as

the amount of acid infused increased.

When alkaline solution was infused, pO_2 ranged from 85.9 to 18.3 mmHg for arterial blood and 45.5 to 8.5 mmHg for mixed venous blood. The range of difference between arterial and mixed venous pO_2 during the alkaline infusion ranged from 9.4 to 48.8 (mean = 23.4 $\pm$ 8.0 mmHg). Mixed venous pO_2 was always less than arterial pO_2. Both arterial and mixed venous pO_2 decreased as the amount of base infused increased.

There were no significant differences between mean values of correlation coefficient, slope and intercept in acidotic or alkalotic states. (See Table 5 and Figure 15.)

$\underline{HCO_3^-}$ - The range of HCO_3^- concentrations for arterial and mixed venous blood during acid infusion ranged from 21.7 to 4.6 mEq/l and from 22.7 to 5.4 mEq/l, respectively. The difference between arterial and mixed venous HCO_3^- concentrations ranged from -2.6 to -.15 (mean = -1.2 $\pm$ 0.61). The HCO_3^- concentration for arterial blood was always lower than that of mixed venous blood. Both arterial and mixed venous HCO_3^- concentrations decreased as the amount of acid infused increased.

During the infusion of alkali, the HCO_3^- concentrations for arterial and mixed venous blood ranged from 29.6 to 79.5 mEq/l and 29.9 to 78.9 mEq/l, respectively. The range of difference between arterial and mixed venous

HCO_3^- concentration ranged from -3.2 to +1.6 (mean = .6 $\pm$ 1.8 mEq/l).

Sometimes arterial HCO_3^- concentrations were greater than mixed venous HCO_3^- concentrations and sometimes less. There did not seem to be a consistent pattern. Both arterial and mixed venous HCO_3^- concentrations increased as the alkaline infusion increased.

No significant difference was found between mean correlation coefficients for HCO_3^- concentrations in acidotic and alkalotic dogs. However, mean slopes were significantly different ($p < 0.02$) as was the difference between mean values of intercepts ($p < 0.001$). (See Table 5 and Figures 16 and 17.)

Table 2

Summary for Means and Standard Deviations for Correlation Coefficients, Slopes and Intercepts: Blood-Gas Parameter versus Amount of Acid or Base Infused per Kilogram Body Weight

	PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
	a**	mv**	a	mv	a	mv	a	mv
Dogs Infused with NH_4Cl:								
$\bar{x}$ r	-.981	-.985	-.828	-.726	.863	.894	-.946	-.943
SD(±) r	.012	.012	.145	.261	.073	.084	.017	.034
$\bar{x}$ slope	-.034	-.035	-.588	-1.113	2.558	1.880	-1.474	-1.438
SD(±) slope	.007	.008	.261	.374	.957	.697	.364	.359
$\bar{x}$ intercept	7.320	7.305	42.701	45.794	82.358*	53.236*	20.047	21.104
SD(±) intercept	.064	.062	3.715	4.484	4.521	4.798	2.422	2.566
Dogs Infused with $NaHCO_3$:								
$\bar{x}$ r	.876	.866	.904	.947	-.930	-.955	.984	.988
SD(±) r	.053	.066	.100	.027	.081	.010	.012	.005
$\bar{x}$ slope	.008	.007	.549	.672	-.919	-.506	1.170	1.212
SD(±) slope	.003	.003	.146	.090	.432	.088	.181	.209
$\bar{x}$ intercept	7.436	7.431	42.741	44.434	75.335*	45.710*	27.461	27.434
SD(±) intercept	.032	.034	6.263	5.778	9.410	1.559	1.837	1.516

*$p < 0.001$ where p is the probability that the values are the same

**a, arterial blood; **mv, mixed venous blood

Table 3

Results of t-Tests for Differences Between Means for Correlation Coefficients, Slopes and Intercepts From Table 2

	PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
	NH_4Cl	$NaHCO_3$	NH_4Cl	$NaHCO_3$	NH_4Cl	$NaHCO_3$	NH_4Cl	$NaHCO_3$
t r	0.483	0.242	-0.681	-0.826	-0.544	0.614	-0.147	-0.568
t slope	0.181	0.475	-2.083	-1.441	1.145	-1.874	-.142	-0.305
t intercept	0.346	0.217	-1.062	-0.397	8.835*	6.212*	-0.599	0.023

df = 6 *$p < 0.001$ where p is the probability that the values are the same

Table 4

Mean Values for Correlation Coefficients,
Slopes and Intercepts:
Mixed Venous Blood versus Arterial Blood

	PH		PCO_2 mmHg		PO_2 mmHg		HCO_3 mEq/l	
	NH_4Cl	$NaHCO_3$	NH_4Cl	$NaHCO_3$	NH_4Cl	$NaHCO_3$	NH_4Cl	$NaHCO_3$
$\bar{x}$ r	0.992	0.996	0.930	0.961	0.850	0.940	0.995	0.997
SD r	0.010	0.001	0.038	0.048	0.126	0.056	0.004	0.002
$\bar{x}$ slope	1.014	0.934	0.770	1.052	0.541	0.664	0.976	1.023
SD slope	0.036	0.014	0.104	0.242	0.115	0.264	0.028	0.014
$\bar{x}$ intercept	-1.126	0.478	14.121	-5.035	10.208	3.361	1.522	-0.522
SD intercept	0.250	0.108	5.229	5.386	10.810	5.248	0.494	0.602

Table 5

T-Tests Comparing the Differences Between Means for Correlation Coefficients, Slopes and Intercepts: Mixed Venous Blood versus Arterial Blood During Acidotic and Alkalotic States

	PH	PCO_2 mmHg	PO_2 mmHg	HCO_3 mEq/l
t r	-0.860	-1.083	-1.306	-1.353
t slope	4.182 (3)	-2.375 (5)	-0.951	-3.092 (4)
t intercept	-4.459 (3)	5.391 (2)	1.152	5.611 (1)

df = 7

(1) $p < 0.001$
(2) $p < 0.005$
(3) $p < 0.01$
(4) $p < 0.02$
(5) $p < 0.05$ where p is the probability that the values are the same

Figure 3

The pH of arterial and mixed venous blood are shown as a function of mEq NH_4Cl infused per kilogram body weight. Each symbol represents one pH value. This graph shows results from four dogs that received NH_4Cl.

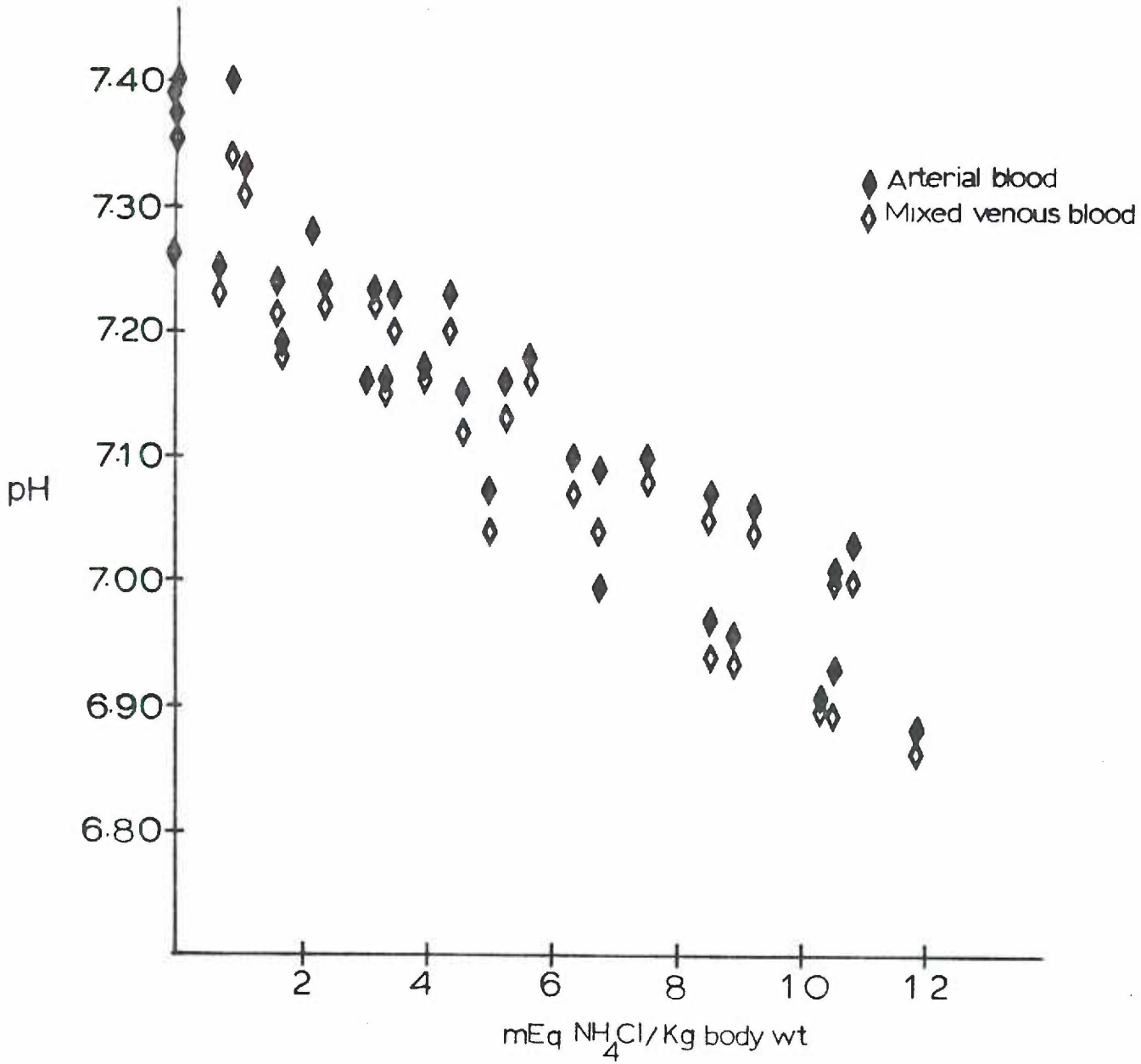

7·40
7·30
7·20
7·10
7·00
6·90
6·80
pH
2
4
6
8
10
12
mEq NH4Cl/Kg body wt
Arterial blood
Mixed venous blood

Figure 4

The pH of arterial and mixed venous blood are shown as a function of mEq $NaHCO_3$ infused per kilogram body weight. Each symbol represents one pH value. This graph shows results from four dogs that received $NaHCO_3$. The isolated pair of values occurred in Dog 9 as a result of severe hypoventilation.

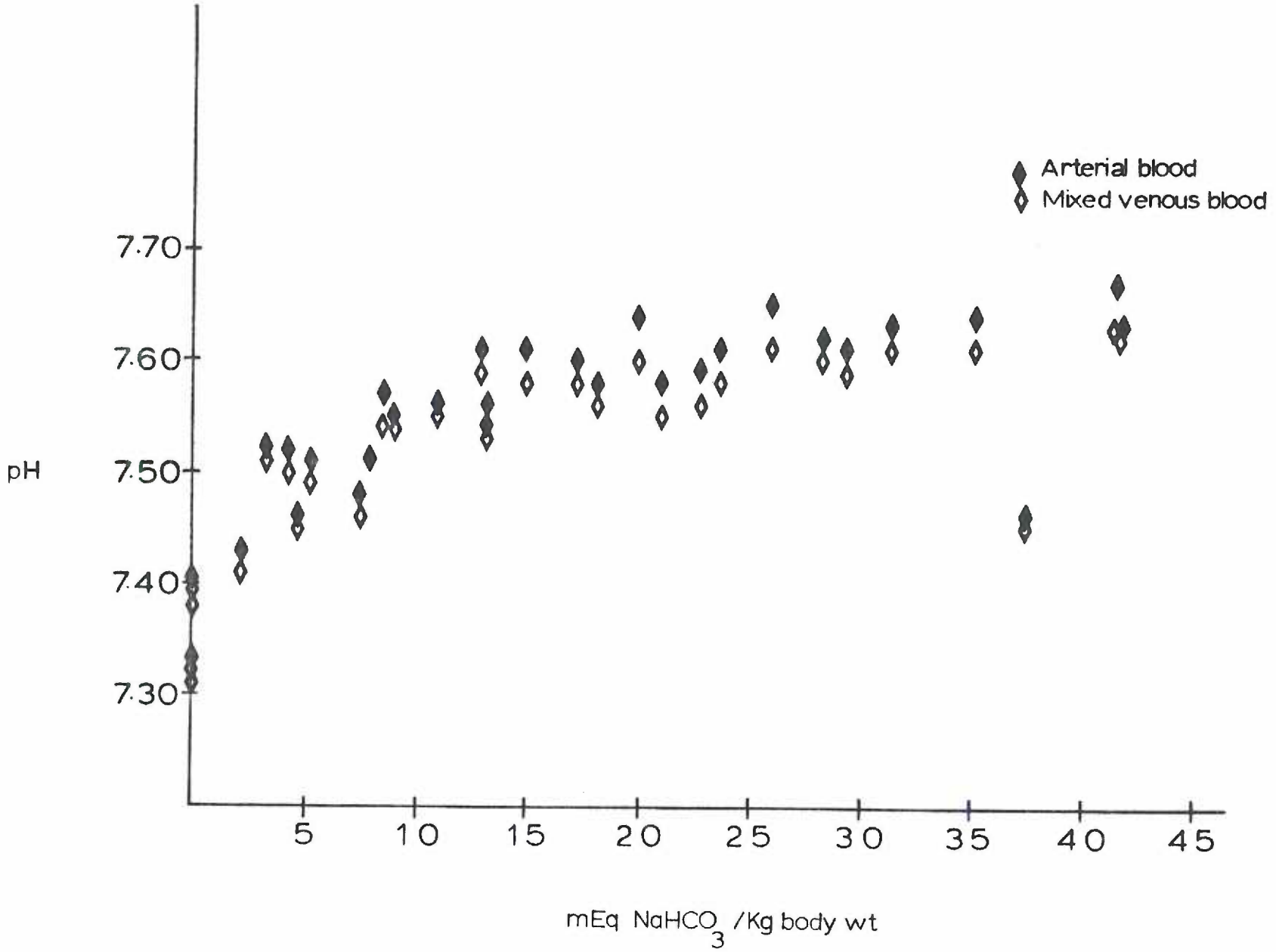

Arterial blood
Mixed venous blood
pH
7.70
7.60
7.50
7.40
7.30
5
10
15
20
25
30
35
40
45
mEq NaHCO3 /Kg body wt

Figure 5

The pCO_2 of arterial and mixed venous blood are shown as a function of mEq NH_4Cl infused per kilogram body weight. Each symbol represents one pCO_2 value. This graph shows results from four dogs that received NH_4Cl.

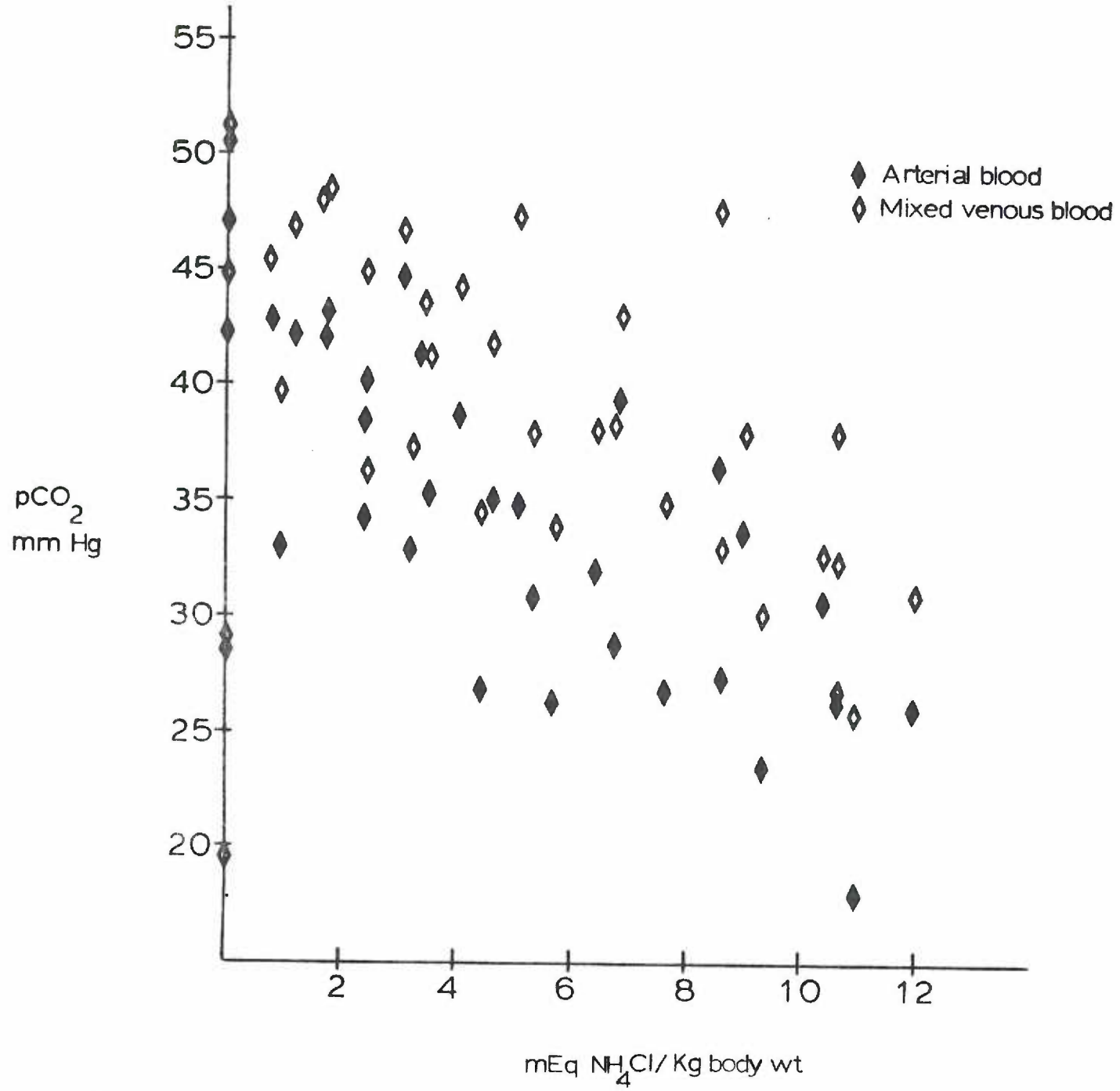

55
50
45
40
35
30
25
20
pCO2
mm Hg
2
4
6
8
10
12
mEq NH4Cl/ Kg body wt
Arterial blood
Mixed venous blood

Figure 6

The pCO_2 of arterial and mixed venous blood are shown as a function of mEq $NaHCO_3$ infused per kilogram body weight. Each symbol represents one pCO_2 value. This graph shows results from four dogs that received $NaHCO_3$. The isolated pair of values occurred in Dog 9 as a result of severe hypoventilation.

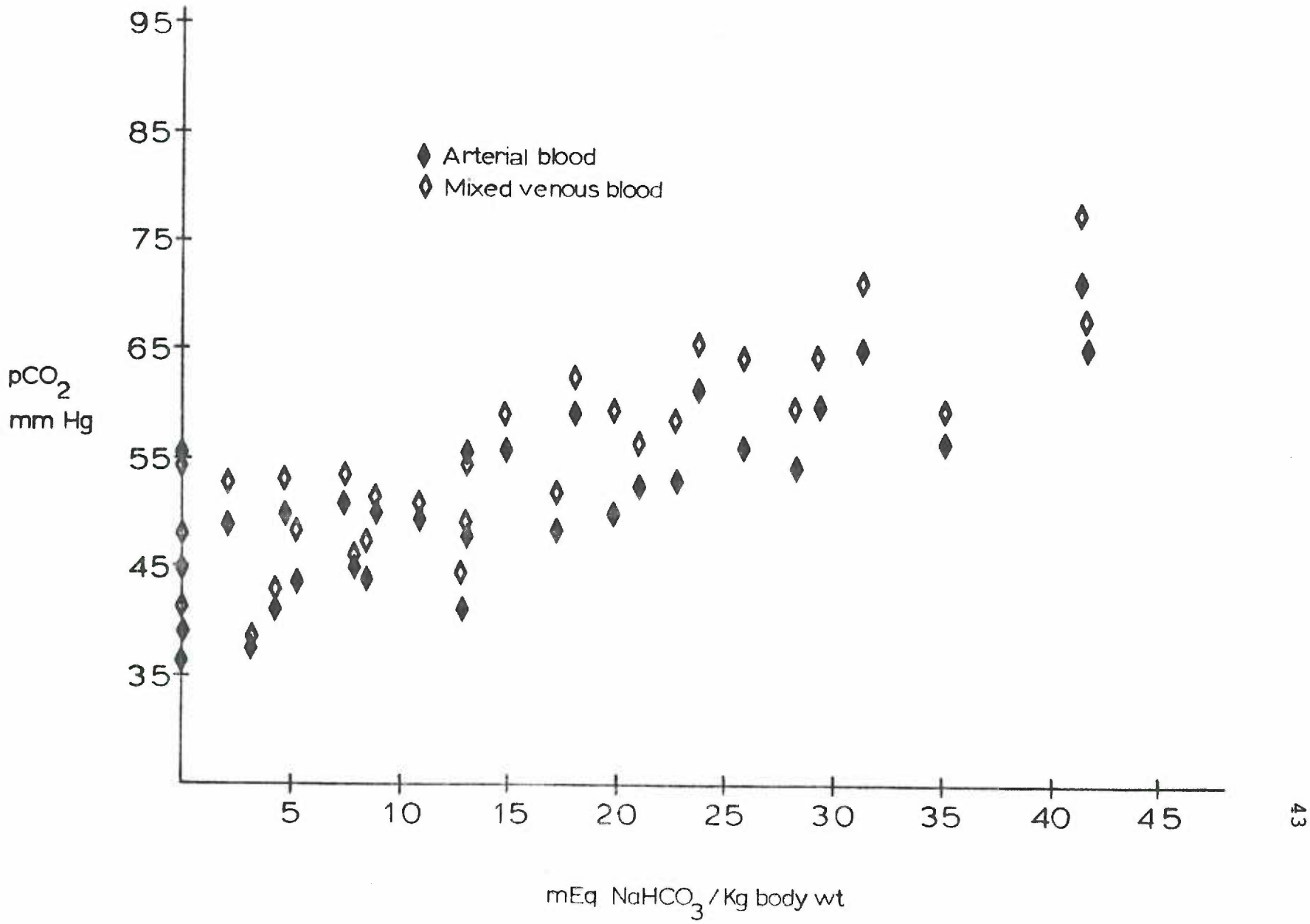

95
85
75
65
55
45
35
pCO2
mm Hg
Arterial blood
Mixed venous blood
5
10
15
20
25
30
35
40
45
mEq NaHCO3 / Kg body wt

Figure 7

The pO_2 of arterial and mixed venous blood are shown as a function of mEq NH_4Cl infused per kilogram body weight. Each symbol represents one pO_2 value. This graph shows results from four dogs that received NH_4Cl.

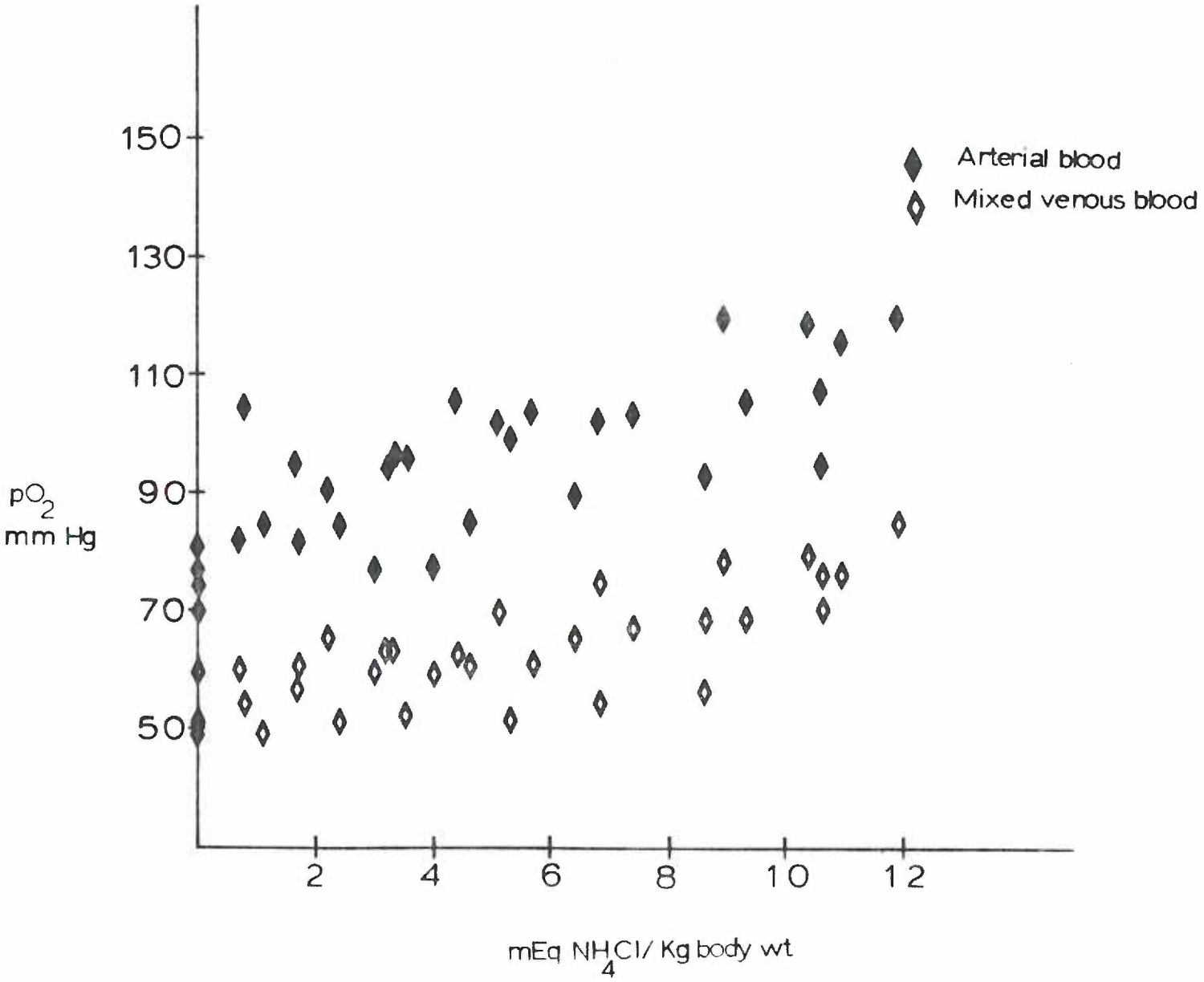

150
130
110
90
70
50
pO2
mm Hg
2
4
6
8
10
12
mEq NH4Cl/ Kg body wt
Arterial blood
Mixed venous blood

Figure 8

The pO_2 of arterial and mixed venous blood are shown as a function of mEq $NaHCO_3$ infused per kilogram body weight. Each symbol represents one pO_2 value. This graph shows results from four dogs that received $NaHCO_3$. The lowest arterial and mixed venous pO_2 occurred in Dog 9 as a result of severe hypoventilation.

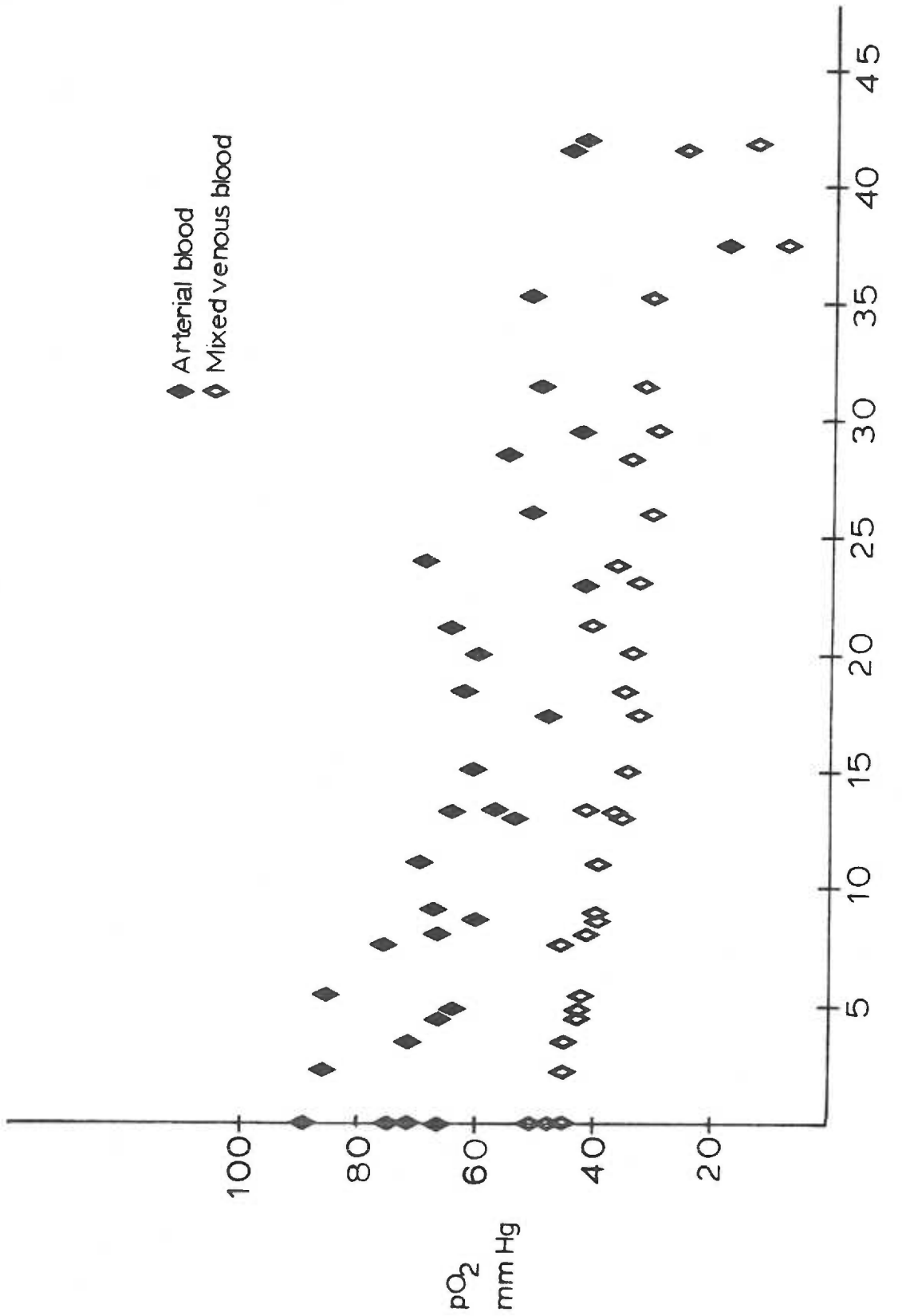

Arterial blood
Mixed venous blood
100
80
60
40
20
pO_2 mm Hg
5
10
15
20
25
30
35
40
45
mEq $NaHCO_3$ / Kg body wt

Figure 9

The HCO_3^- concentrations of arterial and mixed venous blood are shown as a function of mEq NH_4Cl infused per kilogram body weight. Each symbol represents one HCO_3^- concentration. This graph shows results from four dogs that received NH_4Cl.

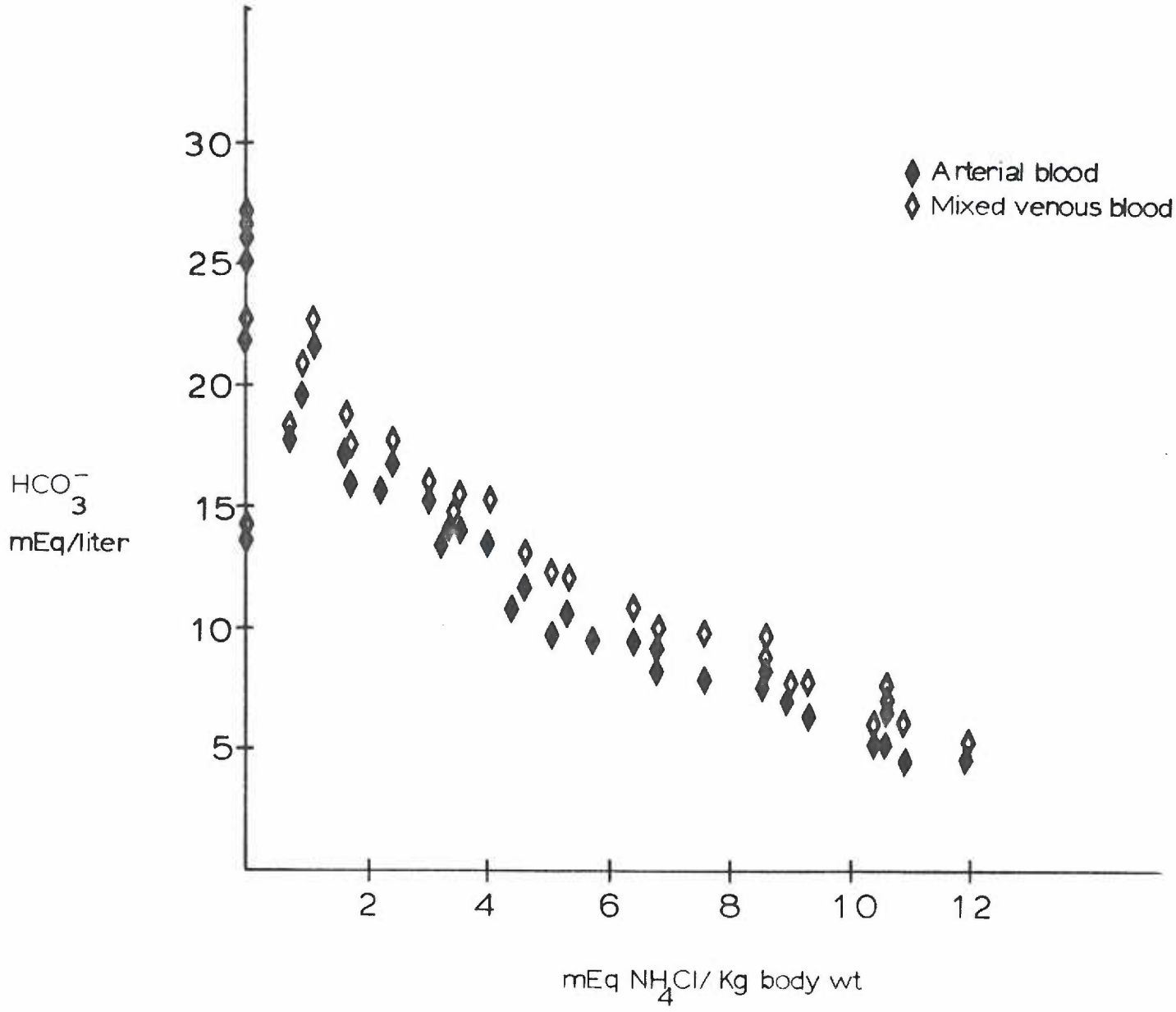

30
25
20
15
10
5
2
4
6
8
10
12
Arterial blood
Mixed venous blood
HCO3−
mEq/liter
mEq NH4Cl/ Kg body wt

Figure 10

The HCO_3^- concentrations of arterial and mixed venous blood are shown as a function of mEq $NaHCO_3$ infused per kilogram body weight. Each symbol represents one HCO_3^- value. This graph shows results from four dogs that received $NaHCO_3$.

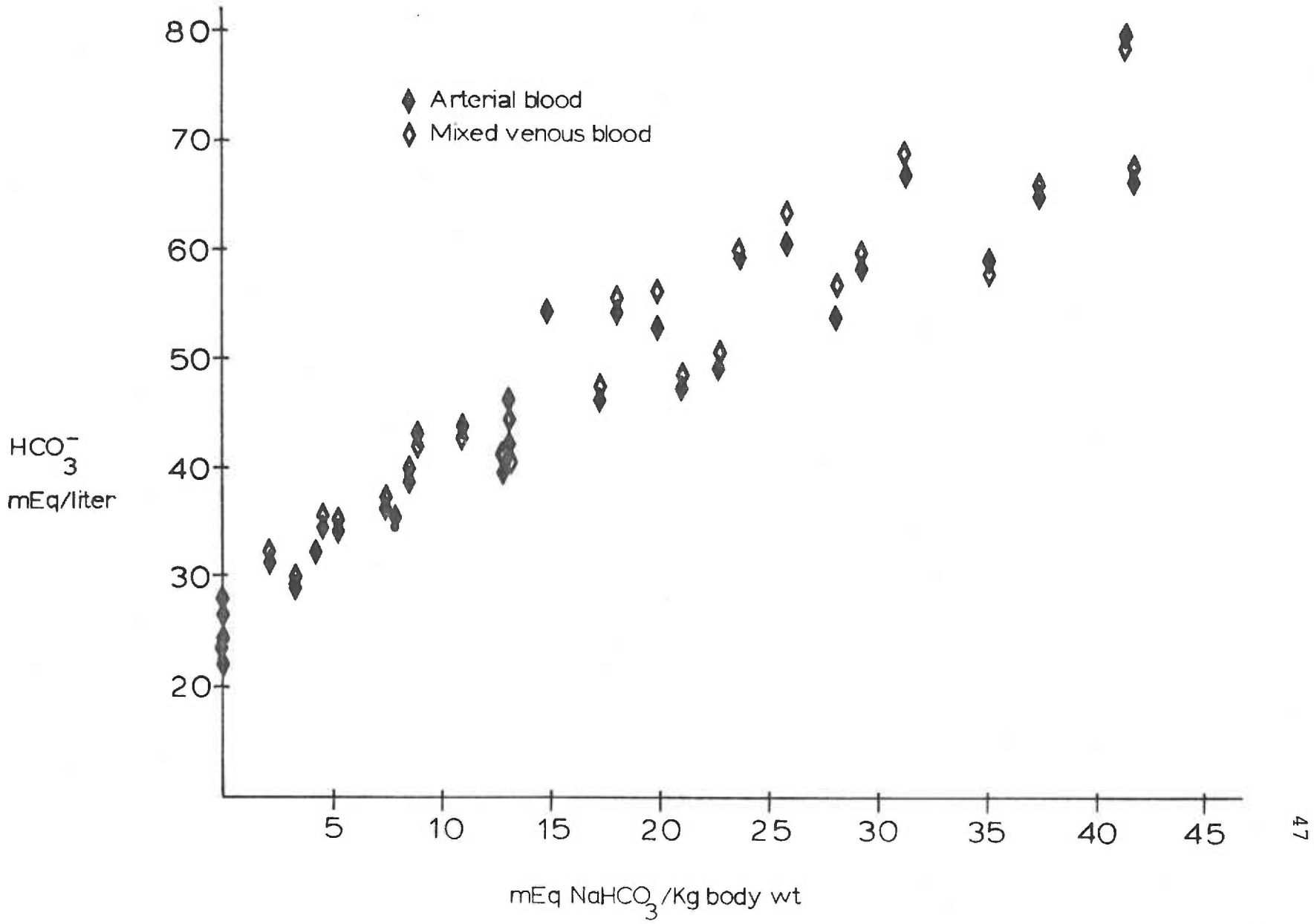

80
70
60
50
40
30
20
Arterial blood
Mixed venous blood
HCO_3^-
mEq/liter
5
10
15
20
25
30
35
40
45
mEq $NaHCO_3$ /Kg body wt

Figure 11

Arterial HCO_3^- concentration is shown as a function of arterial pH during acidotic and alkalotic states. Each symbol represents one pair of values. This graph shows results from nine experimental dogs. The isolated point occurred in dog 9 as a result of severe hypoventilation.

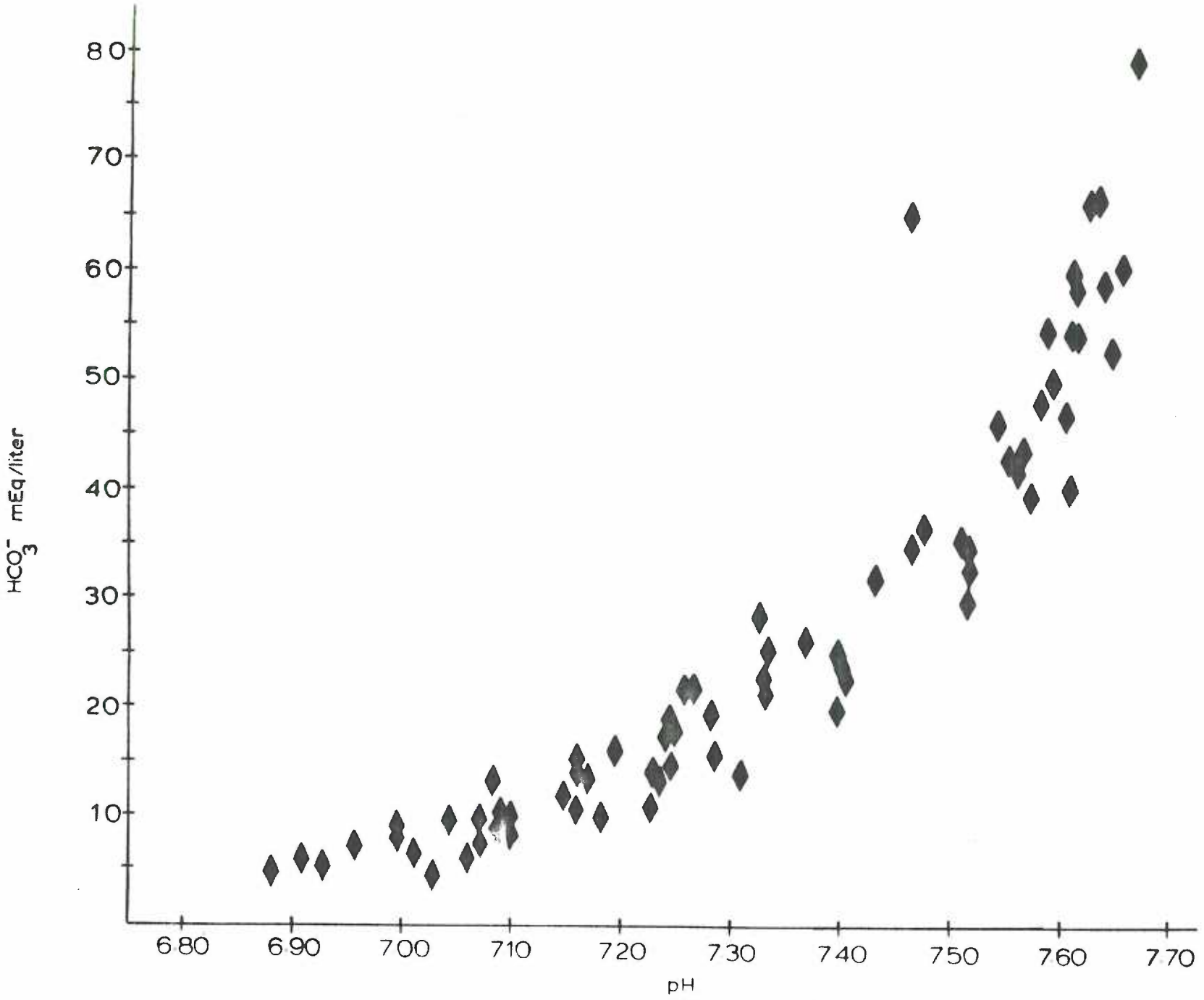

80
70
60
50
40
30
20
10
HCO_3^- mEq/liter
6.80
6.90
7.00
7.10
7.20
7.30
7.40
7.50
7.60
7.70
pH

Figure 12

Mixed venous HCO_3^- concentration is shown as a function of mixed venous pH during acidotic and alkalotic states. Each symbol represents one pair of values. This graph shows results from nine experimental dogs. The isolated point occurred in dog 9 as a result of severe hypoventilation.

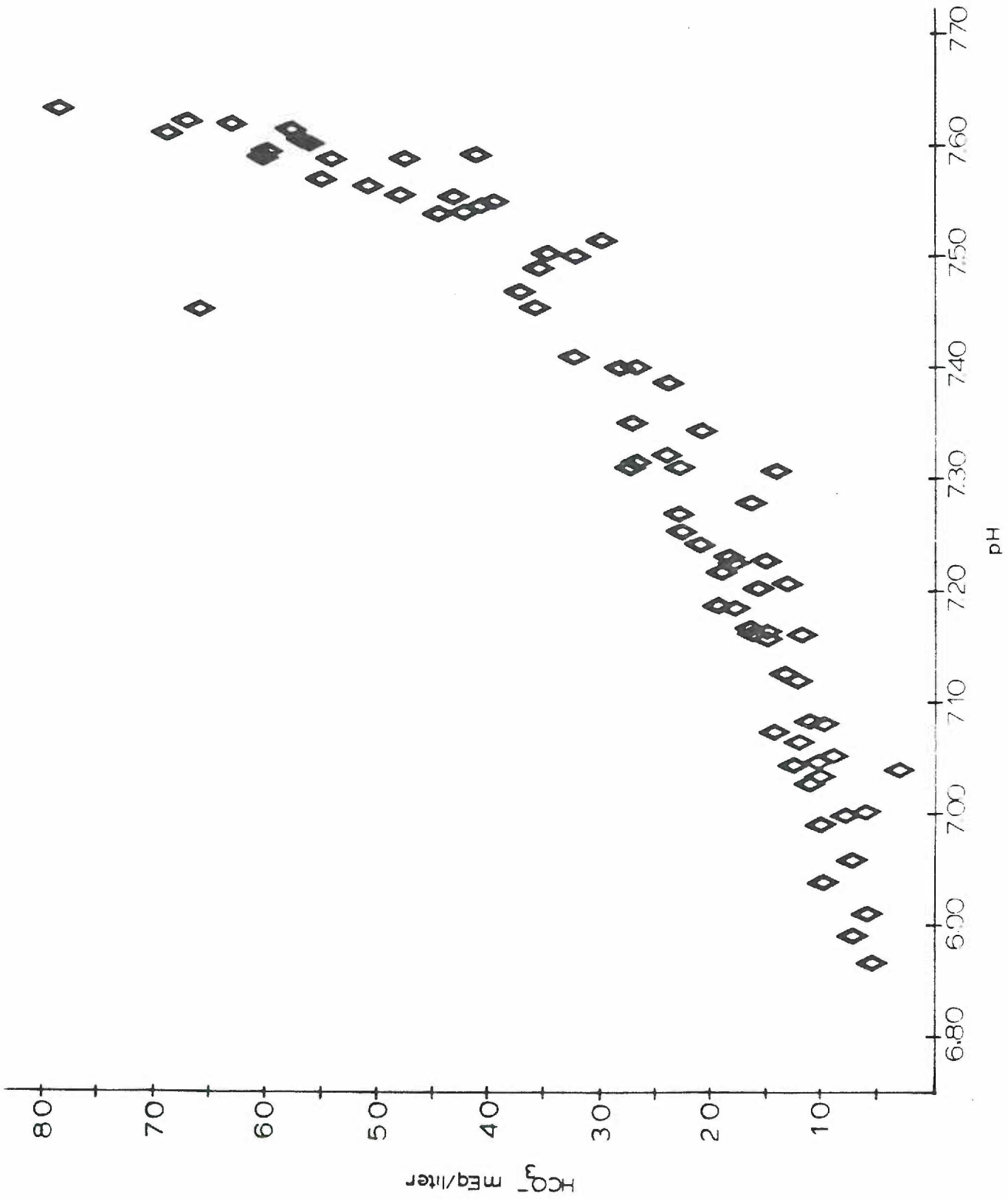

80
70
60
50
40
30
20
10
HCO_3^- mEq/liter
6.80
6.90
7.00
7.10
7.20
7.30
7.40
7.50
7.60
7.70
pH

Figure 13

Identity relationships are shown for all arterial and mixed venous pH values obtained during acidotic and alkalotic states.
Each symbol represents one pair of values.
The identity line shows a correlation coefficient of 1.

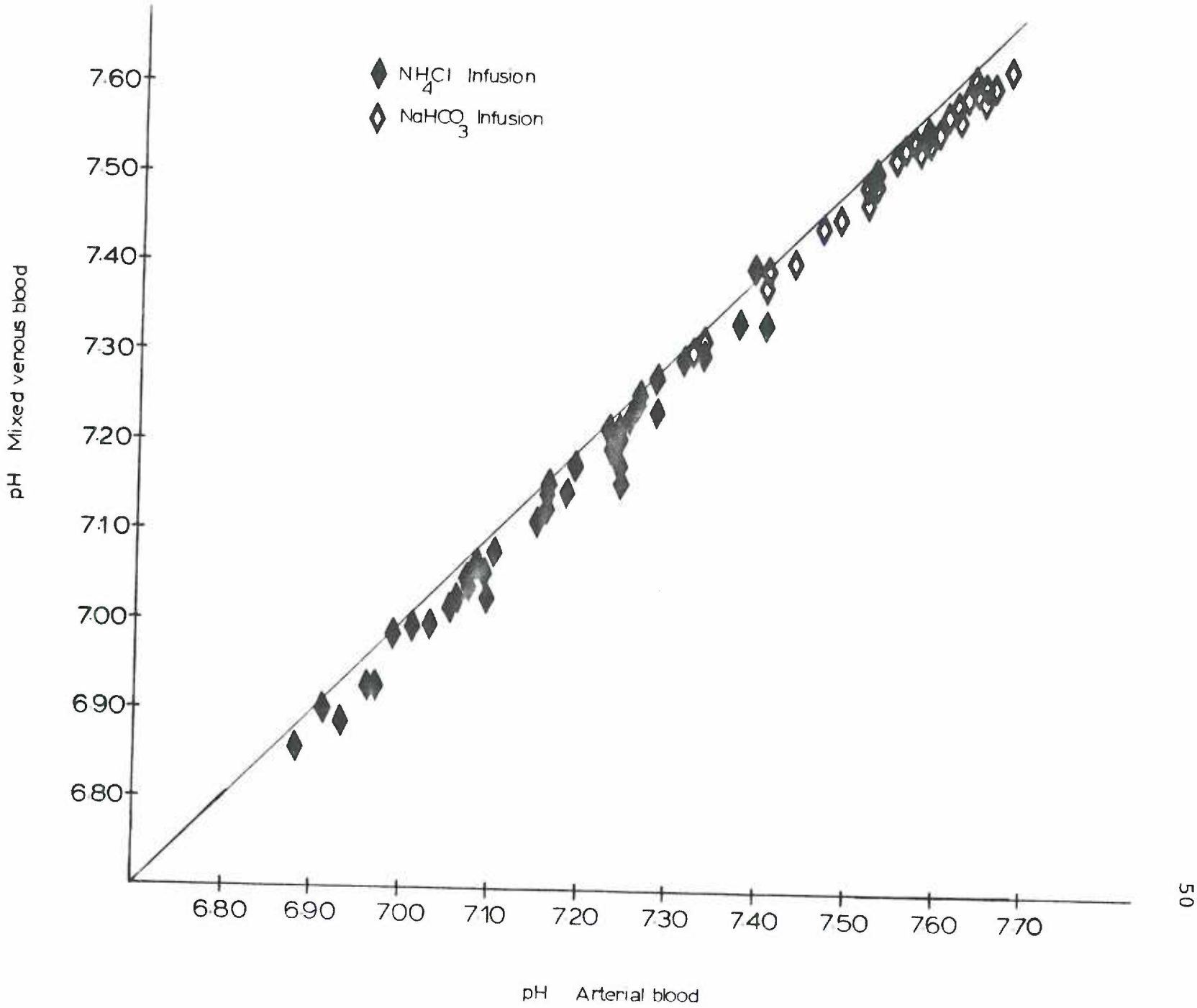

NH4Cl Infusion
NaHCO3 Infusion
pH Mixed venous blood
7.60
7.50
7.40
7.30
7.20
7.10
7.00
6.90
6.80
6.80
6.90
7.00
7.10
7.20
7.30
7.40
7.50
7.60
7.70
pH Arterial blood

Figure 14

Identity relationships are shown for all arterial and mixed venous pCO_2 values obtained during acidotic and alkalotic states. Each symbol represents one pair of values. The identity line shows a correlation coefficient of 1.

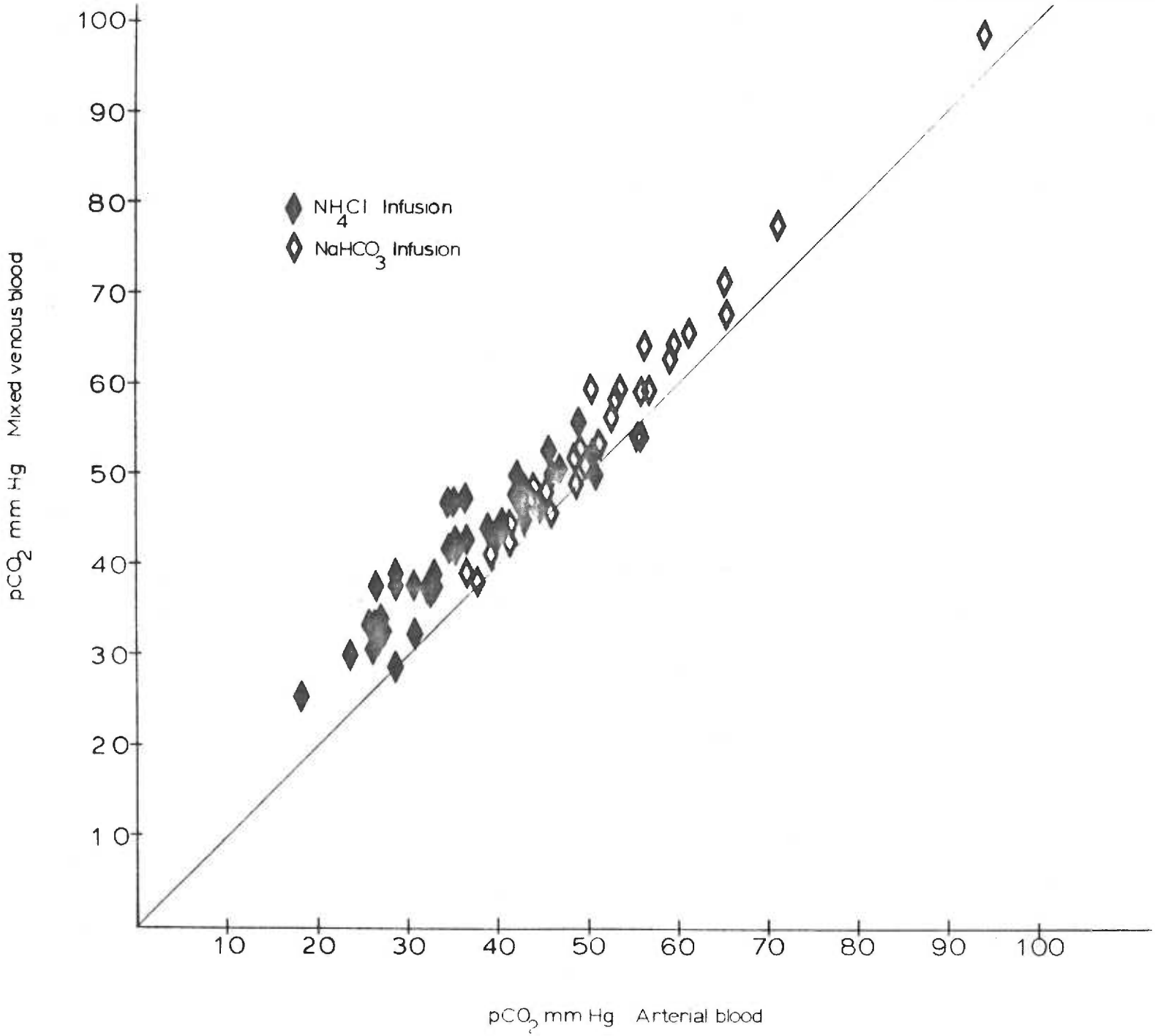

100
90
80
70
60
50
40
30
20
10
NH4Cl Infusion
NaHCO3 Infusion
pCO2 mm Hg Mixed venous blood
10
20
30
40
50
60
70
80
90
100
pCO2 mm Hg Arterial blood

Figure 15

Identity relationships are shown for all arterial and mixed venous pO_2 values obtained during acidotic and alkalotic states. Each symbol represents one pair of values. The identity line shows a correlation coefficient of 1.

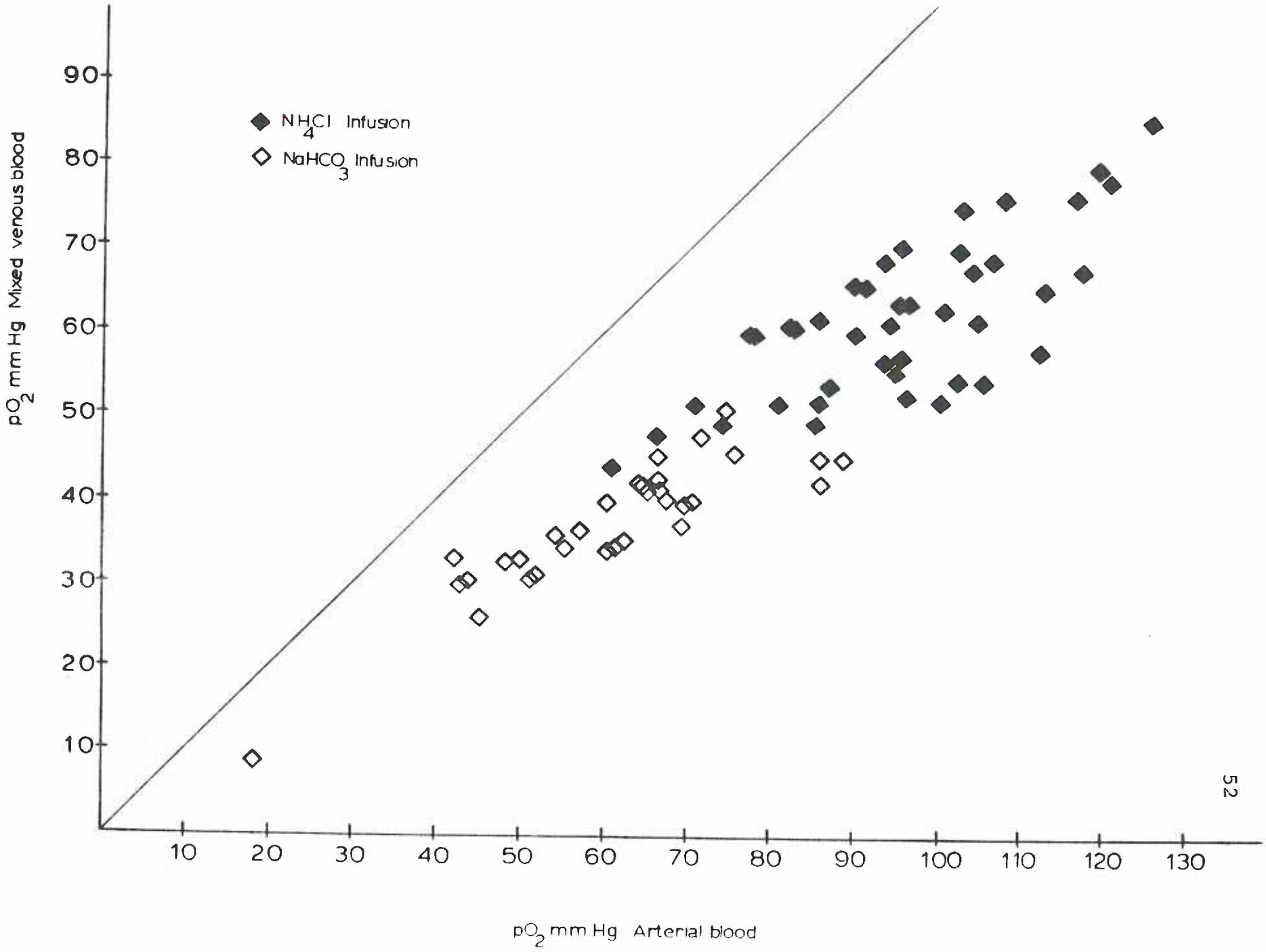

◆ NH_4Cl Infusion
◇ $NaHCO_3$ Infusion
pO_2 mm Hg Mixed venous blood
pO_2 mm Hg Arterial blood
10
20
30
40
50
60
70
80
90
100
110
120
130

Figure 16

Identity relationships are shown for all arterial and mixed venous HCO_3^- concentrations obtained during acidosis. Each symbol represents one pair of values.
The identity line shows a correlation coefficient of 1.

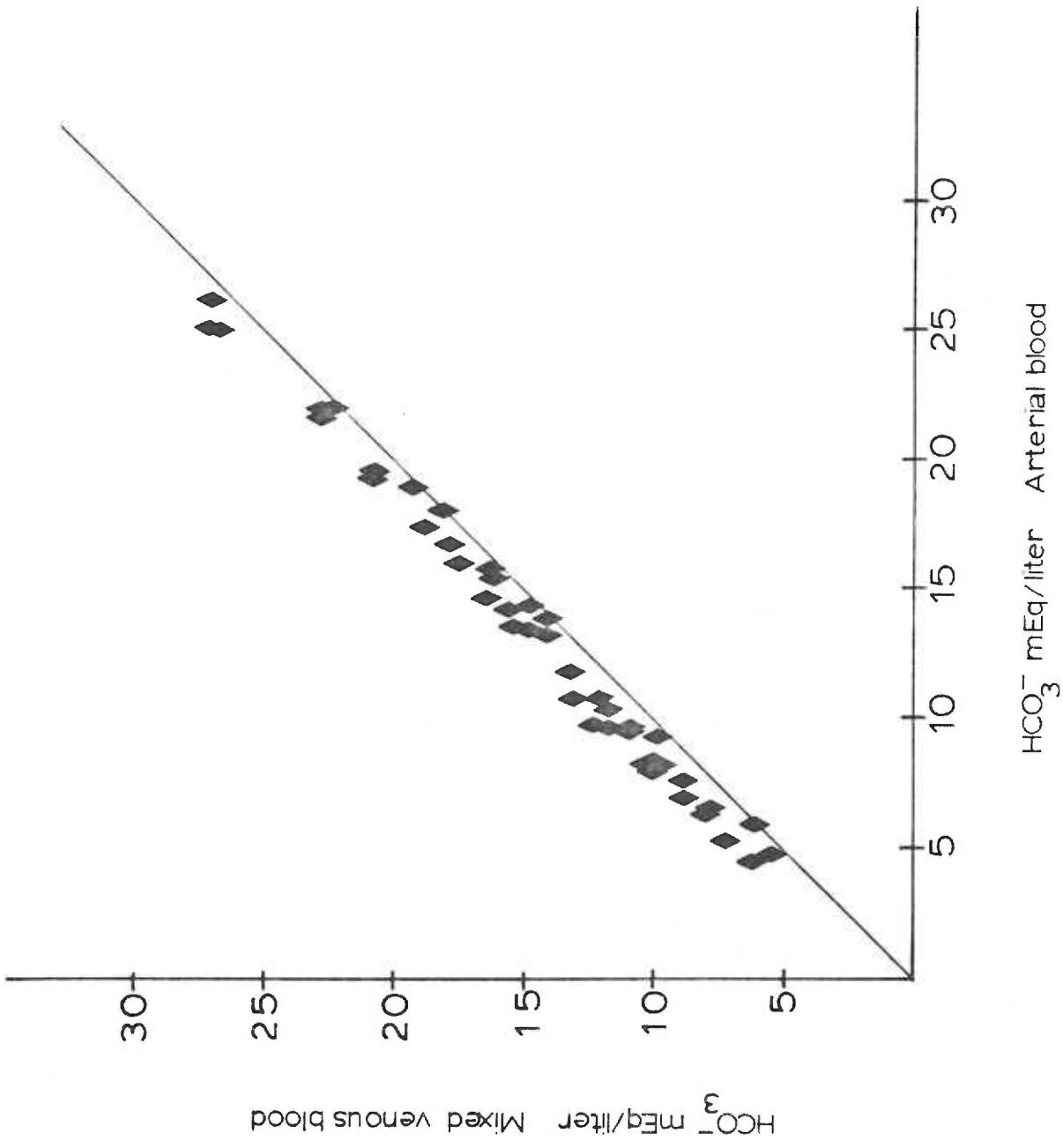
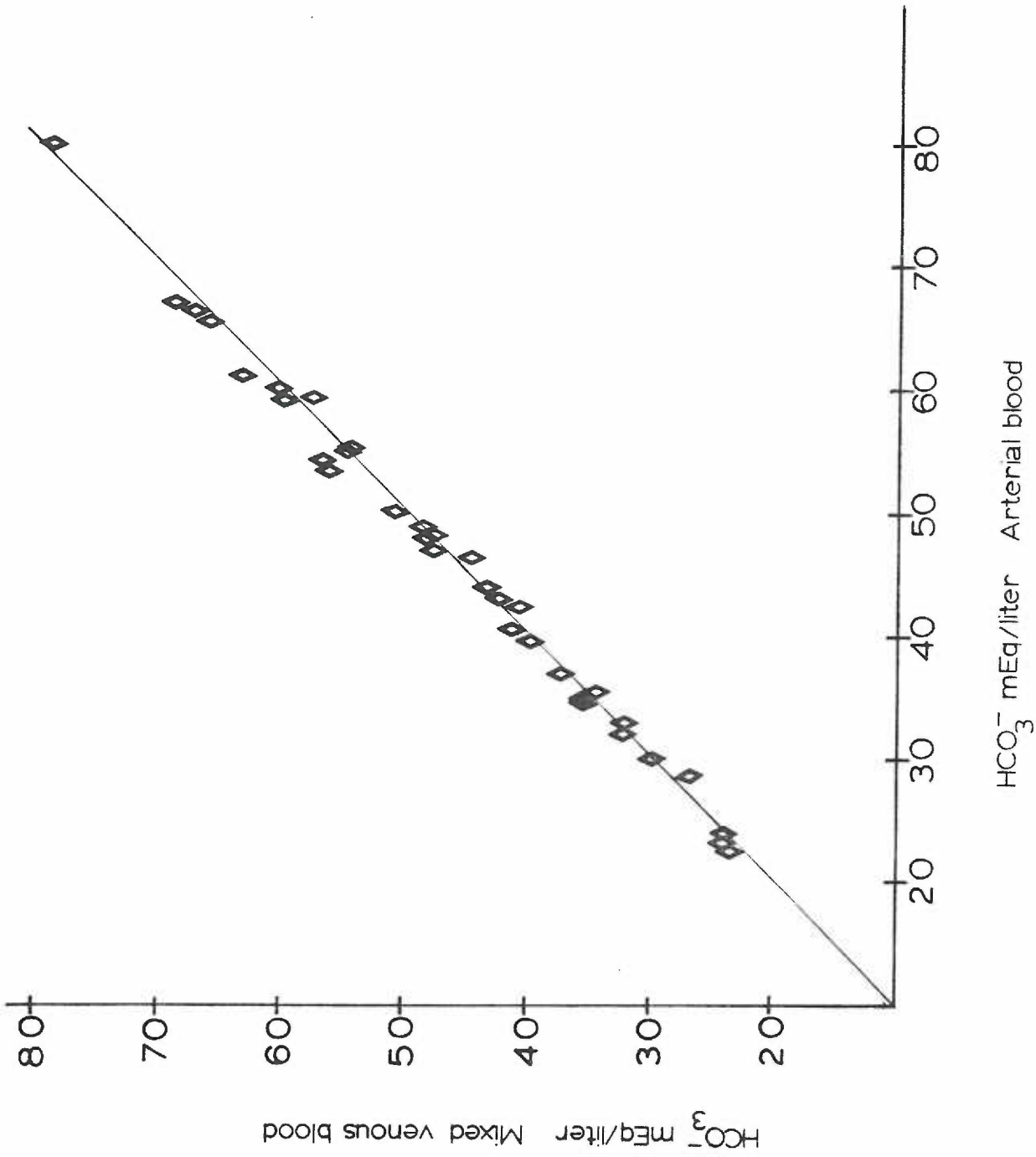

30
25
20
15
10
5
HCO_3^- mEq/liter Mixed venous blood
5
10
15
20
25
30
HCO_3^- mEq/liter Arterial blood

Figure 17

Identity relationships are shown for all arterial and mixed venous HCO_3^- concentrations obtained during alkalosis. Each symbol represents one pair of values. The identity line shows a correlation coefficient of 1.


HCO_3^- mEq/liter Mixed venous blood
20
30
40
50
60
70
80
HCO_3^- mEq/liter Arterial blood
20
30
40
50
60
70
80

CHAPTER IV

DISCUSSION

Metabolic acidosis was induced in the experimental animals with NH_4Cl. In the liver, ammonium chloride is converted to urea and hydrochloric acid. This process is shown in the following equations:

$$2NH_4Cl \rightleftharpoons 2NH_3 + 2H^+ + 2Cl^-$$

$$+$$

$$CO_2$$

$$\downarrow$$

$$(NH_2)_2 - CO + H_2O$$

Since hydrogen ions and chloride ions are formed, administration of NH_4Cl is equivalent to giving the animals hydrochloric acid. Onset of acidosis is as rapid with infusion of 0.3M NH_4Cl as it is with infusion 0.3M HCl (Russell, 1968).

It is apparent from the results of these experiments that there is a predictable pattern to the way mixed venous blood-gas composition changes during states of metabolic acidosis and alkalosis. For all blood-gas parameters in both acidotic and alkalotic states, mixed venous blood appears to mirror the pattern of arterial

blood. This was shown to be true over a wide range of pH values (pH 6.88 to 7.67 for arterial blood and 6.86 to 7.63 for mixed venous blood).

These results support those obtained by Zahn and Weil (1966). In their experiments the pH and pCO_2 of central venous blood was compared to that of arterial blood in critically ill patients. Their results showed that arterial and mixed venous blood resembled each other closely over a wide range of pH values. The range of values obtained from individual patients in their study was not reported. It is unlikely, however, that the range in any given patient varied as widely as those reported for any one dog in this study.

Phillips and Peretz (1969) also found that the pH and pCO_2 of arterial and mixed venous blood correlated highly during states of acidosis and alkalosis in critically ill patients. They reported that venous blood samples are a reliable practical substitute for arterial sampling in the assessment of metabolic acid-base disturbances. Their published results, however, did not provide data that led to this conclusion. The results of this present dog study do support their assertion since all the disturbances in this study were metabolic in origin, and correlations between all arterial and mixed venous blood-gas parameters were high.

It is clear from the results (Figure 13) that mixed venous pH was consistently lower than arterial pH. This result was expected since mixed venous blood is in contact with systemic tissues where lactic acid and carbonic acid are added to the blood (Figure 1). Therefore, one would expect to find a higher acid concentration in mixed venous blood.

Carbon dioxide is removed from mixed venous blood in the lungs. Therefore, arterial blood would be expected to have lower pCO_2 values than mixed venous blood. This was borne out consistently during these experiments (Figures 5 and 6).

Baseline pCO_2 values from the dogs infused with acid vary over a wide range (Figure 5). Low values for pCO_2 may have resulted from the highly excitable state of some of the dogs at the time of induction of anesthesia. High pCO_2 values may reflect the depressor effects of the anesthetic agent (Sodium Pentobarbital) on respiratory neurons in the central nervous system.

A great deal of variance is apparent in pCO_2 values during NH_4Cl infusions (Figure 5). This scatter may reflect the variable responses of the animals to the anesthetic agent. Nevertheless, arterial pCO_2 was consistently lower than that of mixed venous blood. In only one pair of values out of a total of 75 pairs was arterial pCO2 greater than mixed venous pCO_2. In this

instance, the values were not significantly different (Figure 14).

The patterns for arterial and mixed venous pO_2 tended to mirror each other in acidotic and also in alkalotic states. Mixed venous pO_2 was consistently lower than arterial pO_2. During acidotic states, pO_2 values rose (Figure 7). During alkalotic states, however, pO_2 values decreased (Figure 8). The rise in pO_2 during infusion of NH_4Cl may reflect the effects of compensation through hyperventilation. During hyperventilation carbon dioxide content of the blood is reduced and oxygen concentration in the alveoli is increased. Therefore, diffusion of oxygen into the blood from the alveoli is enhanced. Hence, arterial pO_2 will increase. Even though ventilation rate was not measured, these animals hyperventilated since the pCO_2 of both arterial and mixed venous blood decreased during infusion of NH_4Cl (Slonim, 1976).

The following explanations may account for the decrement in pO_2 observed during alkalotic states. It is possible that alkalosis resulted in depression of the dogs' central respiratory neurons and peripheral chemoreceptors. If such were the case, pCO_2 would increase and pO_2 would decrease because of the consequent reduction in alveolar ventilation rate. Thus, there would be a reduced amount of oxygen in the arterial blood. Metabolic requirements of body cells for oxygen

would not be sufficiently met and lactic acidosis could result. If hypercapnea and increased lactic acid production were superimposed on the existing alkalosis, one would expect to see a reduction in pH. Such was the case. In Figures 11 and 12 an isolated point is shifted to the left of the exponential pattern of pH versus HCO_3^- concentration. This point, representing a decrease in pH, occurred after the dog had reached a pH of 7.67 in arterial blood and 7.63 in mixed venous blood. This shift occurred after the animal had received over 400 ml of hypertonic $NaHCO_3$. This animal had severe hypoventilation. The arterial blood was dark in color and looked identical to that obtained from the pulmonary artery. The pO_2 was sufficiently low to cause increased lactic acid production.

Another explanation for the reduction in pO_2 during alkalosis is that respiratory compensatory mechanisms may have been operant. Were this the case, suppression of ventilation would also result in the retention of carbon dioxide in the blood and decreased oxygenation of the blood in the pulmonary circuit. Such compensatory mechanisms would reduce the magnitude of change in pH that would have occurred had these mechanisms not been operating. The changes in pH did diminish as metabolic alkalosis progressed (Figure 4). Respiratory compensation for metabolic alkalosis requires that the HCO_3^- concentration

in cerebral spinal fluid (CSF) increase. Since CSF was not analyzed, the degree to which this mechanism contributed to the changes in blood-gas composition cannot be determined.

The HCO_3^- concentrations of arterial and mixed venous blood showed very high correlations. Mixed venous blood had a consistently higher HCO_3^- concentration than arterial blood during metabolic acidosis (Figure 16). During metabolic alkalosis, however, mixed venous HCO_3^- concentrations sometimes exceeded that of arterial blood while at other times was less than that of arterial blood (Figure 17). One explanation for this is that in metabolic alkalosis the HCO_3^- concentration becomes sufficiently high that differences between arterial and mixed venous blood may become smaller than the experimental error.

An exponential relationship between pH and HCO_3^- concentrations during acidosis and alkalosis is shown in Figures 11 and 12. The patterns for arterial and mixed venous blood appear to be identical. The relationship seems to become asymptotic to the pH isopleth of 7.7. It is possible that depression of the respiratory neurons or respiratory compensation or both prevented larger increases in pH.

Another contributing factor may have been the effect that alkaline states have on the binding of oxygen to hemoglobin. During alkalotic states, oxygen binds more tightly to hemoglobin. Thus, only at low levels of pO_2 can oxygen be released from hemoglobin. At low levels of pO_2, however, metabolic requirements for oxygen may be insufficiently met. Anaerobic metabolism and increased

production of lactic acid may result. Thus, the accumulation of lactic acid may contribute to preventing pH from rising beyond a level of 7.7.

In anesthetized animals that have not received artificial or controlled ventilation, pH of 7.7 may be the highest pH attainable.

Sutton, et al. (1967) compared pH, pCO_2, O_2 saturation and HCO_3^- concentrations of central venous (cv) and arterial blood. Samet, et al. (1969) compared pH, pCO_2 and pO_2 of mixed venous blood (mv) to arterial blood. In both of these studies, high correlations were noted in the identity relationships between arterial and venous blood-gas composition.

When differences (arterial minus venous) or percent change in venous blood-gas values were viewed as a function of their corresponding venous values [e.g., $(a - mv)pCO_2$ plotted as a function of venous pCO_2] predictable relationships could not be found. Based on these results, both groups concluded that mixed venous blood cannot be substituted for arterial blood in assessing acid-base status. The reason for the findings of these authors may be explained as follows.

The carbon dioxide transported in venous blood (mMoles/min) is equal to the amount of carbon dioxide transported in arterial blood (mMoles/min) plus the amount of carbon dioxide added by the tissues due to metabolism. This relationship can be shown in the following equation:

$$\dot{Q}[CO_2]_v = \dot{Q}[CO_2]_a + \dot{V}CO_2 \quad (1)$$

where

$\dot{Q}$ = flow (cardiac output)

$\dot{V}CO_2$ = CO_2 production by the tissues

$[CO_2]_a$ = concentration of CO_2 in arterial blood

$[CO_2]_v$ = concentration of CO_2 in central venous or mixed venous blood

From equation (1) the following derivation can be made:

$$(CO_2)_v - (CO_2)_a = \frac{\dot{V}CO_2}{\dot{Q}} \quad (2)$$

Under resting conditions, CO_2 production ($\dot{V}CO_2$) is reasonably constant. If cardiac output ($\dot{Q}$) is decreased, the difference between mixed venous and arterial CO_2 concentrations will increase. Conversely, if cardiac output increases, then the difference between arterial and venous CO_2 content will decrease.

Samet, et al. (1969) studied patients with a variety of cardiac problems. The subjects studied by Sutton, et al. (1967) were seriously ill. It seems likely that all their patients were bed-fast. Therefore, CO_2 production would be reasonably constant in their patients. The degree to which blood flow (cardiac output) varied among their populations is not reported. It is likely, however, that there were patients with high, moderate and low values of cardiac output. In both studies, the

subjects were treated as a single population. As a result, the effect of blood flow on the differences between arterial and mixed venous blood was an unidentified variable which could account for much of the scatter they observed.

Had they grouped their subjects according to the degree of compromised blood flow, the relationships found between arterial and mixed venous blood-gas values may have been much different. A similar argument can be applied to analysis of pH and pO_2 when differences between arterial and mixed venous blood-gases are viewed as a function of metabolic rates and blood flow.

CHAPTER V

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary and Conclusions

Arterial blood has historically been analyzed to determine acid-base status. Evidence is accumulating, however, indicating that arterial blood does not provide all the information needed to accurately assess acid-base status, especially at the tissue level.

In this study, a model was developed which indicated that mixed venous blood rather than arterial blood might more accurately reflect the acid-base status of systemic

tissues.

The purpose of this study was two-fold:

1. To determine if a predictable pattern could be described for the way mixed venous blood-gas composition changes during states of metabolic acidosis and alkalosis.

2. To determine the manner in which mixed venous blood-gas composition differed from arterial blood-gas composition during states of metabolic acidosis and alkalosis.

To achieve states of metabolic acidosis, five dogs were infused with 0.3M NH_4Cl. Metabolic alkalosis was induced by infusion of $NaHCO_3$ in four dogs. As metabolic acid and alkaline states developed, simultaneously drawn samples of arterial and mixed venous blood were analyzed to determine blood-gas composition.

The results of these experiments showed that mixed venous blood-gas composition mirrored the pattern of arterial blood.

The pH of mixed venous blood was consistently lower than arterial pH. Arterial pCO_2 was consistently lower than that of mixed venous blood. Mixed venous pO_2 was consistently lower than arterial pO_2. The HCO_3^- concentration of mixed venous blood was consistently higher than the HCO_3^- concentration of arterial blood during metabolic acidosis. During metabolic alkalosis the HCO_3^- concentrations of mixed venous blood were sometimes higher

and sometimes lower than those of arterial blood.

Recommendations for Further Study

1. In the last dog in which alkalosis was induced, pH decreased after reaching a pH level of 7.67 in arterial blood and 7.63 in mixed venous blood. Only one set of blood-gas values was obtained during the phenomenon. In further studies, it would be useful to determine if this phenomena would occur in all animals exposed to the same experimental conditions. Should decrements in pH occur after alkalosis is developed, would the pattern and pathway of decreasing pH be consistent and predictable?

2. During these experiments, ventilatory rates and cardiac outputs were not measured or controlled. Both of these factors have a marked effect on blood-gas parameters. It is recommended that this study be replicated controlling these factors.

3. This study attempted to describe the pattern of change of mixed venous blood-gases relative to arterial blood-gases during metabolic acid-base disturbances. It would be useful to describe the changes seen in arterial and mixed venous blood during states of respiratory acid-base disturbances. Planning for this phase is already in progress. With this additional information, the issue of whether mixed venous blood (rather than arterial blood) is a better indicator of tissue status can be addressed more completely.

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APPENDICES

APPENDIX A

Definition of Terms

Definition of Terms

1. pH: The pH of a solution is defined as the negative logarithm of the hydrogen ion (H+) activity in the solution:

   pH = =log (H+) or log (1/H+) (Keyes, 1976).

2. pCO_2: The partial pressure of carbon dioxide (pCO_2) is a measure of the chemical activity of CO_2 that is physically dissolved in the blood. (Keyes, 1974).

3. pO_2: The partial pressure of oxygen (pO_2) is a measure of the chemical activity of O_2 that is physically dissolved in the blood. (Keyes, 1974).

4. (HCO_3^-): The bicarbonate concentration in arterial blood is the third parameter needed for the definitive assessment of acid-base status. The units of concentration are milliequivalents per litre.

5. Fixed acids or nonvolatile acids are acids that must be excreted from the body in water. (Keyes, 1974).

6. Acidosis is a disturbance in acid-base status that results from an increase in acids or loss of bases. (Keyes, 1976; Slonim, 1976).

7. Alkalosis is a disturbance in acid-base status that results from an increase in bases or loss of acids. (Keyes, 1976; Slonim, 1976).

8. Metabolic acidosis is an acid-base disturbance that results when production of fixed acids exceeds excretion of fixed acids. This disturbance may also occur when base (HCO_3^-) is lost from the body. (Keyes, 1976; Slonim, 1976).

9. Metabolic alkalosis is an acid-base disturbance that results when loss of fixed acids exceeds production of fixed acids. This disturbance may also occur when there is an increase in base (HCO_3^-) in body fluids. (Keyes, 1976; Slonim, 1976).

10. Buffers combine either with H+ or yield H+ in response to appropriate changes in body fluid. Therefore, they reduce the magnitude of change in pH that would have occurred had buffers not been present. The major buffer system for buffering fixed acids is the carbonic acid - bicarbonate system. (H_2CO_3 - HCO_3^-). (Keyes, 1976).

APPENDIX B

Protocol for Calibration of Electrodes

Protocol for Calibration of Electrodes

The BMS3 Mark 2 is comprised of three units. The BGA3 component houses the electrodes. The GMA2 precision gas supply is used for the calibration of the blood-gas electrodes and for the equilibration of blood to known pCO_2 values. Pure carbon dioxide entering the GMA2 is infused at a constant rate where it is mixed with atmospheric air to produce two measurable gas concentrations. The two gas mixtures enter the BGA3 component where they are humidified.

The PHM73 pH blood-gas monitor provides a digital readout for pH, pCO_2 and pO_2. Known blood-gas parameters, as measured by the electrode are calibrated with the controls on this component.

Calibration Technique

Preparation for Calibration

The BMS3 Mark 2 system was turned on at least one hour prior to calibration. This allowed the water bath to reach and maintain a temperature of 37°C. Barometric pressure was measured with a mercury barometer. This information is necessary for calibration of the pCO_2 and pO_2 electrodes. Membranes for the pCO_2 and pO_2 electrodes were changed weekly prior to calibration.

pH Calibration

A two buffer calibration technique with precision buffers of pH 7.383 (±0.005) and 6.841 (±0.005) were used to calibrate the pH electrode.

The electrode was calibrated with the high pH buffer followed by the low pH buffer. The electrode was re-checked with the high pH buffer to ensure precision.

The two buffer calibration technique was carried out prior to sample analysis. A one buffer calibration technique (pH buffer 7.383) was used between sample analysis. If this calibration check showed that the reading was not within ±0.001 pH units, then the electrode was recalibrated using both buffers.

pCO_2 Calibration

Pure carbon dioxide was infused into the GMA2 precision mixer at a constant rate. The carbon dioxide was mixed in precise amounts with air to give two gas mixtures of high and low concentrations of carbon dioxide. The concentrations of carbon dioxide in the mixtures were measured in a mass spectrometer. They were found to have concentrations of 5.61% and 11.22% for the low and high concentrations, respectively. Tables of values were used to determine the pCO_2 from the barometric pressure and the known carbon dioxide concentrations in the gas mixtures. The pCO_2 values obtained were

verified using the following equation:

$$pCO_2 = \frac{(BP-W)\text{mmHg} \times x\%}{100}$$

where BP = barometric pressure;
W = vapour pressure of water (47mmHg);
x = the percent of carbon dioxide in the gas mixture

Once the pCO_2 values were determined, the PHM73 was calibrated using these values. A gas selector was used which allowed either high or low carbon dioxide concentrations to flow in contact with the pCO_2 membrane, and hence the electrode. Calibration was done using the low gas concentration first, followed by the high gas concentration. To ensure precision, the low gas concentration was rechecked.

Between samples, the calibration was rechecked using the low gas concentration. If this calibration check showed that the reading was not within ±0.1mmHg, then the electrode was recalibrated using both high and low concentrations.

pO_2 Calibration

The PO_2 electrode was calibrated using both high and low concentrations of oxygen. The high pO_2 was obtained by using a sample of thermostat water that had been in equilibrium with atmospheric air for at least one hour at a temperature of 37°C.

Tables of values were used to determine pO_2 measurements based on barometric pressure. The pO_2 value was verified using the following equation:

$$pO_2 = \frac{(BP-W)\text{mmHg} \times x\%}{100}$$

where BP = barometric pressure;
W = vapor pressure of water (47mmHg);
x = the oxygen concentration in the atmosphere (20.93%)

Using the gas selector in the low pCO_2 position, a reference pO_2 was obtained. Between samples the calibration for pO_2 was rechecked using the reference pO_2. If this calibration check was not within ±1mmHg, then recalibration was carried out using thermostat water.

APPENDIX C

Raw Data from Nine Experimental Animals
Showing Quantities of Acid and Base Infused
and Blood-Gas Parameters Obtained
During the Infusions

Dog #1

December 15, 1978
Weight - 16 Kg

	NH_4Cl PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
Time	a*	mv*	a	mv	a	mv	a	mv
1031	7.332	7.307	49.100	56.200	61.200	43.667	25.210	27.250
1115	7.264	7.250	50.433	52.767	66.400	47.367	22.120	22.410
1145	7.283	7.238	42.200	50.300	87.100	53.700	19.340	20.800
1225	7.243	7.183	45.600	52.900	94.933	55.567	19.080	19.260
1351	7.243	7.161	35.433	47.200	112.367	58.100	14.820	16.360
1425	7.083	7.070	46.333	50.433	90.433	59.867	13.420	14.150
1525	7.092	7.061	35.133	42.833	112.633	65.467	10.380	11.790
1600	7.046	7.024	36.400	43.067	94.233	61.333	9.670	10.890
1630	7.091	7.029	28.867	39.233	117.433	67.633	8.510	10.020

*a, arterial blood; *mv, mixed venous blood

Dog #2

January 9, 1979
Weight - 18 Kg

	Cummulative NH_4Cl Infused			PH		PCO_2mmHg		PO_2mmHg		HCO_3^-mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1155	0	0.0	0.000	7.307	7.304	28.633	29.200	77.500	59.933	13.881	14.059
1235	44	13.2	0.733	7.249	7.227	42.833	45.433	82.560	60.500	18.170	18.320
1305	104	31.2	1.733	7.193	7.182	43.233	48.400	82.200	61.033	16.121	17.596
1340	181	54.3	3.017	7.160	7.159	44.800	46.667	77.600	59.967	15.483	16.091
1410	241	72.3	4.017	7.168	7.163	38.767	44.300	77.867	59.833	13.647	15.416
1425	274	82.2	4.567	7.147	7.122	35.100	41.800	85.900	61.633	11.773	13.236
1515	382	114.6	6.367	7.098	7.079	32.200	38.133	90.033	65.700	9.648	10.936
1550	518	155.4	8.633	7.071	7.049	27.467	33.100	93.667	68.667	7.734	8.818
1620	634	190.2	10.567	7.013	6.997	26.700	32.500	95.667	70.433	6.578	7.717

Dog #3

January 16, 1979
Weight - 15.9 Kg

	Cummulative NH_4Cl Infused			PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1207	0	0.0	0.000	7.260	7.265	50.500	50.400	71.100	51.133	21.971	22.698
1248	85	25.5	1.604	7.239	7.213	42.067	48.233	95.633	57.200	17.438	18.833
1331	177	53.1	3.340	7.161	7.154	41.433	43.500	96.533	63.767	14.352	14.827
1416	268	80.4	5.057	7.073	7.040	34.767	47.433	102.667	70.233	9.834	12.435
1454	360	108.0	6.792	6.994	6.988	39.500	43.100	102.767	75.067	9.314	10.024
1534	475	142.5	8.963	6.956	6.934	33.000	38.000	120.500	78.633	7.130	7.804
1608	550	165.0	10.377	6.908	6.895	30.867	32.700	119.400	79.867	5.971	6.139
1637	630	189.0	11.887	6.881	6.863	26.100	31.133	125.567	85.600	4.745	5.430

Dog #4

January 23, 1979
Weight - 10 Kg

	Cummulative NH_4Cl Infused			PH		PCO_2mmHg		PO_2mmHg		HCO_3^-mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1300	0	0.0	0.000	7.366	7.346	47.100	51.067	80.933	51.533	26.157	27.084
1330	36	10.8	1.080	7.331	7.307	42.267	46.833	85.300	49.267	21.655	22.705
1405	80	24.0	2.400	7.242	7.221	40.300	44.867	85.800	51.600	16.822	17.844
1437	117	35.1	3.510	7.229	7.199	35.367	41.300	96.367	52.633	14.327	15.614
1514	177	53.1	5.310	7.161	7.126	31.000	38.033	100.067	52.000	10.738	12.154
1555	225	67.5	6.750	7.088	7.043	28.767	38.433	101.967	54.600	8.423	10.145
1630	285	85.5	8.550	6.971	6.936	36.633	47.700	93.533	56.600	8.193	9.842
1709	353	105.9	10.590	6.929	6.888	26.800	38.100	108.033	76.333	5.441	7.039

Dog #5

January 30, 1979
Weight - 22.3 Kg

	Cummulative NH_4Cl Infused			PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1210	0	0.0	0.000	7.394	7.396	42.400	44.800	74.234	49.100	25.115	26.659
1235	65	19.5	0.874	7.395	7.340	33.100	39.667	105.300	54.433	19.651	20.749
1310	165	49.5	2.220	7.284	7.275	34.400	36.267	91.367	65.500	15.817	16.333
1335	235	70.5	3.161	7.234	7.222	32.967	37.367	95.733	63.567	13.510	14.895
1410	330	99.0	4.440	7.226	7.203	26.800	34.600	100.633	62.933	10.782	13.202
1445	425	127.5	5.718	7.182	7.157	26.433	34.000	104.533	61.733	9.610	11.669
1525	565	169.5	7.601	7.099	7.077	26.800	34.933	103.933	67.633	8.048	9.972
1600	690	207.0	9.282	7.060	7.037	23.567	30.200	106.300	68.900	6.470	7.863
1635	810	243.0	10.897	7.028	6.999	18.067	25.867	116.333	76.433	4.607	6.170

Dog #6

February 6, 1979
Weight - 11.4 Kg

	Cummulative $NaHCO_3$ Infused			PH		PCO_2mmHg		PO_2mmHg		HCO_3^-mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1225	0	0	0.000	7.328	7.317	45.367	48.333	88.700	45.100	23.084	23.978
1251	25	25	2.193	7.430	7.406	49.267	53.033	85.867	45.000	31.705	32.293
1335	60	60	5.263	7.514	7.485	44.033	48.633	85.900	42.067	34.383	35.522
1410	85	85	7.456	7.475	7.464	51.200	53.633	75.700	45.467	36.546	37.325
1445	125	125	10.965	7.564	7.548	49.667	51.233	69.833	39.500	43.514	43.263
1520	170	170	14.912	7.608	7.583	56.133	59.333	61.467	34.267	54.423	54.308
1600	227	227	19.912	7.644	7.597	50.300	59.467	60.300	34.000	52.983	56.214
1645	295	295	25.877	7.653	7.614	56.400	64.400	51.633	30.600	60.652	63.307

Dog #7

February 20, 1979
Weight - 15.9 Kg

	Cummulative $NaHCO_3$ Infused			PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1200	0	0	0.000	7.403	7.395	36.833	39.367	74.700	50.600	22.274	23.372
1235	52	52	3.270	7.515	7.510	37.833	38.633	71.633	44.900	29.610	29.890
1315	125	125	7.862	7.508	7.497	45.467	46.200	66.567	41.300	35.016	34.690
1400	210	210	13.208	7.558	7.540	48.633	49.233	64.567	41.633	42.024	40.815
1455	335	335	21.069	7.580	7.550	52.667	56.600	65.400	41.000	47.874	48.016
1545	450	450	28.302	7.616	7.599	54.600	59.767	55.533	34.267	53.921	56.758
1625	560	560	35.220	7.638	7.608	56.733	59.500	51.967	31.067	58.939	57.688
1700	665	665	41.824	7.627	7.617	65.433	67.933	43.967	30.433	66.277	67.243

Dog #8

February 27, 1979
Weight - 11.8 Kg

	Cummulative $NaHCO_3$ Infused			PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1155	0	0	0.000	7.325	7.310	55.900	54.633	71.833	47.533	28.247	26.670
1240	55	55	4.661	7.464	7.450	50.067	53.333	64.267	42.200	34.843	35.939
1320	105	105	8.898	7.551	7.535	50.400	51.633	67.567	40.000	42.854	42.315
1350	156	156	13.220	7.540	7.533	55.600	54.567	57.200	36.267	46.094	44.514
1425	215	215	18.220	7.585	7.564	59.400	62.867	62.700	35.000	54.620	55.079
1500	280	280	23.729	7.609	7.584	61.567	65.700	69.400	36.967	59.829	60.274
1540	370	370	31.356	7.632	7.606	65.167	71.267	50.100	32.767	66.772	68.779
1615	490	490	41.525	7.668	7.629	71.433	77.567	45.233	25.933	79.518	78.930

Dog #9

March 6, 1979
Weight - 13.6 Kg

	Cummulative $NaHCO_3$ Infused			PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
Time	ml	mEq	mEq/Kg	a	mv	a	mv	a	mv	a	mv
1140	0	0	0.000	7.398	7.382	39.300	41.400	66.300	45.300	23.494	23.854
1215	58	58	4.265	7.516	7.495	41.433	43.100	66.600	42.367	32.502	32.214
1250	115	115	8.456	7.571	7.544	44.100	47.500	60.500	39.567	39.265	39.743
1330	175	175	12.868	7.606	7.586	41.533	44.834	54.367	35.833	40.083	41.321
1410	235	235	17.279	7.602	7.583	48.833	52.033	48.400	32.633	46.696	47.626
1445	310	310	22.794	7.592	7.559	53.200	58.700	42.267	32.900	49.714	50.840
1525	400	400	29.412	7.612	7.589	59.900	64.600	43.200	29.933	58.613	59.951
1605	510	510	37.500	7.460	7.449	94.467	98.067	18.267	8.567	65.140	65.931

APPENDIX D

Raw Data of Correlation Coefficients, Slopes and Intercepts: Blood-Gas Parameters versus Amount of Acid or Base Infused per Kilogram Body Weight

Dogs Infused with NH_4Cl

		PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
		a*	mv*	a	mv	a	mv	a	mv
January 9	r	-.966	-.968	-.6174	-.425	.878	.922	-.923	-.899
	Slope	-.024	-.025	-1.2345	-.830	1.713	1.060	-1.017	-.944
	Intercept	7.265	7.252	40.9542	43.598	77.252	58.403	17.029	17.720
January 16	r	-.988	-.990	-.936	-.945	.946	.986	-.965	-.980
	Slope	-.034	-.035	-1.669	-1.595	3.925	2.764	-1.371	-1.424
	Intercept	7.265	7.251	47.411	51.387	80.676	53.569	19.583	20.809
January 23	r	-.933	-.995	-.846	-.591	.860	.784	-.952	-.952
	Slope	-.043	-.045	-1.592	-.803	2.176	1.829	-1.854	-1.774
	Intercept	7.369	7.349	43.646	47.133	83.583	46.804	22.839	23.793
January 30	r	-.979	-.989	-.912	-.944	.768	.882	-.942	-.940
	Slope	-.035	-.036	-1.858	-1.224	2.419	1.868	-1.655	-1.610
	Intercept	7.381	7.366	38.794	41.058	87.919	54.168	20.738	22.095

*a, arterial blood; *mv, mixed venous blood

Dogs Infused with $NaHCO_3$

		PH		PCO_2 mmHg		PO_2 mmHg		HCO_3^- mEq/l	
		a*	mv*	a	mv	a	mv	a	mv
February 6	r	.926	.915	.755	.912	.976	.947	.968	.982
	Slope	.012	.010	.373	.588	-1.514	-.621	1.402	1.484
	Intercept	7.402	7.388	46.253	48.359	88.829	46.248	26.966	27.190
February 20	r	.899	.913	.973	.976	-.972	-.956	.991	.991
	Slope	.005	.004	.616	.670	-.662	-.437	.977	.986
	Intercept	7.469	7.459	38.155	39.523	74.281	47.637	26.087	26.232
February 27	r	.878	.862	.941	.942	-.808	-.948	.996	.993
	Slope	.007	.006	.496	.633	.547	-.437	1.210	1.239
	Intercept	7.417	7.418	49.749	50.411	70.714	44.830	30.163	29.631
March 5	r	.803	.775	.948	.960	.963	-.968	.982	.986
	Slope	.007	.006	.709	.798	-.955	-.529	1.092	1.141
	Intercept	7.456	7.458	36.808	39.443	67.518	44.123	26.630	26.683

*a, arterial blood; *mv, mixed venous blood

APPENDIX E

Raw Data for Correlation Coefficients, Slopes and Intercepts: Mixed Venous Blood versus Arterial Blood

		pH	pCO_2 mmHg	PO_2 mmHg	HCO_3^- mEq/l
December 15	r	.974	.941	.917	.994
	Slope	.957	.715	.365	.990
	Intercept	.266	18.963	23.049	1.319
January 9	r	.996	.954	.960	.990
	Slope	1.040	.929	.565	.944
	Intercept	-.304	6.934	15.170	1.719
January 16	r	.997	.866	.946	.992
	Slope	1.019	.814	.640	1.016
	Intercept	-.152	11.474	3.472	.751
January 23	r	.999	.926	.693	1.000
	Slope	1.048	.665	.640	.960
	Intercept	-.372	19.339	-4.580	1.894
January 30	r	.993	.963	.736	.997
	Slope	1.007	.728	.495	.970
	Intercept	-.072	13.890	13.929	1.928
February 6	r	.996	.890	.929	.996
	Slope	.915	1.156	.393	1.039
	Intercept	.612	-3.410	11.037	-.525
February 20	r	.994	.990	.966	.996
	Slope	.930	1.074	.649	1.005
	Intercept	.514	-1.304	-.703	.104
February 27	r	.997	.975	.866	.998
	Slope	.942	1.269	.591	1.025
	Intercept	.418	-13.010	.985	-1.340
March 5	r	.998	.988	.998	1.000
	Slope	.948	.709	1.025	1.024
	Intercept	.367	-2.418	2.123	-.333

AN ABSTRACT OF THE THESIS OF

MARLENE BIEBER

For the MASTER OF NURSING

Date Receiving this Degree:

Title: The Use of Mixed Venous Blood in Determining Acid-Base Status of Systemic Tissues When Metabolic Input is Manipulated

Approved: [redacted]
Jack L. Reyes, PhD. Thesis Advisor

Arterial blood has historically been analyzed to determine acid-base status. Evidence is accumulating, however, indicating that arterial blood does not provide all the information needed to accurately assess acid-base status, especially at the tissue level.

In this study, a model was developed which indicated that mixed venous blood rather than arterial blood might more accurately reflect the acid-base status of systemic tissues.

The purpose of this study was two-fold:

1. To determine if a predictable pattern could be described for the way mixed venous blood-gas composition changes during states of metabolic alkalosis and acidosis.

2. To determine the manner in which mixed venous

blood-gas composition differed from arterial blood-gas composition during states of metabolic acidosis and alkalosis.

To achieve states of metabolic acidosis, five dogs were infused with 0.3mNH_4Cl. Metabolic alkalosis was induced by infusion of $NaHCO_3$ in four dogs. As metabolic acid and alkaline states developed, simultaneously drawn samples of arterial and mixed venous blood were analyzed to determine blood-gas composition.

In identity relationships of mixed venous versus arterial blood-gas composition, correlations were high for all blood-gas parameters.

When mixed venous and arterial blood-gas compositions were viewed as a function of the amount of acid or base infused per kilogram body weight, the pattern for venous blood-gas composition mirrored the pattern of arterial blood-gas composition.

The pH of mixed venous blood was consistently lower than arterial pH. Arterial pCO_2 was consistently lower than that of mixed venous blood. Mixed venous pO_2 was consistently lower than arterial pO_2. The HCO_3^- concentration of mixed venous blood was consistently higher than the HCO_3^- concentration of arterial blood during metabolic acidosis. During metabolic alkalosis the HCO_3^- concentrations of mixed venous blood were sometimes higher and sometimes lower than those of arterial blood.

Recommendations were made for further study.