THE USE OF MIXED VENOUS BLOOD FOR ASSESSMENT OF ACID-BASE STATUS IN STATES OF DECREASED CARDIAC OUTPUT

by

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TABLE OF CONTENTS

Chapter		Page
I.	INTRODUCTION AND THEORETICAL FRAMEWORK	1
	Nursing Implications	3
	Review of the Literature	6
	The Difference Between in vitro and in vivo Blood Buffer Curves	7
	Theoretical and Experimental Considerations Regarding the Differences Between Mixed Venous and Arterial Blood-Gas Compositions	10
	Predictability of Mixed Venous Blood-Gas Composition Over a Wide Range of Altered Acid-Base States . . .	21
	The Effects of Decreased Cardiac Output on Arterial and Mixed Venous Blood-Gas Compositions	28
	Clinical Uses of Central and Mixed Venous Blood-Gas Analysis for Assessment of Patients	32
	Summary of the Review of the Literature	36
	Statement of the Problem	36
II.	METHODS	38
	Statement of the Variables	38
	Design	38
	Procedure	38
III.	RESULTS	42
	General Description	42
	Blood-Gas Parameters	43
	Arterio-Venous Differences	44
	pH/ $\{HCO_3^-\}$ Relationship	45

IV. DISCUSSION 64

How Does Arterial Blood-Gas Composition Compare To Mixed Venous Blood-Gas Composition in States of Decreasing Cardiac Output? 64

Does Mixed Venous Blood-Gas Composition Follow a Predictable Pattern in States of Decreased Cardiac Output? 67

Possible Complications Resulting from Repeated Sampling of Mixed Venous Blood 69

Implications for Nursing Practice 72

Limitations of the Study 73

V. SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary and Conclusions 75

Recommendations for further study 76

REFERENCES 77

APPENDIX. 80

A. Raw Data from 10 Experimental Animals Showing Blood-Gas Parameters Obtained During Induced States of Decreased Cardiac Output 81

LIST OF TABLES

TABLE		PAGE
I	Control Values for Heart Rate, Respiratory Rate, Hematocrit, Protein, Cardiac Output and Temperatures for Dogs 1-10	47
II	Final Values for Heart Rate, Respiratory Rate, Hematocrit, Protein Concentration, Cardiac Output, Temperature and Blood Volume Removed for Dogs 1-10	48
III	Control Values for Blood-Gas Parameters (pH, pCO_2, $\{HCO_3^-\}$ and pO_2) for Dogs 2-10 for Arterial and Mixed Venous Blood	49
IV	Final Values for Blood-Gas Parameters (pH, pCO_2, $\{HCO_3^-\}$ and pO_2) for Dogs 2-10 for Arterial and Mixed Venous Blood	50
V	Arterial-Venous Differences for Dogs 2-10 at Each Level of Cardiac Output. Cardiac Output at Time of Sample Reported as % of Control as Recorded in Last Column	51
VI	Results of Paired t Test Between Control and Final Values for Arterial-Venous Differences for Dogs 2-10	53
VII	Means and Standard Deviations for the A-V Differences for Each Blood-Gas Parameter According to Four Divisions of Percent Control of Cardiac Output	54

LIST OF FIGURES

FIGURE		PAGE
1	Model: Arterial versus Venous Blood	2
2	Effect of Added Carbon Dioxide on the Bicarbonate Concentration of Blood, Interstitial Fluid, and Intracellular Fluid	9
3	Normal In Vivo CO_2 Titration Curve of True Oxygenated Mixed Venous Blood and Two In Vitro Curves Obtained on Mixed Venous Blood	12
4	The Effect of Doubling the A-V Difference for Oxygen Saturation Between Arterial and Mixed Venous Blood with Constant Arterial Blood-Gas Tensions	15
5	The Oxyhemoglobin Dissociation Curve	31
6	Arterial-Mixed Venous pH Differences as a Function of Percent of Control Cardiac Output	55
7	Arterial-Mixed Venous pCO_2 Differences as a Function of Percent of Control Cardiac Output	56
8	Arterial-Mixed Venous pO_2 Differences as a Function of Percent of Control Cardiac Output	57
9	Arterial-Mixed Venous Bicarbonate Concentration Differences as a Function of Percent of Control Cardiac Output	58
10	Bar Graph of Mean Arterial-Mixed Venous pH Differences as a Function of Percent of Control Cardiac Output	59
11	Bar Graph of Mean Arterial-Mixed Venous pCO_2 Differences as a Function of Percent of Control Cardiac Output	60
12	Bar Graph of Mean Arterial-Mixed Venous pO_2 Differences as a Function of Percent of Control Cardiac	61
13	Bar Graph of Mean Arterial-Mixed Venous Bicarbonate Concentration Differences as a Function of Percent of Control Cardiac Output	62

LIST OF FIGURES (Continued)

FIGURE		PAGE
14	The Last 3 Values of Arterial and Mixed Venous Blood-Gas Parameters for Dogs 2-10 Plotted on a ph/$\{HCO_3^-\}$ Diagram.	63
15	pH/$\{HCO_3^-\}$ Diagram Depicting Areas of Compensated Metabolic Acidosis and Combined Metabolic and Respiratory Acidosis.	68

CHAPTER I

INTRODUCTION AND THEORETICAL FRAMEWORK

Acid-base status is assessed from analysis of the gas composition of a blood sample. Arterial blood is used almost exclusively in this assessment. This analysis is also used to help assess cardiopulmonary function in critically ill patients. Either repeated arterial punctures or an indwelling arterial catheter is used to obtain blood samples. In the past ten to fifteen years, mixed venous blood has been suggested as a possible alternative to arterial blood in acid-base assessment.

The physiological model for the use of mixed venous blood in acid-base assessment is shown in Figure 1. Blood flows through the pulmonary capillaries of the lungs where gas exchange with alveoli occur. The blood then flows into the left side of the heart where it is mixed in the left ventricle. Thus, blood obtained from any systemic artery will have uniform composition and could be used for assessment purposes. It can be seen from this model that arterial blood represents the output of the respiratory system. Arterial blood-gas composition reflects the balance between ventilation and perfusion of pulmonary capillaries. Therefore, pulmonary function may be assessed in part by analysis of the blood-gas composition of arterial blood.

Mixed venous blood represents the flow weighted output of the tissues. As is apparent from the model, venous blood is derived from many different tissues and organs. Blood flow to organ systems varies and in addition will change in response to the metabolic activity of the tissue. Therefore, the blood gas composition of a sample of venous blood will depend on the sampling site. The right ventricle is the site of mixing of returning venous blood and thus the blood-gas composition

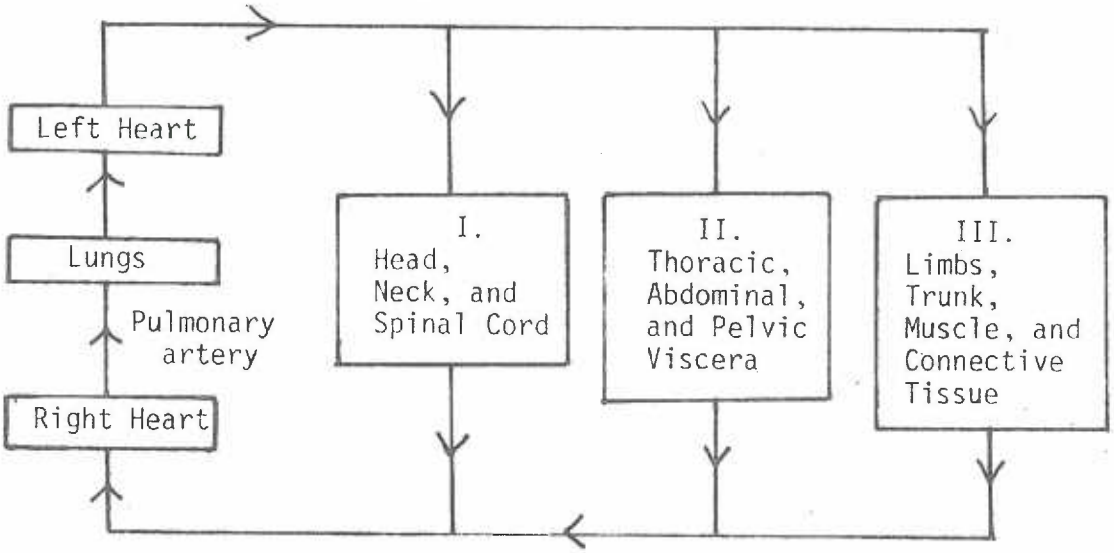


FIGURE 1

Arterial blood is the output from the lungs and represents input to the systemic tissues. Venous blood is the output from systemic tissues. The difference between arterial and venous blood is what the lungs add and remove: i.e., oxygen and carbon dioxide, respectively. Pathways I., II., and III. reflect blood flow through the parallel systemic circulation which contributes to mixed venous blood.

Model modified from Griffith, 1980.

of blood in the pulmonary artery is a flow weighted average of all systemic venous blood. Thus, mixed venous blood can be obtained from the pulmonary artery.

In systemic capillaries blood equilibrates with the interstitial fluid (ISF) that surrounds cells. Therefore, the blood-gas composition of blood draining a given tissue should be the same as the blood-gas composition of the ISF of that tissue. Venous blood from all systemic tissues flows to the right side of the heart where it is mixed in the right ventricle and pumped into the pulmonary artery. The blood-gas

composition of this mixed venous blood is a flow weighted average of all systemic venous blood. Since this mixed venous blood has been equilibrated with the ISF or internal milieu of the body it should have a gas composition that is an "average" of all ISF. Since acid-base status of the body is in fact the acid-base status of the ISF it is only reasonable to conclude that the blood-gas composition of mixed venous blood would be a better indicator of systemic acid-base status than that of arterial blood.

Prior to the use of mixed venous blood for assessment purposes it must be determined whether mixed venous blood varies in a predictable pattern over wide variations in physiological states. The altered states that need to be considered are respiratory and metabolic acid-base disturbances and reduced cardiac output. In the following review it will be established that mixed venous blood has varied predictably over wide ranges of hydrogen ion concentrations in both respiratory and metabolic acid-base changes. However, the effect of stepwise decreases in cardiac output on mixed venous blood-gas composition has not been extensively studied. The overall purpose of this study is to determine the changes in blood-gas composition of mixed venous blood as compared to that of arterial blood when cardiac output decreases.

NURSING IMPLICATIONS

The definition of nursing and the services and activities which the profession includes encompasses a wide range of personal, philosophical and theoretical concepts and beliefs. There are several basic assumptions common to nurses regardless of individual beliefs regarding nursing theory. These assumptions include the belief that human beings

are complex bio-psychosocial beings who interact with others and their environment in complex, ever changing ways. Nurses deal with these individuals in a variety of situations and during various states of wellness and illness. Nursing assessment is not complete until the triad of biological, psychological and social states of individuals are evaluated. Only then can the nurse begin to understand the person as an individual and plan effective, comprehensive, and safe nursing intervention. Nurses may need to assign immediate priority to one aspect of the triad over the other two at certain times in the nurse-patient relationship depending upon the setting, the individuals involved, and the patient's position on the health-illness continuum.

In acute care settings, as well as at times of crises, the nurse might be immediately involved in urgent, critical, physiological assessment of a patient's status. This is not at the exclusion of the other important factors but rather an immediacy because of the critical nature of the patient's situation which may be life threatening.

Nurses are the only professional group who maintain 24 hour surveillance for patients in hospital settings. Therefore they provide a unique dimension of continuity regarding ongoing assessment of the patient's status. Acutely ill patients are especially dependent on these critical nursing assessments. For many of these patients this assessment includes monitoring of acid-base status through observation of color, perfusion, mental status and vital signs, obtaining arterial blood for blood-gas analysis, and the interpretation of these results. In order to function competently in these acute care settings it is imperative that the nurse has the ability to assess patient status, can safely and correctly perform the procedure, understands acid-base physiology, and

can correctly interpret the results in order to plan intervention accordingly.

The results of this research may demonstrate a different approach to this assessment of acid-base status. An animal model is used as an initial step in testing the hypothesis for obvious methodological and ethical reasons. The primary outcome from knowledge generated in an animal model and further tested in clinical settings will significantly impact the understanding of acid-base physiology and affect the manner in which nurses obtain blood-gas samples and interpret the results.

If it can be shown that mixed venous blood provides significant information regarding tissue acid-base status in states of reduced cardiac output, then the nurse will need to consider these data in her assessment. If pulmonary function is to be assessed, arterial blood-gas analysis will provide the information needed. If a patient is being ventilated and decreased cardiac output is suspected, a mixed venous sample may give added information. At certain times, the blood-gas components of both arterial and mixed venous blood may be necessary. The nurse will need to consider all aspects of the patient's physiological status to coordinate nursing interventions appropriately. Close monitoring of physiological data in collaboration with physicians and allied health professionals regarding the ongoing assessment will optimize patient management.

Another implication for nursing centers around the procedure for obtaining blood samples for blood-gas analysis. Arterial sampling involves an arterial puncture most commonly obtained from the brachial or radial artery. This procedure is not only painful to the patient but also presents the possibility of complications such as hematoma, infec-

tion and hemorrhage. If the patient already has a flow directed catheter (Swan-Ganz) in the pulmonary artery for assessment of fluid volume and cardiac function, sampling from this site may provide the best information regarding tissue acid-base status without the additional discomfort due to an arterial puncture.

Finally, nurses must continually increase their knowledge base and improve their clinical expertise in order to keep pace with ever-changing and advancing technology. New knowledge and understanding in the area of physiology will help increase the nurse's ability to accurately assess the patient's status and plan nursing interventions accordingly. Collaborative and interdisciplinary research is imperative in order to provide new knowledge and understanding upon which to base quality and safe patient care.

REVIEW OF THE LITERATURE

The review of the literature is organized under the following headings:

1) The difference between in vitro and in vivo buffer curves.
2) Theoretical and experimental considerations regarding differences in mixed venous and arterial blood-gas composition.
3) Predictability of mixed venous blood-gas composition over a wide range of altered acid-base states.
4) The effects of reduced cardiac output on arterial and mixed venous blood-gas compositions.
5) Clinical uses of central and mixed venous blood-gas analysis for assessment of patients.

Difference Between In Vitro and In Vivo Blood Buffer Curves.

For the following discussion, buffer capacity will be defined as the slope of the carbon dioxide (CO_2) titration curve (Israel, 1981). Buffer capacity varies with hemoglobin (Hb) concentration. When it is necessary to eliminate this variable for comparison purposes, the buffer capacity will be factored by the Hb concentration and referred to as buffer value.

In addition, for the following discussion the relationship between carbon dioxide, bicarbonate concentration and hydrogen ion concentration can be expressed by equation 1:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons \begin{matrix} B^- \\ + \\ H^+ \\ \Updownarrow \\ HB \end{matrix} + HCO_3^- \qquad (1)$$

To obtain in vitro buffer curves, blood is removed from the subject and titrated with varying concentrations of carbon dioxide. After equilibration, the sample is analyzed for pH and pCO_2. The $\{HCO_3^-\}$ can be determined from the Henderson-Hasselbalch equation.

The buffers available in vitro are hemoglobin and plasma proteins. Hemoglobin is the major buffer of the blood. From equation 1 it can be seen that protein and hemoglobin buffers (B^-) can bind hydrogen ions shifting the equation to the right and thereby increasing the bicarbonate concentration. The reverse reaction also occurs. The greater the amount of hemoglobin and plasma proteins available the greater the change in $\{HCO_3^-\}$ and the smaller the change in pH for a given change in pCO_2.

With in vivo titration, the change in pCO_2 is made prior to removal of the blood sample. Thus added carbon dioxide diffuses quickly from the blood into the ISF and also into the cells. Any change in plasma $\{HCO_3^-\}$ also results in changes in ISF $\{HCO_3^-\}$ (Figure 2, arrow 1). Interstitial fluid has a very low concentration of protein and no hemoglobin so it is a less effective buffer for carbon dioxide than blood. The ISF with its low buffer capacity has a dilutional effect on the total buffer capacity. This dilution tends to decrease the slope of the in vivo buffer curve in comparison to the in vitro buffer curve (see Figure 3).

In addition, body cells are affected by changes in the carbon dioxide concentration of the blood. Carbon dioxide diffuses across ISF into the cells. Cellular buffering of hydrogen ions causes increased production of bicarbonate which diffuses out of the cells into the ISF and plasma (Figure 2, arrow 2) (Davenport, 1974).

Prys-Roberts, Kelman, and Nunn (1966) demonstrated the difference between in vitro and in vivo titration curves in human subjects. They studied nine anesthetized patients while undergoing minor elective surgery. All had been previously examined to rule out any existing cause for acid-base disturbance.

Five patients had hypercapnea followed by hyperventilation experiments, three were studied during hyperventilation only and one was studied during hypercapnea only. An indwelling arterial catheter was inserted into a radial artery. Arterial blood was sampled at 10 minute intervals throughout the study and 5 minutes after each change in pCO_2. The pH, pCO_2, and pO_2 were measured on each blood sample. The naso-

pharyngeal temperature was monitored. Hemoglobin and lactic acid concentrations were also measured on each sample. The slope of the in vivo CO_2 titration curves was determined by changing arterial pCO_2 as described above. In vitro slopes were determined by titrating a sample of the patient's arterial blood in a tonometer.

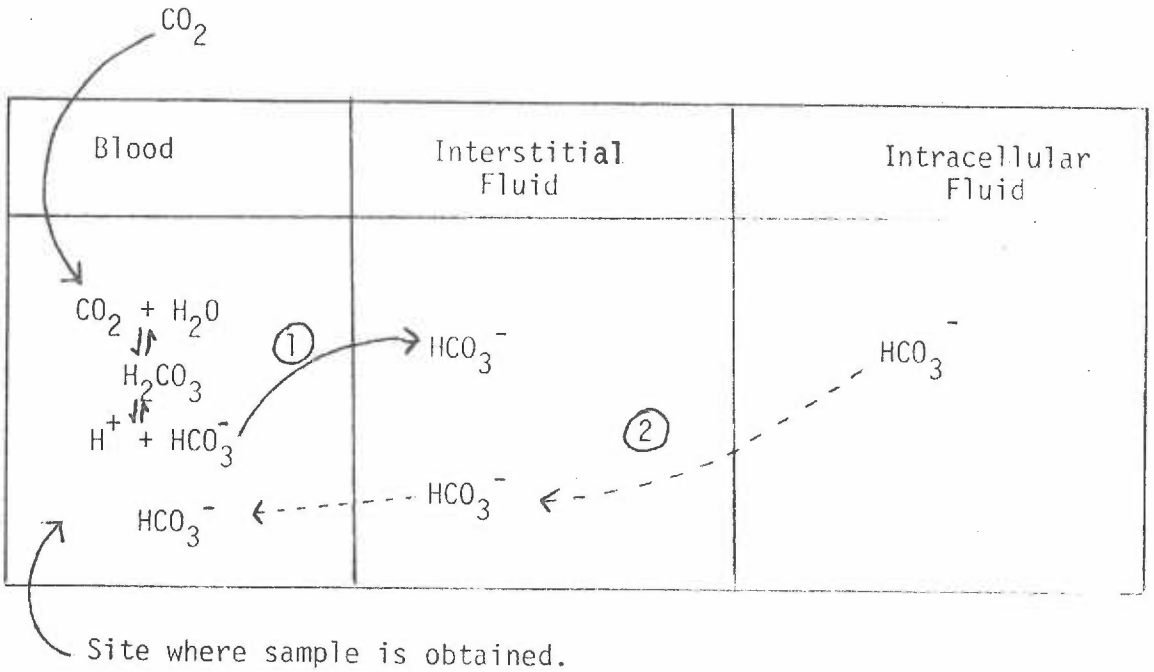


FIGURE 2

Effect of Added Carbon Dioxide on the Bicarbonate Concentration of Blood, Interstitial Fluid, and Intracellular Fluid.

The pH range in the experiments extended from 7.120 to 7.666. The pCO_2 and pO_2 varied over a range of 15.7-84 mmHg and 89-135 mmHg respectively. When pH (abscissa) was plotted against $\{HCO_3^-\}$ (ordinate), the mean in vitro slope for whole blood was 33 mEq./L·pH. The mean in vivo slope was 19 mEq./L·pH. This difference between the in vivo and in vitro slopes was statistically significant. The in vivo and in vitro slopes were related in a consistent manner with the mean ratio being

0.58:1 (p. 504).

In effect, in vivo titration has two opposing influences on the slope of the buffer curve. One tends to decrease the $\{HCO_3^-\}$ because of the dilution effect of ISF, the other tends to raise $\{HCO_3^-\}$ due to cellular buffering with generation of new HCO_3^- . The sum of these two processes alters the in vivo slope such that it is less than the in vitro slope, hence, the dilution effect predominates.

In summary, the in vivo buffer curve is affected by three factors. First, the larger the ratio of ISF volume to plasma volume, the flatter the slope of the buffer curve. Second, cellular buffering increases the slope. Finally there is a change in buffering over time. As time increases there may be increased exchange of hydrogen for sodium and potassium ions across the cell membrane causing decreased concentrations of hydrogen ions in the plasma. Decreasing hydrogen ion shifts equation 1 to the right increasing bicarbonate concentration (Davenport, p. 59).

Theoretical and Experimental Considerations Regarding the Differences Between Mixed Venous and Arterial Blood-gas Compositions.

In 1967, Roos and Thomas published a discussion on the theory of the in vitro and in vivo carbon dioxide buffer curves. They compared the slope of the arterial curve to that of mixed venous blood. They concluded that the slope of the arterial CO_2 buffer curve was closer to that of the in vitro curve while the slope of the CO_2 buffer curve of mixed venous blood was the true slope of the in vivo titration curve.

From an anatomical viewpoint the volume of arterial blood flowing through the pulmonary capillaries is large compared to the pulmonary ISF volume. This minimizes the dilutional effect of ISF on the buffer

capacity and thus removal of CO_2 in pulmonary capillaries is equilibrated to an in vitro titration. Mixed venous blood, however, originates from systemic capillaries and thus equilibrates with a larger volume of ISF, namely all of the ISF within the body except pulmonary. Therefore, the CO_2 buffer curve of mixed venous blood is the true in vivo titration curve.

Roos and Thomas used a mathematical model to predict differences between the in vitro and in vivo titration curves of a sample of mixed venous blood. The two different curves can be seen in Figure 3. Blood for this model was assumed to be 100% saturated with oxygen. This assumption was made to avoid the complications of the Bohr and Haldane effects on the titration curve.

It can be seen from Figure 3 that the slope of the in vivo line is less steep than the in vitro line. The dissimilarity in the slopes results from the differences in concentrations of hemoglobin and protein buffers between blood alone and blood in equilibrium with a large volume of ISF. In their calculations, Roos and Thomas did not consider the effect of cellular buffering. The in vivo slope is then quantitatively the combined buffer capacity of the two fluid compartments, blood and ISF.

Michel (1968) in a discussion of the theory of the buffering behavior of blood during hypoxaemia and respiratory exchange lends support to the proposal that the true in vivo CO_2 titration curve is that of mixed venous blood. Comparisons of how the Haldane phenomenon alter the arterial and mixed venous blood were presented as well as explanations and rationale for the differences noted.

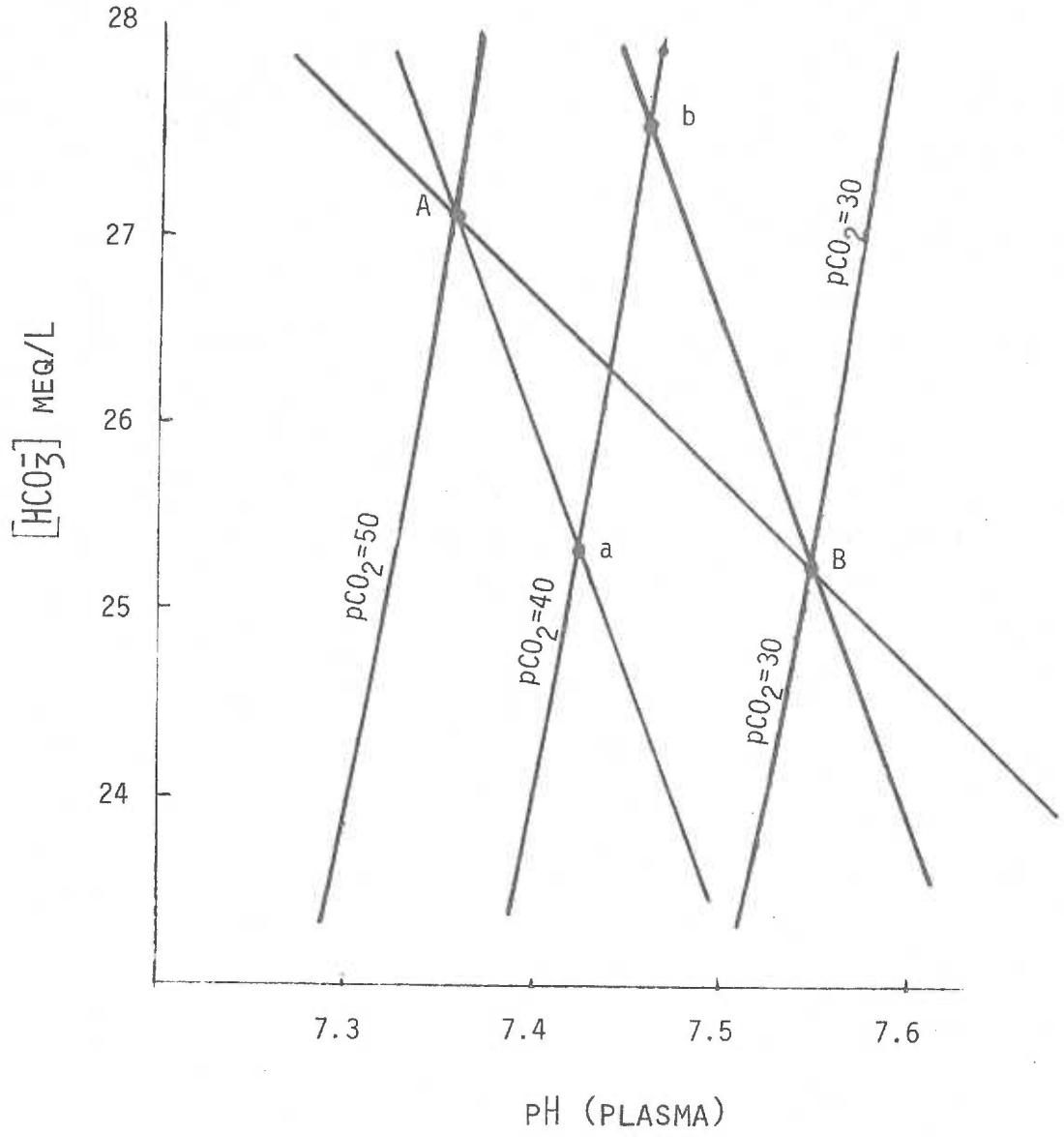


FIGURE 3

"Normal in vivo CO_2 titration curve of true oxygenated mixed venous plasma (AB) and two in vitro curves (Aa and Bb), obtained on mixed venous blood withdrawn at pCO_2 = 50 (A), and 30 (B), respectively." (Note: These results are based on theoretical analysis of a mathematical model. The mood of the verb is intended to be subjunctive).

Roos and Thomas, 1967, p. 1050.

When oxygenated blood is deoxygenated in vitro, at constant pCO_2, the pH rises slightly due to the Haldane effect. This is accompanied by a slight rise in $\{HCO_3^-\}$. The reduced hemoglobin is a weaker acid than oxyhemoglobin and hence the $\{H^+\}$ also decreases. As a result more CO_2 is converted to HCO_3^- (equation 1) and the $\{HCO_3^-\}$ increases. When deoxygenation occurs in vivo the HCO_3^- ions diffuse into the ISF and thus the increase in $\{HCO_3^-\}$ is not as great as in vitro.*

Michel's arguments support the idea that the blood-gas composition of arterial blood represents in vitro equilibration and that of mixed venous blood represents in vivo equilibration. He cited evidence that strongly suggests that HCO_3^- ions do not exchange with extravascular components in the pulmonary circulation. This lack of exchange decreases the dilution effects of ISF and makes the blood buffering behave as though the process occurred in vitro. In mixed venous blood the HCO_3^- ions equilibrate with ISF, thus, the slope of the CO_2 titration curve for mixed venous blood is the in vivo buffer capacity. He concluded that mixed venous blood-gas composition is determined by in vivo buffering conditions and that arterial blood-gas composition is related to mixed venous blood-gas composition via in vitro titration conditions during respiratory exchange in the lungs.

Michel considered instances in which arterial pCO_2 and pO_2 might remain constant even though the pCO_2 and pO_2 of mixed venous blood change. This could be predicted to occur if there were changes in blood flow and/or metabolic rate. In the discussion, the arterial pCO_2 and pO_2 were assumed to remain constant and changes in the arterial-venous difference

* It should be remembered that cellular buffering also occurs and affects $\{HCO_3^-\}$.

(A-V difference) were due to changes in blood flow or metabolism (p. 287).

If the A-V difference for saturation of hemoglobin with oxygen is doubled the effect is similar to doubling the desaturation of the venous blood. The magnitude of the Haldane effect is dependent on the change in oxygen saturation (ΔSO_2). Figure 4 shows the changes in arterial and mixed venous blood as the A-V difference for oxygen saturation increases. Assume this increased A-V difference is due to reduced cardiac output. For purposes of discussion, also assume that there is no change in metabolic acid composition of the blood and that the gas exchange is a multistep process. Let point A_o represent the original arterial value. First, assume that as blood flows through the tissues, oxygen leaves the blood. This shifts point A_o to point B due to the Haldane effect. Next, CO_2 is added to the blood from the tissues shifting point B to point V_o via an in vivo titration curve and resulting in a venous pCO_2 of 46 torr. If blood flow is reduced due to decreased cardiac output, oxygen saturation can be assumed to decrease due to continued oxygen use by the tissue. This shifts point V_o to point C due to the Haldane effect. Tissue metabolic CO_2 production continues and due to the low blood flow accumulates in venous blood shifting the blood-gas composition from point C to point V_f (pCO_2 = 53.5). Again note that this is an in vivo titration.

When the blood returns to the lungs and is oxygenated the oxygen saturation returns to 100%. The blood-gas composition shifts initially from point V_f to D as a result of oxygenation. Removal of CO_2 from the blood in the pulmonary capillaries causes the blood-gas composition to

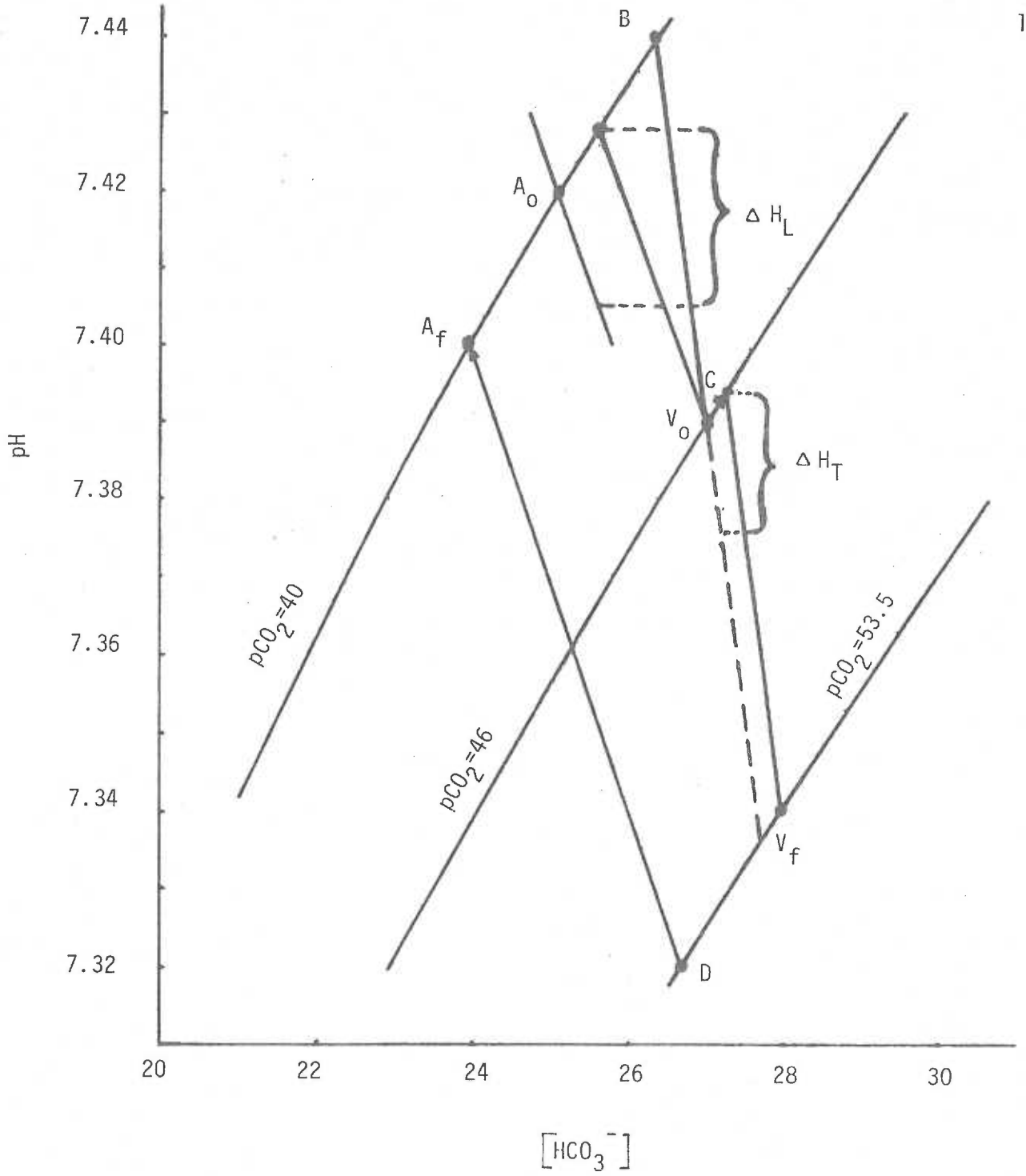


FIGURE 4

The effect of doubling the A-V difference for oxygen saturation between arterial and mixed venous blood with constant arterial blood-gas tensions. A_o and V_o represent initial arterial and mixed venous values respectively. (A_f and V_f represent final values). Lines BV_o and CV_f represent in vivo titration curves. The lines passing through A and A_fD represent in vitro titration curves. ΔH_L is the magnitude of the Haldane effect in the lungs for a SO_2 of 30%. ΔH_T is the Haldane effect in the tissues for a ΔSO_2 of 30%. (Note: The slope of the in vivo titration curves are steeper than the in vitro slopes because the variables on the graph have been reversed with pH on the ordinate and $\{HCO_3^-\}$ on the abscissa.)

Modified from Michel, 1968, p. 288.

shift from point D to point A_f. The latter shift is an in vitro titration of blood in pulmonary capillaries.

Thus it can be seen that increasing the A-V difference for oxygen saturation results in shifting the arterial point to a lower pH and $\{HCO_3^-\}$ but constant pCO_2. Michel concluded that an assessment of arterial blood-gas composition in this situation could lead the examiner to the erroneous conclusion that a metabolic acidosis was present.

In summary, Michel concluded the CO_2 titration curve for mixed venous blood was the true in vivo curve and that arterial blood is related to mixed venous blood via in vitro dissociation curves (p. 290). He also concluded that mixed venous blood was important in determining acid-base status. He stated, "It means that changes in arterial pH with changes in P_aCO_2 cannot be predicted by any sort of dissociation curve without reference to the mixed venous blood" (p. 291).

Garcia, Lai, Attebery, and Brown (1971) investigated the differences between the slopes of the in vivo buffer curves of arterial and mixed venous blood. Twelve dogs were anesthetized and the aorta and pulmonary artery cannulated for sampling arterial and mixed venous blood, respectively. A cuffed endotracheal tube was inserted and the dog spontaneously breathed 100% oxygen.

Six of the dogs were connected to a positive pressure respirator and pulmonary ventilation increased to reduce the pCO_2 to values less than 15 torr. Simultaneous arterial and mixed venous blood samples were obtained at 10 minutes, 1 hour, and 2 hours, after increasing ventilation. The dogs were then disconnected from the respirator and blood samples obtained at 10 and 60 minutes.

Six dogs were rendered hypercapnic by increasing inspired carbon dioxide ($FICO_2$) to 10% CO_2 in 90% O_2. The ventilation was controlled with use of tubocurarine chloride and pressure ventilation to keep pCO_2 at 70 torr. Simultaneous arterial and mixed venous samples were obtained at 15 minutes, 1, 2, 3, 4, and 6 hours. The animals were then given 100% O_2 to breathe without mechanical ventilation. Blood samples were obtained 15 minutes after the change.

The investigators measured pO_2, pCO_2, and pH. Hemoglobin concentration and oxygen saturation were also measured using a spectrophotometer. The plasma $\{HCO_3^-\}$ was calculated from the Henderson-Hasselbalch equation. Blood lactate and pyruvate concentrations were determined by enzymatic methods. The buffer capacity was calculated as $\Delta\{HCO_3^-\}$ / ΔpH.

With the decrease in pCO_2, (from 37.9 to 16.7 torr in arterial blood), plasma $\{HCO_3^-\}$ decreased by 4 mmole/liter. The pH increased to 7.61. Within 10 minutes the sum of the lactate and pyruvate concentrations increased from 1.07 to 1.80 mmole/liter (p. 240). There was an increase in the A-V oxygen difference attributed to either a decreased cardiac output or an increased oxygen consumption. When ventilation rate was decreased, values returned toward normal and within 10 minutes the sum of the pyruvate and lactate concentrations decreased to 2.88 mmole/liter and the A-V O_2 difference decreased (p. 240).

Hypercapnea produced an increase in plasma $\{HCO_3^-\}$ and decreased pH. During the first 15 minutes of hypercapnea, the A-V O_2 difference decreased but after 6 hours this difference increased 83% from the control value indicating a decreased cardiac output or increased oxygen consumption.

The in vivo buffer slopes of arterial and mixed venous blood did not differ significantly with the increase in pCO_2. "The buffer slope calculated from arterial blood values was larger than venous buffer slope with both increase and decrease in pCO_2 on the hyperventilated dogs. Decreasing the elevated pCO_2 after six hours of hypercapnea increased the difference between arterial and mixed venous slopes but the difference was not statistically significant" (p.240).

The difference between the slope of the CO_2 titration curves of arterial and mixed venous blood, even though not statistically significant, was similar to that predicted from the model of Roos and Thomas(1967). The higher values for the slope of the arterial titration curve is in part due to the effect of changing pCO_2 on cardiac output.

The authors concluded that the differences between the arterial and mixed venous slope, over the pCO_2 ranges investigated, were not significant nor important enough to be of value in assessing acid-base status.

Kappagoda, Stoker, Snow and Linden (1972) investigated the differences between the CO_2 titration curves of arterial and mixed venous blood in vivo. In addition they were interested in determining the usefulness of using mixed venous blood for assessment of acid-base status.

Their experiments involved dogs and humans. Four dogs were anesthetized, the femoral veins and arteries cannulated and a pulmonary artery catheter inserted. Body temperature, arterial blood pressure, heart rate, electrocardiogram, and end-tidal pCO_2 were monitored. The dogs were artificially ventilated and the stroke volume of the ventilator was set to keep the p_aCO_2 at 40 torr. Metabolic acid-base states were varied by intravenous infusions of 1 M-HCl (acidosis) or 8.4%

$NaHCO_3$ (alkalosis). In these altered states of metabolic disturbances, the p_aCO_2 was lowered in some experiments by increasing the minute volume of the respirator. In other experiments the p_aCO_2 was increased by increasing the $FICO_2$.

Six human subjects were studied at the time of cardiac catheterization. Arterial blood was sampled from either the brachial artery or from a catheter in the aorta. Mixed venous blood was obtained from the pulmonary artery via a double lumen catheter. Arterial blood pressure, oral temperature, and electrical activity of the heart were monitored continuously. The p_aCO_2 was lowered by having the patients hyperventilate. The p_aCO_2 was elevated by increasing the inspired CO_2 to 10% in 90% O_2.

In both animals and humans, simultaneous arterial and mixed venous samples were obtained in heparinized syringes within 5-10 minutes after each change in inspired gas composition and ventilation rate. After changing ventilation rate the subjects were returned to their original respiratory conditions and final control blood samples were obtained. Results supported the differences predicted by Roos and Thomas (1967), that is, the slopes of the in vivo titration curves were less than those of the in vitro curves.

"Non-respiratory pH values" were determined for the corresponding arterial and mixed venous values obtained. The authors defined non-respiratory pH as the pH that would occur if the pCO_2 of arterial blood in vivo (p_aCO_2) was adjusted to 40 mmHg (p. 533). This value can be determined by extrapolation from the titration curve obtained. The reason for determining this value was to attempt to separate the

metabolic components of acid-base regulation from the respiratory components. Results showed the mixed venous non-respiratory pH was consistently greater than the associated arterial non-respiratory pH values. This was explained as being due to the Haldane effect in the lungs when carbon dioxide is expired and the blood is oxygenated. As hemoglobin is oxygenated it gives up hydrogen ions thereby decreasing the pH of arterial blood.

Finally, the slope of the titration curve of mixed venous blood in vivo was slightly less than that calculated for arterial blood. The authors concluded that mixed venous blood could be used for assessing acid-base status but there would be no practical advantage for doing so. This conclusion was based on the fact that there was no statistically significant differences between the slopes of the in vivo arterial and mixed venous titration curves. However, it should be noted that this conclusion is valid only when their assumed conditions are met, i.e., constant cardiac output and constant carbon dioxide differences.

Summarizing the literature reviewed in this section one can conclude the following facts:

1) From an anatomical viewpoint, the change in blood-gas composi- in the lungs follows an in vitro titration curve. Mixed venous blood equilibrates with ISF and cells and thus represents in vivo buffering conditions.

2) A similar conclusion can be made from a biochemical-biophysical point of view. Experimental evidence suggests that HCO_3^- ions do not diffuse out of pulmonary capillaries during a single passage through the lungs.

3) Increasing A-V oxygen saturation differences can be shown to affect arterial and mixed venous blood-gas composition differently. The true in vivo CO_2 titration curve is that of mixed venous blood.

4) Based on the above, under conditions of varying cardiac output, arterial blood-gas composition may be interpreted erroneously for assessing systemic acid-base status.

Predictability of Mixed Venous Blood-gas Composition Over a Wide Range of Altered Acid-base States.

Prior to the use of mixed venous blood it must be demonstrated that mixed venous blood varies predictably in various acid-base disturbances. Samet, Linhart, Barold, and Hildner (1969) investigated the reliability of using mixed venous blood to monitor blood-gas parameters. They obtained simultaneous arterial and mixed venous blood samples from fifty cardiac patients during cardiac catheterization. None of the fifty patients was acutely ill or in shock at the time of the study. Blood samples were analyzed for pH, pO_2, pCO_2, and base excess.

The authors reported that arterial and mixed venous CO_2 tensions correlated positively with a correlation coefficient of 0.77 ($p = 0.01$). They then analyzed the data in terms of the difference between the pulmonary and systemic arterial (SA) pCO_2 values plotted on the ordinate and the pulmonary arterial (PA) pCO_2 tension plotted on the abscissa. When examined in this manner the coefficient of correlation was only 0.29.

The remaining variables were analyzed similarly with the following results. The coefficient of correlation for oxygen tension was 0.31.

When difference between PA and SA was plotted against the PA values the correlation was -0.26. The correlation for pH values of PA and SA was 0.78. When pH difference between PA and SA was plotted against the PA value this correlation was -0.20. Base excess values of PA and SA were correlated at 0.41. The difference between base excess values in PA and SA blood plotted against the corresponding PA blood value had a correlation coefficient of -0.65.

Based on the above analysis, the authors concluded that, "the especially poor correlation between the difference in systemic and pulmonary arterial sampling sites and the absolute level of the pulmonary arterial sample for pCO_2, pO_2, and pH clearly depicts why reliance on venous blood from any source is untenable " (p. 134). They felt the use of mixed venous blood was unjustifiable in acutely ill patients.

Samet et al.can be criticized not only for poor syntax but also for the conclusions stated from their analysis. Griffith (1980) discussed the relationships between variables which are linearly related (x and y) and how these relate when y-x is plotted against y. Griffith's example (p. 69) helps to clarify these relationships and precedes a discussion of the findings of Samet et al.

Let two variables, x and y, be linearly related. Plotting these 2 variables on a graph with y being the ordinate and x being the abscissa will yield a straight line. The following equation describes the relationship.

$$y = a + bx$$
where a = the y intercept
b = the slope

To evaluate the relationship let b = 0.5 and a = 0. Solving the equation gives the following:

$$y = 0 + 0.5x$$
$$y = 0.5x$$

then if:	y	x	y-x
	y = 1	x = 2	-1
	y = 2	x = 4	-2
	y = 3	x = 6	-3

slope of y-x vs. y = -1.0

This example shows that if 2 variables are linearly correlated with a slope of 0.5 then the difference y-x plotted as a function of y yields a slope of negative 1.0.

If 2 variables are related with a slope of 1.0 then a plot of the relationship y-x vs. y yields a line of zero slope. Now consider,

If:	y	x	y-x
	y = 1	x = 1	0
	y = 2	x = 2	0
	y = 3	x = 3	0

Then the slope of y - x vs. y = 0.

It can be seen that as the slope of y vs. x approaches 1.0, the slope of y - x vs. y approaches 0. It can be argued that the data obtained from the experiments of Samet et al. were responding exactly the way they should for linearly related data. The 0.77 coefficient of correlation (with slope approaching 1.0) obtained for carbon dioxide relationships show a strong correlation and the fact that PA-SA plotted against PA was only correlated with a coefficient of 0.29 does not weaken the relationship but in fact is exactly what one would expect from such a positive correlation between two variables. The rejection of mixed venous blood based on their analysis is unfounded.

Griffith (1980) compared arterial and mixed venous blood gas compositions over a wide range of pH during induced respiratory acid-base disturbances. Ten, healthy, mongrel dogs were anesthetized, curarized,

and a tracheotomy performed. The tracheal tube was connected to a ventilator. A Swan-Ganz flow directed catheter was inserted into the pulmonary artery with confirmation of placement assessed by pressure and wave form changes monitored on a polygraph recorder, (Grass) model 7C. Arterial blood was sampled from a femoral artery.

After a stabilization period, hypercapnea was produced by increasing fractional concentrations of carbon dioxide in oxygen. These increments were as follows; 3% CO_2 in 97% O_2, 5% CO_2 in 95% O_2, and 10% CO_2 in 90% O_2. Simultaneous arterial and mixed venous blood samples were obtained at 20 and 60 minutes following each step increase in fractional concentration of inspired carbon dioxide ($FICO_2$). After sampling at the 10% CO_2 level, the $FICO_2$ was decreased in reverse order with blood samples obtained at 20 and 60 minutes after each change.

Hyperventilation was accomplished by mechanically ventilating the animal using room air as the inspired gas mixture ($FICO_2 = 0$). The respiratory rate was kept constant and tidal volume increased in stepwise fashion 150 ml increments from an initial volume of 200-350 ml to a maximum of 650-750 ml. Actual volumes depended on the weight of the animal. Tidal volume was then reduced in reverse order. Samples were obtained in similar fashion and timing to those used in the hypercapnea experiments.

Samples were obtained anaerobically in glass syringes. They were capped, placed on ice and analyzed immediately.

Results showed that over a wide range of respiratory acid-base disturbances, mixed venous blood-gas composition varied predictably and was closely correlated with that of arterial blood. In hypercapnea the

correlation coefficients (Pearson's r) between mixed venous and arterial blood for pH, pCO_2, $\{HCO_3^-\}$ identity plots and the pH/$\{HCO_3^-\}$ relationship were greater than 0.83. For the PO_2 the correlation was 0.69 (p. 42). In the hyperventilation experiments correlation coefficients greater than 0.86 were obtained for pH, pCO_2, $\{HCO_3^-\}$ and the pH/$\{HCO_3^-\}$ relationship. The correlation coefficient for pO_2 was 0.12.

The blood-gas parameters obtained followed closely the predictions of Roos and Thomas (1967) and also fulfill the predictions that one would assume based on the model presented in Figure 1. The pH of mixed venous blood was always lower than the pH of arterial blood. This can be attributed to the acids from metabolic activity in tissue cells added to capillary blood which flows into the veins.

The pCO_2 in mixed venous blood was always higher than that in arterial blood. This might have been predicted from the following equation: (Griffith, p. 63).

In a steady state:

$$\dot{Q}\ \{CO_2\}_{mv} = \dot{Q}\ \{CO_2\}_{a} + \dot{V}CO_2 \cdot f \qquad (2)$$

where:

$\dot{Q}$ = cardiac output

$\{CO_2\}_{mv}$ = concentration of physically dissolved carbon dioxide in mixed venous blood

$\{CO_2\}_{a}$ = concentration of physically dissolved carbon dioxide in arterial blood

$\dot{V}CO_2$ = Metabolic CO_2 production

f = that fraction of the CO_2 produced that is transported as physically dissolved CO_2

From equation 2 it may be seen that $\{CO_2\}_{mv}$ depends on flow and also on the amount added from cellular metabolic activity.

In the hyperventilation experiment, the pO_2 of arterial blood did not change significantly but the pO_2 of mixed venous blood decreased significantly. This decrease was explained by using the following equation: (p. 64)

$$\{O_2\}_a \cdot \dot{Q} = \{O_2\}_{mv} \cdot \dot{Q} + \dot{V}O_2 \qquad (3)$$

where:

$\{O_2\}_a$ = O_2 concentration in arterial blood

$\dot{Q}$ = cardiac output

$\{O_2\}_{mv}$ = O_2 concentration in mixed venous blood

$\dot{V}O_2$ = oxygen uptake

thus:

$$\{O_2\}_a - \{O_2\}_{mv} = \frac{\dot{V}O_2}{\dot{Q}}$$

Since the animals were anesthetized and curarized, ventilation was controlled and the body temperature remained constant, the oxygen consumption was assumed to remain constant. Therefore, increased differences between the mixed venous and arterial pO_2 values were probably due to a decrease in cardiac output resulting from mechanical ventilation.

The HCO_3^- concentrations between mixed venous and arterial blood were closely correlated. The $\{HCO_3^-\}$ in mixed venous blood was always higher than in arterial blood. This can be predicted from equation 1 (p. 4) where it can be seen that increased carbon dioxide will shift the equation to the right and increase $\{HCO_3^-\}$.

The CO_2 titration curve of mixed venous blood had a lower slope than that of arterial blood as predicted by Roos and Thomas (1967).

Arterial and mixed venous titration curves were, however, still closely correlated with no significant difference between the slopes. This finding ran contrary to the prediction of Roos and Thomas; however, in their analysis they ignored the effect of cellular buffering. According to Pitts (1974), in respiratory acidosis, 97% of the buffering is due to cellular buffering while in respiratory alkalosis, this figure is 99% (pp. 194, 195).

Griffith concluded that arterial and mixed venous blood gas compositions are closely correlated over wide ranges of respiratory acid-base changes when cardiac output is stable. Griffith further concluded that the changes in mixed venous were predictable and thus mixed venous blood could be used for acid-base assessment. The low pO_2 found in mixed venous blood in states of hyperventilation was not closely correlated to arterial blood. However, it was concluded that the mixed venous pO_2 may more accurately predict ISF pO_2.

Bieber (1979) compared mixed venous and arterial blood gas compositions over a wide range of induced metabolic acid-base disturbances. Nine mongrel dogs were used for the experiments. Arterial blood from a femoral artery and mixed venous blood from the pulmonary artery were used for blood-gas analysis. The animal's temperature, heart rate, and respiratory rate, were monitored throughout the experiment. Metabolic acidosis and alkalosis were induced by intravenous infusions of ammonium chloride and sodium bicarbonate respectively.

Results showed that the blood-gas composition of arterial and mixed venous blood were very closely correlated over wide ranges of metabolic acid-base disturbances. Changes in mixed venous blood gas composition

closely mimicked those changes in arterial blood over a wide range of pH values (6.88-7.67 for arterial blood and 6.86-7.63 for mixed venous blood).

Blood gas parameters of mixed venous and arterial blood followed the same pattern as that predicted by the model, Figure 1. Mixed venous pH was consistently lower, and $\{HCO_3^-\}$ and pCO_2 values higher than values in arterial blood. The pH/$\{HCO_3^-\}$ relationship between mixed venous and arterial blood appeared almost identical.

The mixed venous pO_2 was always lower than arterial pO_2. In metabolic acidosis the pO_2 in both arterial and mixed venous blood increased, and was thought to be caused by compensatory hyperventilation. In states of metabolic acidosis, the hydrogen ion stimulates ventilation and as ventilation increases CO_2 is expired in an attempt to return blood pH toward normal.

The pO_2 decreased in the alkalotic states in both mixed venous and arterial blood. This was thought to be caused by hypoventilation which results from depression of respiratory neurons and peripheral chemoreceptors during alkalosis (p. 58).

Bieber concluded that mixed venous blood does mimic arterial blood over wide ranges of pH in metabolic acid-base disturbances. In addition, it was suggested that mixed venous blood might more accurately reflect the tissue acid-base status than arterial blood.

The Effects of Decreased Cardiac Output on Arterial and Mixed Venous Blood Gas Composition.

Tung, Bettice, Wang, and Brown (1976) investigated the effects of hemorrhagic shock on arterial and mixed venous blood gas compositions

and on intracellular acid-base changes. Twenty-one anesthetized mongrel dogs were bled to decrease arterial blood pressure to a mean of 50 torr. This level of hypovolemia was maintained for two hours by either infusing fluids or bleeding as necessary. After the mean blood pressure of 50 was obtained, the animal was allowed to stabilize. After stabilization simultaneous arterial and mixed venous blood samples were obtained at 30, 60, 90 and 120 minutes. Body temperature was monitored throughout the experiment and decreased from a mean of 37.9 $\pm$ 0.2 to 37.4 $\pm$ 0.2C.

Results showed that there were differences in the response of arterial and mixed venous blood gas values in states of decreased cardiac output. The bicarbonate concentration decreased in both arterial and mixed venous blood but the decrement was more precipitous in the arterial blood resulting in a widening of the arterial-venous $\{HCO_3^-\}$ difference. The mixed venous blood always had higher values for $\{HCO_3^-\}$ than arterial blood.

The pCO_2 of mixed venous blood increased during the hemorrhagic states but the pCO_2 in arterial blood decreased. Thus, there was a widening of the arterial-venous pCO_2 difference. These changes can be explained based on the decreased cardiac output. Decreased perfusion to the tissues leads to tissue hypoxia, anaerobic metabolism and a metabolic acidosis. The increased hydrogen ion concentration stimulates ventilation which results in a lowered arterial pCO_2. In mixed venous blood, decreased cardiac output results in retarded blood flow to the tissues. Cell metabolic activity continues production of carbon dioxide and because of the decreased flow CO_2 accumulates and increases the CO_2

concentration in mixed venous blood.

The pH decreased in both arterial and mixed venous blood with a more precipitous fall in the mixed venous sample. Again this resulted in a widening of the arterial-venous difference.

The pO_2 in arterial blood increased by a mean value of 14 torr. This can be explained by the increased ventilation due to the acidosis. The increase in oxygen saturation caused by the increase in pO_2 was minimal. The mixed venous pO_2, however, decreased precipitously from 36 to 16 torr. This decrement represented such a reduction that there were profound effects on the oxygen saturation. At low pO_2 values the oxygen dissociation curve is more linear and there is increased sensitivity to pO_2 changes (Figure 5). The decreased mixed venous pO_2 is due to a reduced oxygen delivery to systemic tissues which is caused by the decreased cardiac output. It represents a state of acute tissue hypoxia even though arterial pO_2 is within normal limits or even slightly higher than normal.

In summary, in moderate to severe hemorrhage, arterial blood reflected a state of metabolic acidosis with respiratory compensation. The mixed venous blood reflected both a metabolic acidosis and an associated respiratory acidosis. The low pH, low $\{HCO_3^-\}$ and increased pCO_2 in mixed venous blood is due to inadequate perfusion. It should be noted that Tung et al. stated the term "respiratory" is used in its broadest sense and not just to describe the adequacy of the pulmonary ventilation (p. 235).

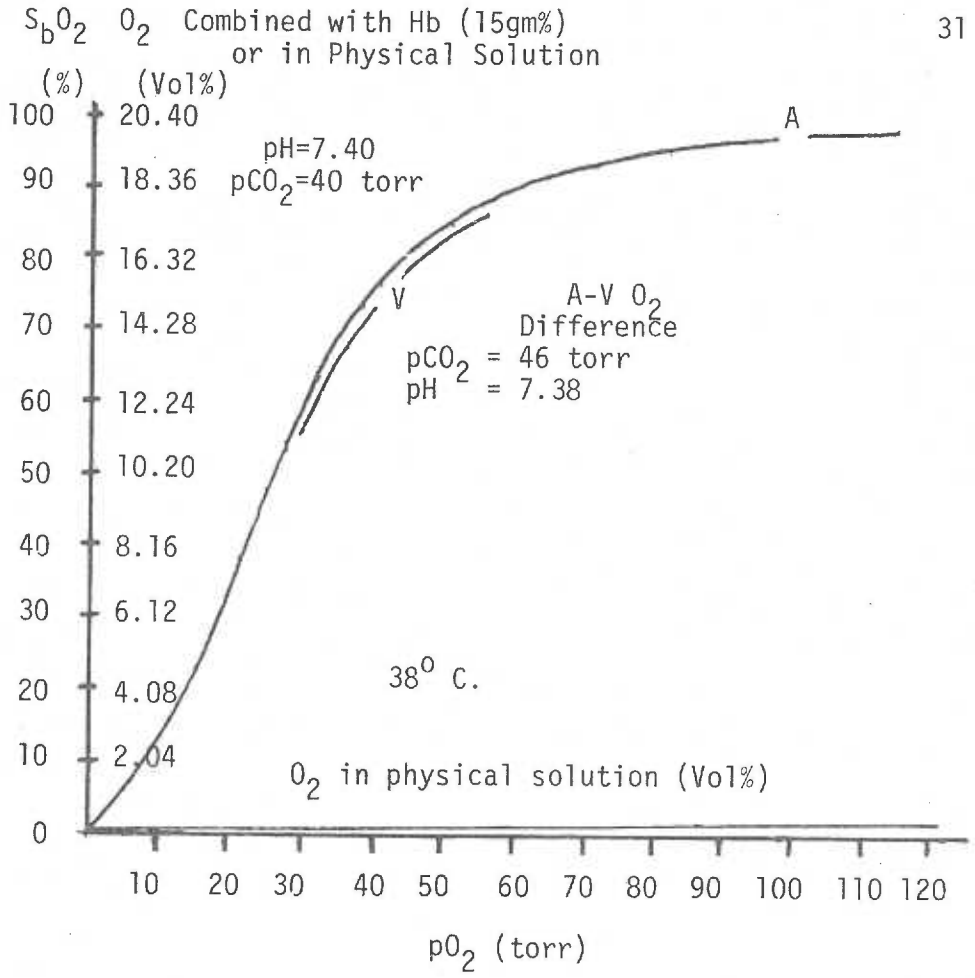


FIGURE 5

"The oxyhemoglobin dissociation curve, showing the basic relationship of blood O_2 transport. Its shape has great physiologic importance. The full curve above applies to the arterial blood of healthy man at rest, whereas the small section to its right applies to venous blood. Point A represents normal values for arterial blood and point V for venous blood. Changes in CO_2 tension, pH, or temperature displace the oxyhemoglobin dissociation curve to the right or left. A physiologic shift from the venous to the arterial curve takes place as blood flows through the pulmonary capillaries, losing CO_2 and increasing in pH. The reverse shift occurs as blood flows through the systemic capillaries. Note that this effect, termed the Bohr shift, facilitates O_2 dumping in the tissues. Note also the relatively small amount of O_2 carried by the blood in physical solution in the physiologic range of O_2 tension."

Source: Slonim, and Hamilton, 1976 (p. 82).

Clinical Uses of Central and Mixed Venous Blood-Gas Analysis for Assessment of Patients.

A limited number of articles pertaining to actual clinical use of venous blood were found in the literature. Although one article suggests use of central venous blood it is included only as an example of how ventilatory support might alter cardiovascular status to the point that tissue oxygenation may be influenced.

Wilson (1978) supported the use of central venous blood in assessment of acutely ill patients. He advocated use of simultaneous arterial and venous samples for blood-gas analysis to increase the accuracy of results and to give added information on the cardiac indices by calculating physiologic shunting and calculating oxygen transport. He found that if the systemic arterial - central venous O_2 difference (A-V difference) was 3.5 volumes % or greater, the central venous blood-gas values correlated well with pulmonary artery values ($r = 0.85$). However, if this A-V difference was less than 3.5 vol. %, the correlation coefficient decreased ($r = 0.35$). The author concluded that obtaining simultaneous blood-gas samples, although more expensive, would serve to give much more accurate information on both the pulmonary and hemodynamic function of the patient.

Based on the physiologic model (Figure 1) it can be argued that the pulmonary artery is the site for obtaining blood which reflects the flow weighted average of returning systemic venous blood. However, Wilson does give one clinical example that should help clarify the proposition that venous blood does give more information regarding the tissue acid-base status than does arterial blood. He states that the addition

of positive end expiratory pressure (PEEP) to a ventilator will decrease cardiac output and reduce oxygen transport. Increasing PEEP will often improve pulmonary function and arterial blood-gas composition but if cardiac output decreases, the tissue status may be worsened and yet not reflected in the arterial blood-gas analysis. The following examples of these values are: (pp. 399-400)

A mechanically ventilated patient, FIO_2 = 0.6

	PEEP (cm/H_2O)	0	5	10	15
arterial	pH	7.43	7.46	7.47	7.48
	pCO_2	40	41	42	43
	pO_2	60	62	64	67
	SaO_2	91%	92%	93%	94%
	Compliance	35	35	37	40

	PEEP (cm/H_2O)	0	5	10	15
venous	cardiac index ($L/min/m^2$)	3.0	3.0	2.8	2.4
	O_2 transport ($ml/min/m^2$)	444	450	423	367
	shunting	31%	29%	26%	21%

It can be seen, that even though arterial blood looks as if status were improving with each incremental step in PEEP, the hemodynamic status determined by use of venous blood shows deterioration in cardiac output and oxygen transport. It can be argued further that based on the model (Figure 1) and the work of Tung et al. the blood-gas composition of mixed venous blood might be used to determine tissue acid-base status. Further, arterial blood samples need not be drawn simultaneously in every case.

Kazarian and Del Guercio (1980) described the use of mixed venous blood-gas determinations in patients with traumatic shock. They collected data from 10 patients arriving in the emergency room of a metropolitan

hospital in profound shock from trauma and hemorrhage. All of the patients were given resuscitation, fluid therapy and blood transfusions, and underwent surgery to control hemorrhage. They were all intubated and either a central venous or Swan-Ganz catheter inserted. Samples of arterial and mixed venous blood were analyzed for blood-gas composition in the resuscitative, operative and postoperative periods.

Of the 10 patients only 4 survived. Results showed that the mixed venous oxygen saturation (S_vO_2) averaged 46% in the survivors and about 25% in the non-survivors. Average arterial pH of survivors was 7.34 and for non-survivors was 7.158. Because all patients were intubated and receiving an FIO_2 of 1.0, arterial oxygen tensions were greater than 100 mmHg and arterial oxygen saturation (S_aO_2) greater than 90%.

The authors contend that mixed venous blood gas values were better predictors of survival and better indices for monitoring the patients response to treatment than arterial blood-gas values. They believed the S_vO_2 was an important predictor of survival. Of the six non-survivors, four had an initial S_vO_2 less than 30%, while only one of the survivors had an initial value this low (p. 181). They stated that mixed venous blood-gas composition reflects circulatory adequacy. "The percentage of oxygen saturation in mixed venous blood can be correlated with the amount of oxygen delivered to the cell and the oxygen consumed" (p. 180).

Several letters to the editor following publication of this article criticized the authors both for method and statistical analysis. Lipton (1980) argued that it was impossible to tell from the data if the 10 patients were truly similar. He asserted that the essence of emergency care was in treatment of shock and rapid pulmonary and circulatory resuscitation. He believed that valuable time would be wasted inserting

catheters at this time. He objected to the use of S_vO_2 as a predictor of survival and stated, "To be able to predict which patients will or will not survive is not appropriate in such critically ill patients" (p. 597).

In rebuttal, Kazarian and Del Guercio (1980) stated that the magnitude of the trauma was similar, that no time was lost in treatment, and that initial samples were taken from whatever central lines were present. In the operative and post-operative phases, all patients had a Swan Ganz catheter in place. However, in the post-operative phase if the S_vO_2 failed to improve the patient expired.

Piantadosi and Bradley (1980) criticized the conclusions of Kazarian and Del Guercio on statistical grounds. They argued that no data were provided regarding patient variables that might influence survival, such as age or sex. Second, when they analyzed the data using a statistical analysis system they concluded that S_vO_2 was not the best predictor for survival and in fact some of the arterial values were better discriminators. Finally, they stated that a larger sample was needed to see if the relationships hold.

In reply, Kazarian and Del Guercio contended that all 10 patients were male, nine of whom ranged in age from 19-38 with one survivor aging 63 years of age. All were given ventilatory support and 100% oxygen. They stated that they did not claim statistical significance since the size of the sample was small. They agreed that studies with larger groups were necessary. They also stated that "because the influence of the resuscitative measures on the arterial blood gases (P_aO_2, P_aCO_2, and S_aO_2) is so great, a statistical analysis of these would not be as meaningful in assessing the metabolic status of the

trauma-shocked patient as in the S_vO_2" (p. 599).

SUMMARY OF THE REVIEW OF THE LITERATURE

1) The in vivo CO_2 titration curve differs from the in vitro curve.

2) The CO_2 titration curve of mixed venous blood represents the in vivo curve while the slope for arterial blood reflects an in vitro curve.

3) Arterial blood represents the output of the lungs while mixed venous blood represents the output of the tissues.

4) It has been demonstrated that there are close correlations for values of pH, $\{HCO_3^-\}$, pCO_2, and the pH/$\{HCO_3^-\}$ relationship between arterial and mixed venous blood over wide ranges of metabolic and respiratory acid-base states.

5) The effect of decreased tissue perfusion associated with decreased cardiac output can be expected to affect the mixed venous blood-gas parameters in a manner different from arterial blood-gas values. The mixed venous blood would more accurately indicate acid-base status of systemic tissues.

STATEMENT OF THE PROBLEM

In this study, the following questions will be answered:

1) How does arterial blood-gas composition compare to mixed venous blood-gas composition in states of decreasing cardiac output?

2) Does mixed venous blood-gas composition follow a predictable pattern in states of decreasing cardiac output?

It can be predicted that by decreasing cardiac output the difference between arterial and mixed venous values for all blood-gas parameters will be increased.

In addition, decreased oxygen delivery due to decreased perfusion can be predicted to cause a metabolic acidosis and a superimposed respiratory acidosis in mixed venous blood (low pH, low $\{HCO_3^-\}$ and increased pCO_2). In contrast, decreased cardiac output can be predicted to cause a metabolic acidosis plus partial respiratory compensation in arterial blood (low pH, low $\{HCO_3^-\}$, and decreased pCO_2).

CHAPTER II

METHODS

Statement of the Variables

The independent variable was the change in cardiac output produced by bleeding the animal several times throughout the experiment.

The dependent variables were the pH, pCO_2, pO_2, and $\{HCO_3^-\}$ of arterial and mixed venous blood. Control baseline values for cardiac output, pH, pCO_2, pO_2, and $\{HCO_3^-\}$ were obtained. After each decrement in cardiac output, samples of mixed venous and arterial blood were obtained.

Design

The design of this study is experimental. Repeated measures were obtained and each subject served as its own control. An animal model was used for the experiment.

Procedure

Ten mongrel dogs weighing from 12.7 to 22.7 kilograms were anesthetized with an intravenous injection of Sodium Pentobarbital (30 mg/kg). Anesthesia was maintained with 30-45 mg doses administered intravenously as needed. The animal was then intubated and breathed room air spontaneously throughout the experiment.

A number 7 French flow-directed (Swan-Ganz) catheter was placed into the right external jugular vein. The catheter was connected to a pressure transducer to monitor pulmonary artery pressure. Placement of the catheter into the pulmonary artery was accomplished by monitoring pressure wave changes recorded on a polygraph recorder (Grass Model 7C). The left external jugular vein was cannulated for

administration of and maintenance of anesthesia. A femoral artery was cannulated for monitoring blood pressure and sampling arterial blood. All catheters were kept patent with periodic infusions (1-3 ml) of heparinized saline (1000 units of sodium heparin in 100 ml of normal saline).

After the surgical procedures were completed the animal was allowed to stabilize for at least 45 minutes. Baseline data were collected on the following: heart rate, respiratory rate, and pulmonary artery blood temperature. A baseline cardiac output was obtained using the thermodilution technique.

An Edwards Laboratories Cardiac Output Computer (Model 9520A) was used to determine cardiac output. The computer was attached to a strip chart recorder (Edwards Laboratories, Model 9810) to obtain thermodilution curves. This computer has an accuracy of $\pm$ 3% to 0.02 L/min. and a repeatability better than $\pm$ 2%. Three milliliter volumes of 5% glucose in water were drawn into 10 ml plastic syringes, capped, and then cooled to 0-5^{o}C and maintained at this temperature in an ice bath. These were used for determination of cardiac output measurements according to the instrument manual. At least four to six successive measurements were obtained for each cardiac output determination. The mean of the three closest values was used.

The plungers and barrels of one milliliter glass syringes were lubricated with silicone stopcock grease to prevent air leakage. Approximately 0.1 milliliter of sodium heparin was drawn into the syringe (100 u/ml). A small volume ($\sim$0.08 ml) of mercury was also drawn into the syringe to provide a seal and to allow for gentle mixing of the sample prior to analysis.

Control blood samples were obtained after the animal stabilized. Prior to obtaining the sample, irrigation fluid was removed from the catheter in an amount equal to at least twice the deadspace volume. The prepared syringe, with excess heparin removed was then attached to the end of the Swan-Ganz catheter and a one milliliter sample was withdrawn over a minimum period of time of one minute.

Arterial blood was obtained from the femoral artery at the same time the mixed venous sample was obtained. This sample was also collected anaerobically in a previously prepared glass syringe. After the blood samples were obtained the syringes were capped and placed on ice until analyzed. The hematocrit and plasma protein concentration were determined from a separate arterial blood sample.

After baseline samples were obtained the animal was bled from the femoral artery to reduce blood volume and thus decrease cardiac output. The initial amount removed (175-250 ml) depended on the animal's weight and estimated blood volume. Vital signs and temperature were monitored closely after this procedure. After blood was removed the animal was allowed to stabilize for at least 45 minutes. During this time period the previous blood samples were analyzed.

A Radiometer Model BGA 3, Mark 2 blood gas analyzer was used for analysis of blood gas composition. This analyzer has a reproducibility $\pm$ 0.001 pH units, $\pm$ 0.1 torr pCO_2, and $\pm$ 1.0 torr pO_2. Samples were analyzed in random order. On each sample the pH readings were obtained until readings agreed within 0.005 pH units of each other. The pO_2 and pCO_2 readings were recorded until three values were obtained that agreed within 1.0 mmHg. The blood gas analyzer was calibrated frequently according to the instrument manual to insure accuracy of analysis.

After the stabilization period following hemorrhage a cardiac output determination was repeated. Again, arterial and mixed venous blood samples were obtained simultaneously. Another measurement of hematocrit and plasma protein concentration was made. The animal was then bled again. These steps were repeated until systolic arterial pressure was reduced to less than 100 mmHg. At least four separate paired samples were obtained.

At the end of the experiment the animal was sacrificed and if there was any question of Swan-Ganz catheter placement a post-morten examination was done to confirm the location.

CHAPTER III

RESULTS

General Description

Ten mongrel dogs of both sexes ranging in weight from 12.7-22.7 kg were used for this study. Heart rate, respiratory rate and body temperature were monitored. The animals were warmed or cooled as necessary to maintain body temperature within normal limits. Hematocrit and protein concentrations were obtained initially when control blood samples were obtained and thereafter with each successive set of blood samples.

Since animals were bled in steps to reduce cardiac output many individual measurements of change were made. To avoid becoming lost in the vast amount of data it is useful to compare control and final values obtained from the animals (Tables I-IV). Control values were obtained prior to the first bleeding episode while the final values were obtained after the last bleeding episode when cardiac output was at its nadir.

Hematocrit increased in two dogs (2 and 3) even though sufficient blood had been removed to reduce cardiac output to less than 50% of control. Furthermore, hematocrit never decreased to values less than 0.36 regardless of significant blood loss (Table II). Dogs are known to have profound splenic contraction following hemorrhage. When the spleen contracts red blood cells from splenic storage sites are infused into the circulating blood.* The spleen in these animals was greatly reduced in size at the end of the experiments.

Cardiac output is a function of body mass, i.e., the greater the weight of the animal the greater the cardiac output. Since animals of

* Personal communication, Mr. Fred Arfmann.

many different weights were used changes in cardiac output are shown in Figures 6-13 and Table IV in terms of percent of control.

The rather high heart rate and low respiratory rate seen during control periods is most likely due to the barbiturate anesthetic (Table I). It should be noted that some animals (2,5,7,8, and 9) were in a respiratory acidosis during the control period (Table III). Again this most likely reflects the depressant properties of general anesthesia.

Blood Gas Parameters

Control values for pH, pCO_2, pO_2 and $\{HCO_3^-\}$ from arterial and mixed venous blood are shown in Table III. Final values are shown in Table IV. It was discovered at the fourth sample obtained from dog number one that the pulmonary artery catheter was no longer properly placed in the pulmonary artery and the samples included blood from the pulmonary capillary bed. Due to low blood flow it was impossible to reposition the catheter correctly. Thus data from dog number one were not used in the analysis.

The mean pH during control periods for arterial blood was 7.33 and that for mixed venous blood was 7.31 (Table III). The pH of arterial blood increased in 5 of 9 animals and decreased in 4 while the pH of mixed venous blood decreased in 7 of the 9 animals as a result of bleeding (Table IV). The mean values for pH in arterial and mixed venous blood after bleeding were 7.31 and 7.21 respectively (Table IV).

The mean control values for pCO_2 in arterial and mixed venous blood were 47.8 and 53.4 torr respectively. The pCO_2 of arterial blood decreased in all dogs as a result of the bleeding. The pCO_2 of mixed venous blood increased in dogs 2,4,6, and 10 and remained essentially the same in dog 9. In dogs 3,5, and 7 the pCO_2 of mixed venous blood decreased.

The mean final arterial and mixed venous pCO_2 values were 31.9 and 52.1 torr, respectively.

The mean control values for arterial and mixed venous $\{HCO_3^-\}$ were 28.6 and 30.8 mEq/L respectively (Table III). The $\{HCO_3^-\}$ in arterial blood decreased in all dogs as a result of the hemorrhage. The final mean values for $\{HCO_3^-\}$ for arterial and mixed venous blood were 16.6 and 20.4 mEq/L respectively. This represents a 44% decrease in arterial $\{HCO_3^-\}$ and a 34% decrease in mixed venous $\{HCO_3^-\}$ (Table IV).

The mean control values for arterial and mixed venous pO_2 were 76.2 and 50.3 torr respectively. The pO_2 of arterial blood <u>increased</u> while the pO_2 in mixed venous blood <u>decreased</u> in all dogs as a result of hemorrhage. The mean final values for pO_2 in arterial and mixed venous blood were 93.5 and 27.4 torr respectively. This represents a 23% increase in arterial pO_2 and a 46% decrease in mixed venous pO_2.

<u>Arterial-Venous Differences</u>

Table V shows the arterial-venous (A-V) differences for dogs 2-10 at control and for each level of decreased cardiac output. Note that cardiac output is reported in terms of percent of control cardiac output.

From Table V it can be seen that there were progressive increases in the A-V differences for each blood-gas parameter as cardiac output decreased. These increments in A-V differences are displayed graphically in Figures 6,7,8 and 9.

A paired t-test was performed using the mean control and final values for each parameter. The values for means, standard deviations, and t-tests are shown in Table VI. The mean values for control were significantly different from final values for all parameters ($p < 0.001$).

Arterial-venous differences were divided according to four arbitrarily chosen divisions of cardiac output. These four divisions were 85-100% of control, 70-85%, 55-70%, and less than 55% of control. The results of organizing data into these intervals are shown in Table VII and graphically depicted in Figures 10,11,12, and 13. It is apparent that at cardiac outputs less than 55% of control the A-V differences increase markedly.

pH{HCO_3^-} Relationship

Figure 14 is a pH/[HCO_3^-] diagram on which the last three pH and {HCO_3^-} data points from each dog (2-10) are plotted. This diagram is used to assess acid-base status based on the relationship between pH, pCO_2, and {HCO_3^-} expressed by the Henderson-Hasselbalch equation. Acid-base disturbances can also be assessed by plotting values on this graph.

In Figure 14, 17 of 27 values (63%) determined from arterial samples fall in the area of compensated metabolic acidosis. Five arterial samples had pCO_2 values between 40 and 46 torr, however, the initial respiratory acidosis of some animals contributed to a higher than expected pCO_2 during hemorrhage. The pCO_2 in all cases decreased from the initial value during the stepwise decrements in cardiac output. The two highest arterial [HCO_3^-] with pCO_2 values greater than 46 torr occurred at cardiac outputs greater than 60% of control.

Twenty (74%) of the blood-gas values determined from mixed venous blood fell into the range of mixed metabolic and respiratory acidosis. Seven of these values fell between pCO_2 values of 40-46 torr and again this may be due to some of the initial acid-base disturbances seen in some of the animals. The lone mixed venous value with a pCO_2 less than 40 torr was found in one dog despite the fact that the cardiac output was

only 36% of control. In addition, the pO_2 increased from the previous sample despite a further decrement in cardiac output (Appendix A). Either sampling error or shunting could explain the apparent anomalous position of this point.

TABLE I

Control Values for Heart Rate, Respiratory Rate, Hematocrit, Protein, Cardiac Output and Temperatures for Dogs 1-10.

	Heart Rate (per min)	Respiratory Rate (per min)	Hematocrit	Plasma Protein (Concentration) (gm%)	Cardiac Output (L/min)	Temperature (Centigrade)	Estimated Blood Volume ml
Dog 1	192	18	0.50	6	2.61	38.1	1300
2	128	20	0.28	6.8	1.53	37.2	890
3	128	11	0.43	5.2	1.85	37.0	920
4	168	7	0.44	5.7	3.25	38.4	1340
5	96	5	0.44	6.7	1.86	35.3	1110
6	168	5	0.46	6.2	3.10	38.0	1340
7	180	7	0.44	6.0	3.12	37.6	1430
8	144	11	0.37	5.1	2.00	35.6	1080
9	144	15	-	-	2.95	37.4	1110
10	192	14	0.51	6.6	3.73	-	1590
$\bar{X}$	154	11	0.43	6.0	2.60	37.2	
S.D.	31	5	0.07	0.6	0.74	1.1	
Range	96-192	5-20	0.28-0.51	5.1-6.8	1.53-3.73	35.3-38.4	

TABLE II

Final Values for Heart Rate, Respiratory Rate, Hematocrit, Protein Concentration, Cardiac Output, Temperature and Blood Volume Removed for Dogs 1-10.

	Heart Rate	Respiratory Rate	Hematocrit	Plasma Protein (Concentration) (gm%)	Cardiac Output (4 min)	Temperature	Volume Blood Removed (ml)
Dog 1	180	24	0.45	4.9	1.31	38.8	950
2	150	30	0.43	4.2	0.51	-	570
3	120	46	0.47	4.0	0.67	37.2	600
4	210	13	0.42	4.8	0.67	38.8	740
5	142	16	0.42	4.5	0.87	36.1	765
6	156	40	0.39	5.0	0.76	39.7	725
7	150	12	0.41	5.0	0.87	98.6 (R)	775
8	138	36	0.36	4.1	0.73	35.4	610
9	172	32	0.41	4.6	1.36	38.2	740
10	180	36	0.43	5.2	1.22	-	1195
$\bar{X}$	160	28.5	0.42	4.63	0.90	37.74	
S.D.	26	11.8	0.03	0.41	0.30	1.57	
Range	120-210	12-46	0.36-0.47	4.1-5.0	0.51-1.36	35.4-39.7	

TABLE III

Control Values for Blood-Gas Parameters (pH, pCO_2, $\{HCO_3^-\}$ and pO_2) for Dogs 2-10 for Arterial and Mixed Venous Blood.

	pH		pCO_2		$\{HCO_3^-\}$		pO_2	
	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous
Dog 2	7.35	7.32	46.2	50.8	24.9	25.5	83.0	41.7
3	7.33	7.30	42.3	40.2	21.7	23.3	87.2	53.7
4	7.37	7.36	38.9	43.8	21.8	23.9	73.2	47.3
5	7.24	7.24	57.7	62.7	24.1	26.3	86.4	54.3
6	7.36	7.38	43.5	43.8	23.7	25.2	51.5	44.9
7	7.27	7.26	50.1	53.8	22.2	23.4	64.2	48.8
8	7.27	7.25	59.0	65.4	26.4	27.9	74.7	49.8
9	7.37	7.34	49.0	55.2	49.0	55.2	83.0	50.5
10	7.35	7.33	43.3	46.8	43.3	46.8	82.5	61.8
$\bar{X}$ *	7.33	7.31	47.8	53.4	28.6	30.8	76.2	50.3
S.D.	$\pm$0.04	$\pm$0.05	6.9	7.7	10.2	11.7	11.9	5.9

Values for pCO_2 and pO_2 are in units of torr while those for $\{HCO_3^-\}$ are in units of mEq/L.

* Since the pH scale is exponential the mean pH values were determined by first converting pH to $\{H^+\}$ and then average $\{H^+\}$ reconverted back to pH.

TABLE IV

Final Values for Blood-Gas Parameters (pH, pCO_2, $\{HCO_3^-\}$ and pO_2) for Dogs 2-10 for Arterial and Mixed Venous Blood.

	pH		pCO_2		$\{HCO_3^-\}$		pO_2		
	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous	Cardiac Output % Control
Dog 2	7.22	7.09	34.6	61.9	13.7	18.2	107.3	24.0	33.5%
3	7.37	7.31	24.4	34.0	13.6	16.4	94.3	44.4	36.1%
4	7.26	7.12	23.8	55.5	12.9	17.5	96.9	18.3	21%
5	7.28	7.20	37.0	60.6	16.8	22.8	95.5	27.3	46.8%
6	7.30	7.24	30.9	48.7	14.8	20.0	78.5	19.4	24.4%
7	7.37	7.28	25.4	42.0	14.1	19.0	97.5	30.1	27.9%
8	7.32	7.22	37.3	57.4	18.8	22.5	103.6	24.6	36.3%
9	7.38	7.27	33.9	55.4	19.5	24.4	94.5	32.2	46.1%
10	7.31	7.25	39.8	53.7	19.5	22.6	73.3	26.5	33%
$\bar{X}$ *	7.31	7.21	31.9	52.1	16.0	20.4	93.5	27.4	33.9%
S.D.	$\pm$0.05	$\pm$0.07	6.1	9.1	2.7	2.8	11.0	7.8	8.8%

Values for pCO_2 and pO_2 are in units of torr while those for $\{HCO_3^-\}$ are in units of mEq/L. Final cardiac output is reported as percentage of control.

* Since the pH is exponential the mean pH values were determined by first converting pH to $\{H^+\}$ and then the average $\{H^+\}$ reconverted to pH.

TABLE V

Arterial-Venous Differences for Dogs 2-10 at Each Level of Cardiac Output. Cardiac Output at Time of Sample Reported as % of Control as Recorded in Last Column.

		pH	pCO_2	pO_2	$\{HCO_3^-\}$	% C.O. of Control
	#1 Control Sample	0.03	-4.57	41.30	-0.67	100%
	#2	0.03	-6.57	44.90	-1.41	78.2%
Dog 2	#3	0.05	-11.87	54.03	-2.78	71.5%
	#4	0.08	-18.80	69.20	-3.93	41.1%
	#5	0.13	-27.30	83.30	-4.57	33.5%
	#1 Control Sample	0.04	-6.87	33.50	-1.55	100%
	#2	0.07	-13.83	43.83	-3.27	79.4%
Dog 3	#3	0.04	-9.83	45.53	-2.60	54.4%
	#4	0.05	-9.73	50.77	-2.57	52.8%
	#5	0.07	-13.67	61.13	-3.73	59.1%
	#6	0.06	-9.60	49.90	-2.86	36.1%
	#1 Control Sample	0.01	-4.90	25.90	-2.13	100%
	#2	0.01	-2.70	22.30	-0.52	57%
Dog 4	#3	0.11	-17.80	60.80	-4.40	38%
	#4	0.09	-19.63	70.97	-6.2	29%
	#5	0.14	-31.70	78.57	-4.56	21%
	#1 Control Sample	0.00	-5.00	32.10	-2.21	100%
	#2	0.05	-11.50	66.30	-3.22	93.5%
Dog 5	#3	0.06	-14.30	56.90	-3.59	52.5%
	#4	0.07	-19.80	53.20	-4.03	47.8%
	#5	0.08	-23.60	68.20	-5.94	46.8%
	#1 Control Sample	0.02	-0.33	6.60	-1.50	100%
	#2	0.05	-7.33	16.27	-1.29	72.9%
Dog 6	#3	0.04	-6.67	31.63	-1.63	56.5%
	#4	0.07	-17.80	59.10	-5.21	24.4%
	#1 Control Sample	0.01	-3.70	15.40	-1.15	100%
	#2	0.00	-2.40	24.20	-1.30	79.2%
Dog 7	#3	0.03	-7.70	47.30	-2.60	59.6%
	#4	0.05	-10.70	55.90	-2.99	31.7%
	#5	0.09	-16.60	67.40	-4.89	27.9%

TABLE V (Continued)

		pH	pCO_2	pO_2	$\{HCO_3^-\}$	% C.O. of Control
	#1 Control Sample	0.02	-6.40	24.93	-1.50	100%
	#2	0.05	-12.63	53.80	-2.86	72.4%
Dog 8	#3	0.00	-7.23	47.17	-2.89	61.1%
	#4	0.06	-15.20	65.83	-3.42	44.7%
	#5	0.11	-20.13	78.97	-3.79	36.3%
	#1 Control Sample	0.03	-6.20	32.50	-1.67	100%
	#2	0.03	-9.50	32.60	-2.07	89.2%
Dog 9	#3	0.01	-13.40	31.30	-5.25	77.6%
	#4	0.06	-18.10	48.10	-4.78	55.3%
	#5	0.12	-21.50	62.30	-4.85	46.1%
	#1 Control Sample	0.01	-3.43	20.67	-1.18	100%
	#2	0.04	-7.87	35.30	-2.05	69%
Dog 10	#3	0.05	-9.80	42.17	-2.69	54%
	#4	0.06	-12.60	43.13	-3.71	43%
	#5	0.06	-13.87	46.77	-3.16	33%

TABLE VI

Results of Paired t Test Between Control and Final Values for Arterial-Venous Differences for Dogs 2-10.

	Control A-V Difference		Final A-V Difference		Paired t	DF
	$\bar{X}$	S.D.	$\bar{X}$	S.D.		
pH	0.01	0.02	0.10	0.03	7.8490	8.000
pCO_2	-4.6	2.0	-20.2	6.8	6.7008	8.000
pO_2	25.9	10.5	66.1	12.9	8.7081	8.000
$\{HCO_3^-\}$	1.51	0.48	-4.48	1.0	9.2995	8.000

* $p < 0.001$

TABLE VII

Means and Standard Deviations for the A-V Differences for Each Blood-Gas Parameter According to Four Divisions of Percent Control of Cardiac Output.

	Cardiac Output in Percent of Control			
	85-100%	70-85%	55-70%	<55%
	N = 11	N = 7	N = 7	N = 20
pH	$\bar{X}$ = 0.02 S.D.= 0.01	$\bar{X}$ = 0.04 S.D.= 0.03	$\bar{X}$ = 0.04 S.D.= 0.03	$\bar{X}$ = 0.08 S.D.= 0.03
pCO_2	$\bar{X}$ = 5.7 S.D.= 3.0	$\bar{X}$ = 9.7 S.D.= 4.3	$\bar{X}$ = 9.1 S.D.= 5.1	$\bar{X}$ = 17.0 S.D.= 6.1
pO_2	$\bar{X}$ = 30.2 S.D.= 15.4	$\bar{X}$ = 38.3 S.D.= 14.7	$\bar{X}$ = 41.8 S.D.= 12.9	$\bar{X}$ = 60.4 S.D.= 12.3
$\{HCO_3^-\}$	$\bar{X}$ = 1.7 S.D.= 0.7	$\bar{X}$ = 2.6 S.D.= 1.4	$\bar{X}$ = 2.6 S.D.= 1.4	$\bar{X}$ = 4.0 S.D.= 1.1

Figure 6.

Arterial-mixed venous (A-mv) differences

for pH as a function of cardiac output

expressed as percent of control

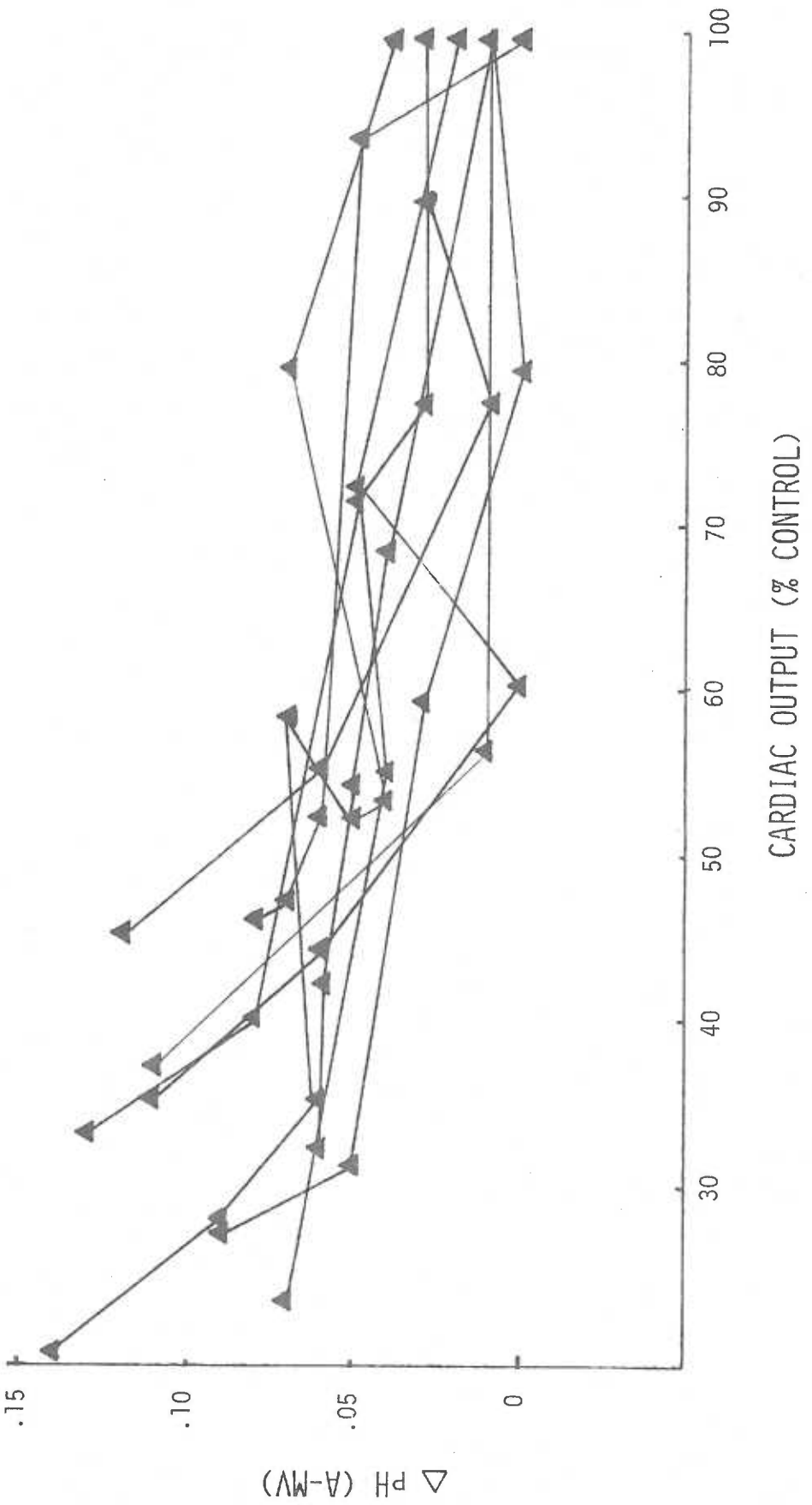

.15
.10
.05
0
Δ pH (A-MV)
30
40
50
60
70
80
90
100
CARDIAC OUTPUT (% CONTROL)

Figure 7.

Arterial-mixed venous pCO_2 differences

as a function of percent of

control of cardiac output

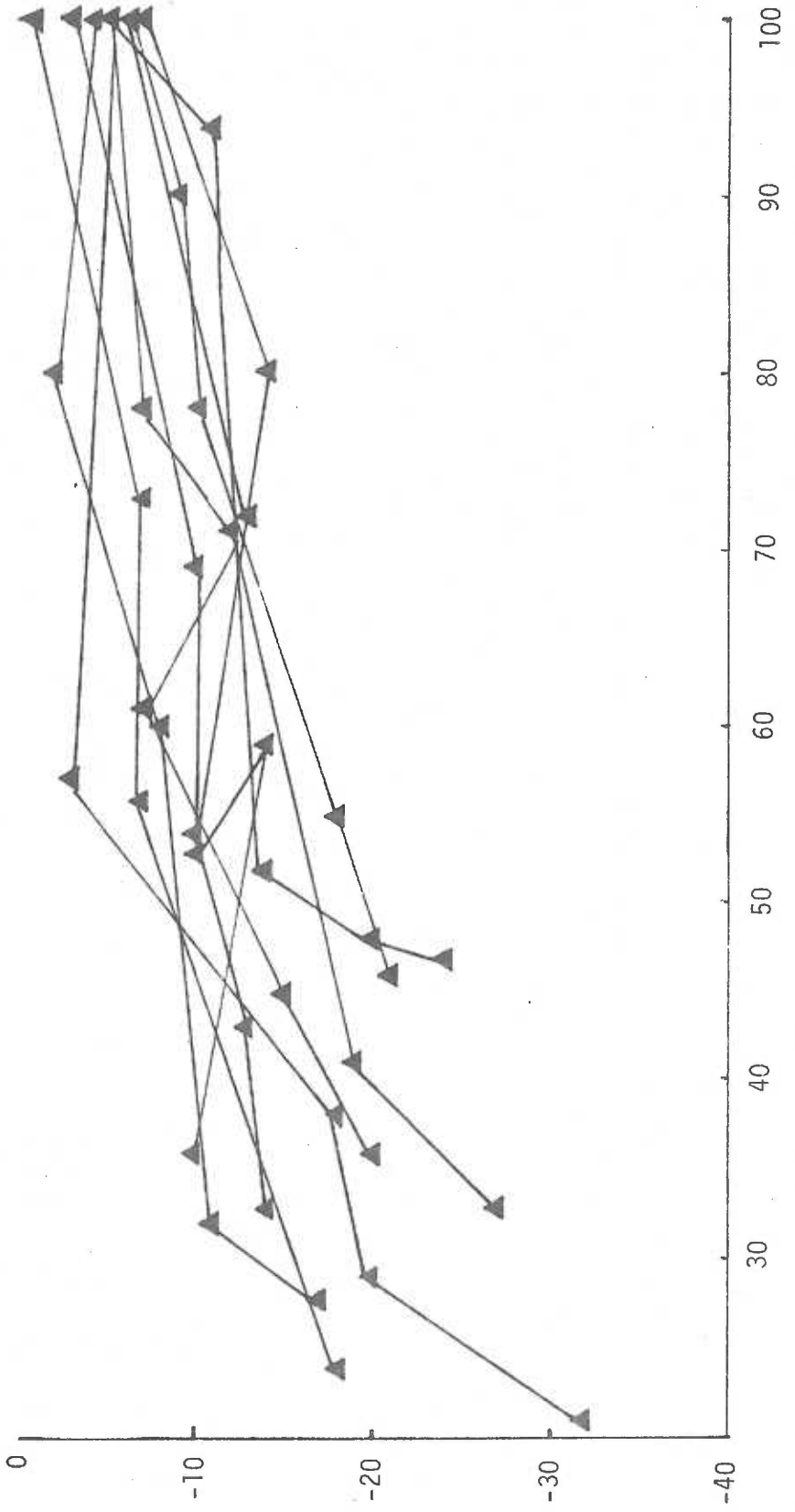

0
-10
-20
-30
-40
30
40
50
60
70
80
90
100
CARDIAC OUTPUT (% CONTROL)
Δ PCO2 (A-MV)

Figure 8.

Arterial-mixed venous PO_2 differences

as a function of percent of

control cardiac output

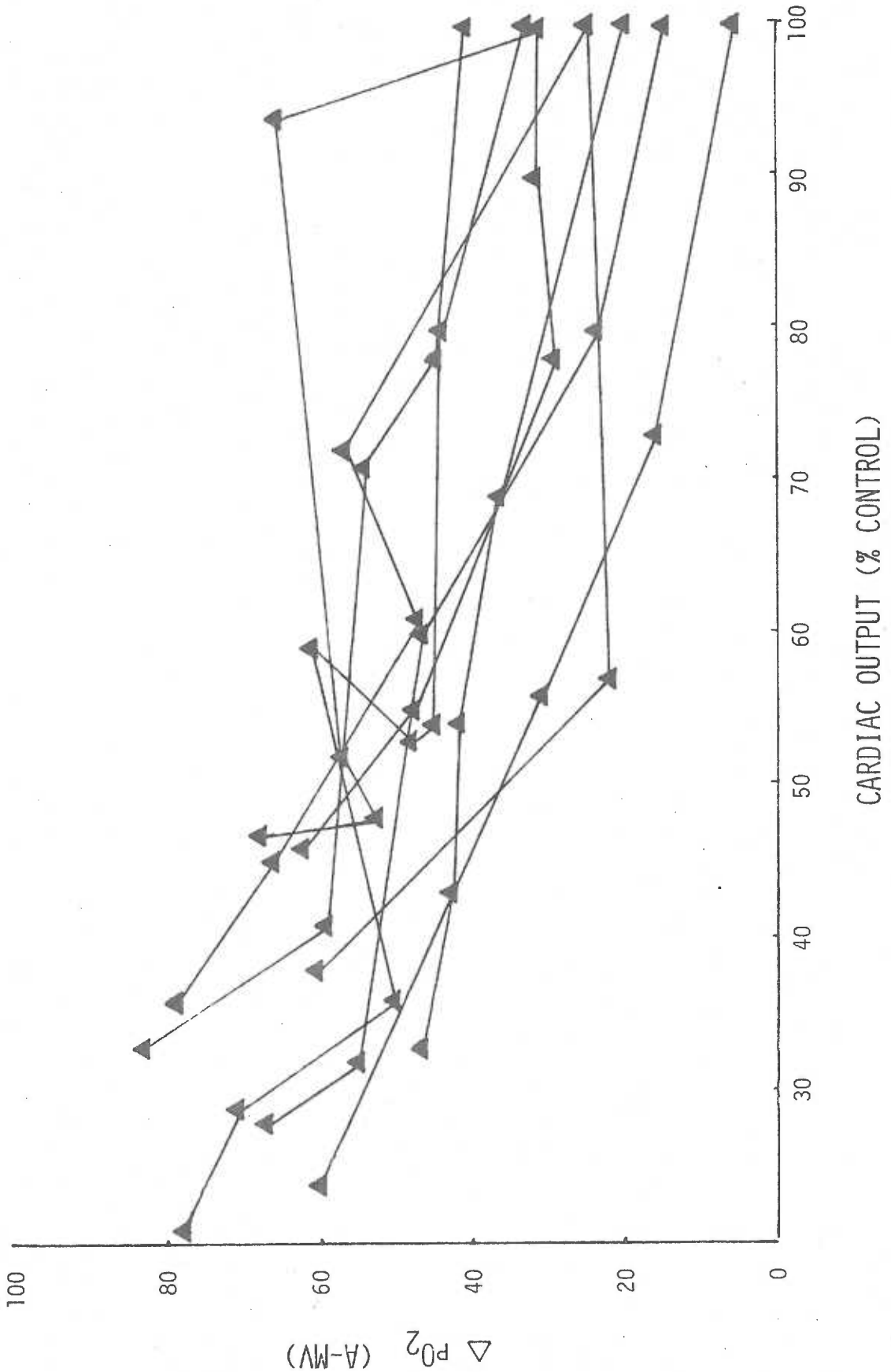

100
80
60
40
20
0
△ P_{O_2} (A-MV)
30
40
50
60
70
80
90
100
CARDIAC OUTPUT (% CONTROL)

Figure 9.

Arterial-mixed venous (HCO_3^-) Differences

as a function of percent of

control cardiac output

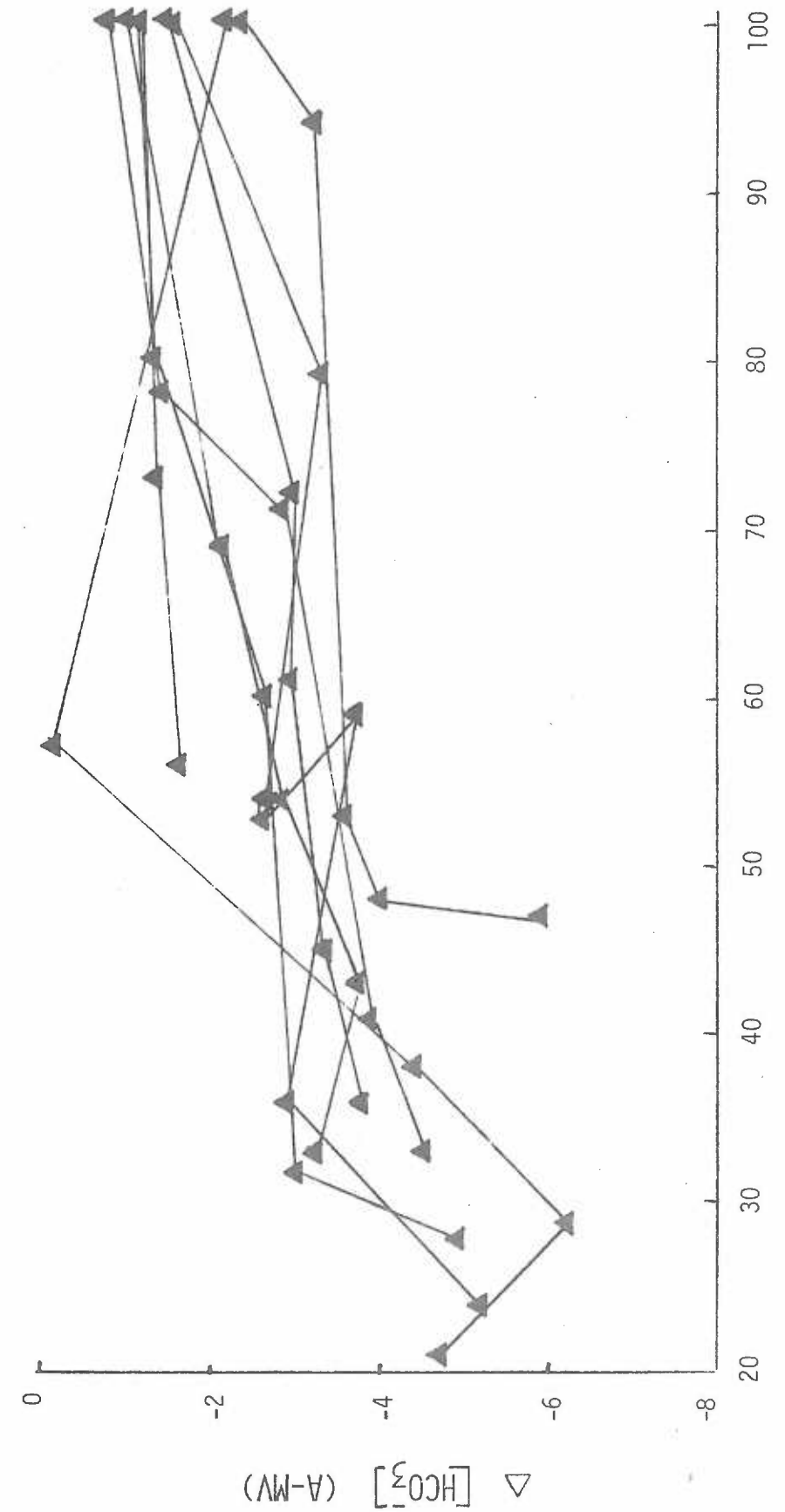

0
-2
-4
-6
-8
20
30
40
50
60
70
80
90
100
CARDIAC OUTPUT (% CONTROL)
Δ [HCO3-] (A-MV)

Figure 10.

Bar graph of mean arterial-mixed venous pH differences as a function of percent of control cardiac output

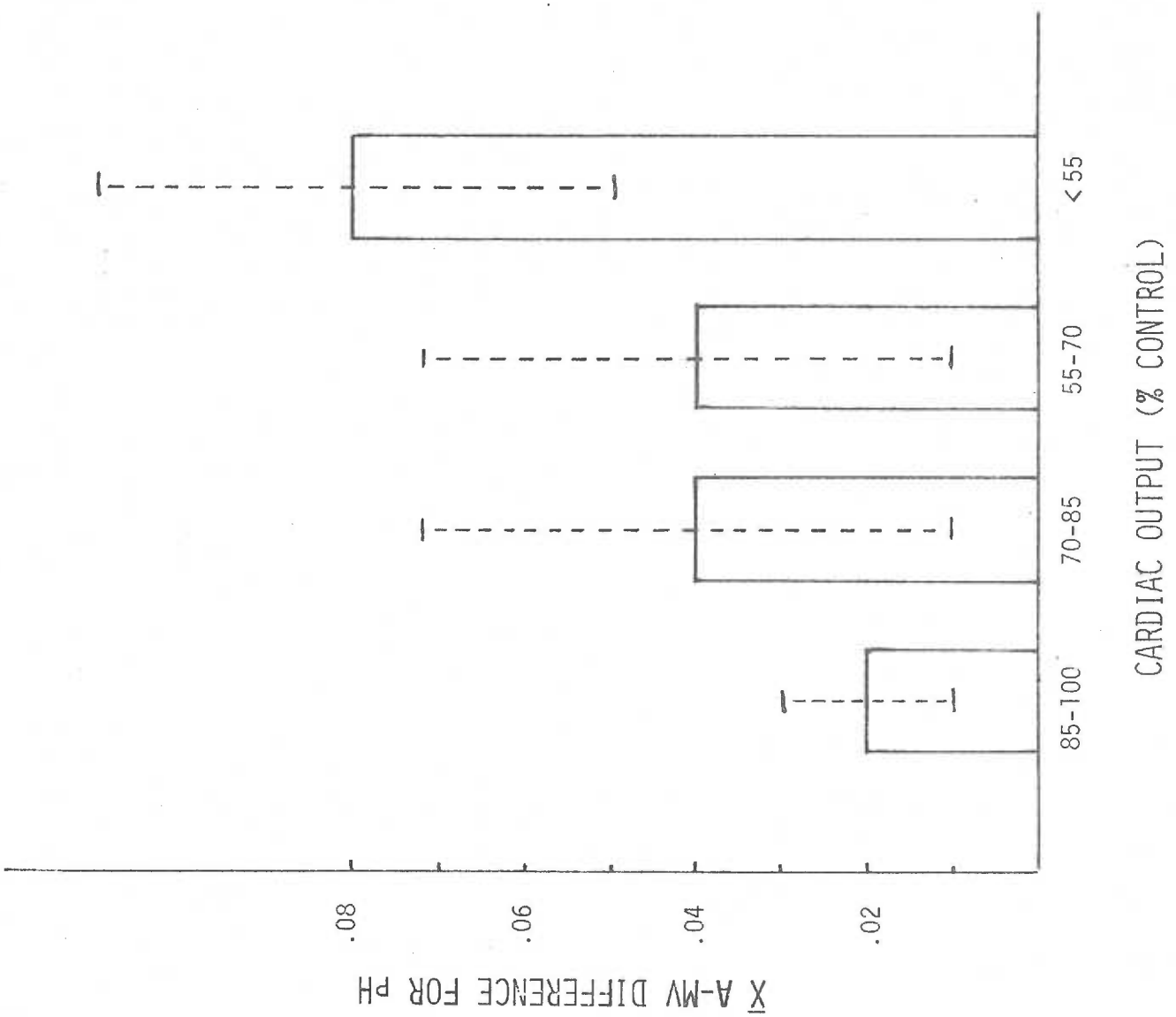

X A-MV DIFFERENCE FOR pH
.08
.06
.04
.02
CARDIAC OUTPUT (% CONTROL)
< 55
55-70
70-85
85-100

Figure 11.

Bar graph of mean arterial-mixed venous pCO_2 differences as a function of percent of control cardiac output

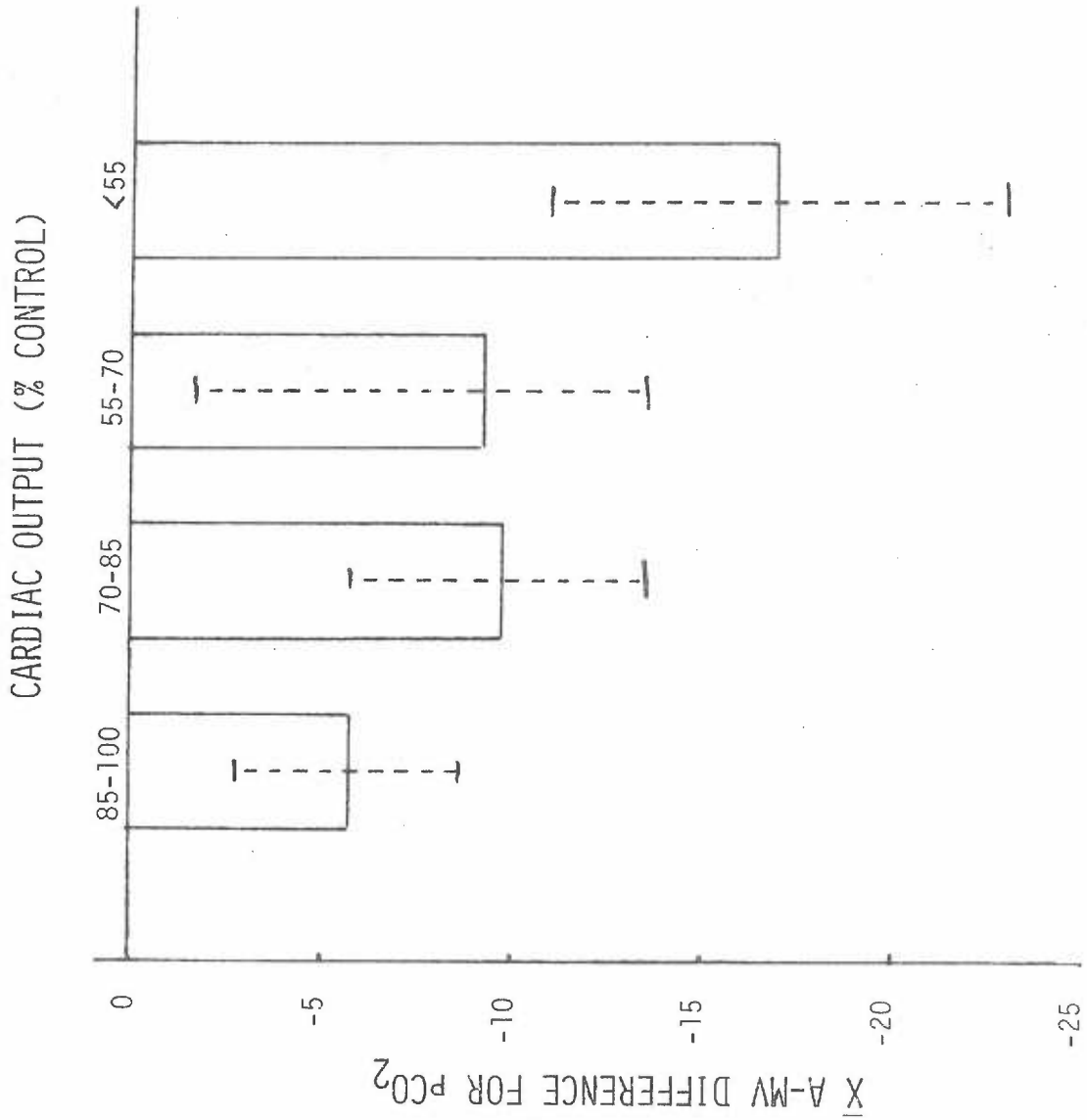

CARDIAC OUTPUT (% CONTROL)
<55
55-70
70-85
85-100
0
-5
-10
-15
-20
-25
$\bar{X}$ A-MV DIFFERENCE FOR PCO_2

Figure 12.

Bar graph of mean arterial-mixed venous PO_2 differences as a function of percent of control cardiac output

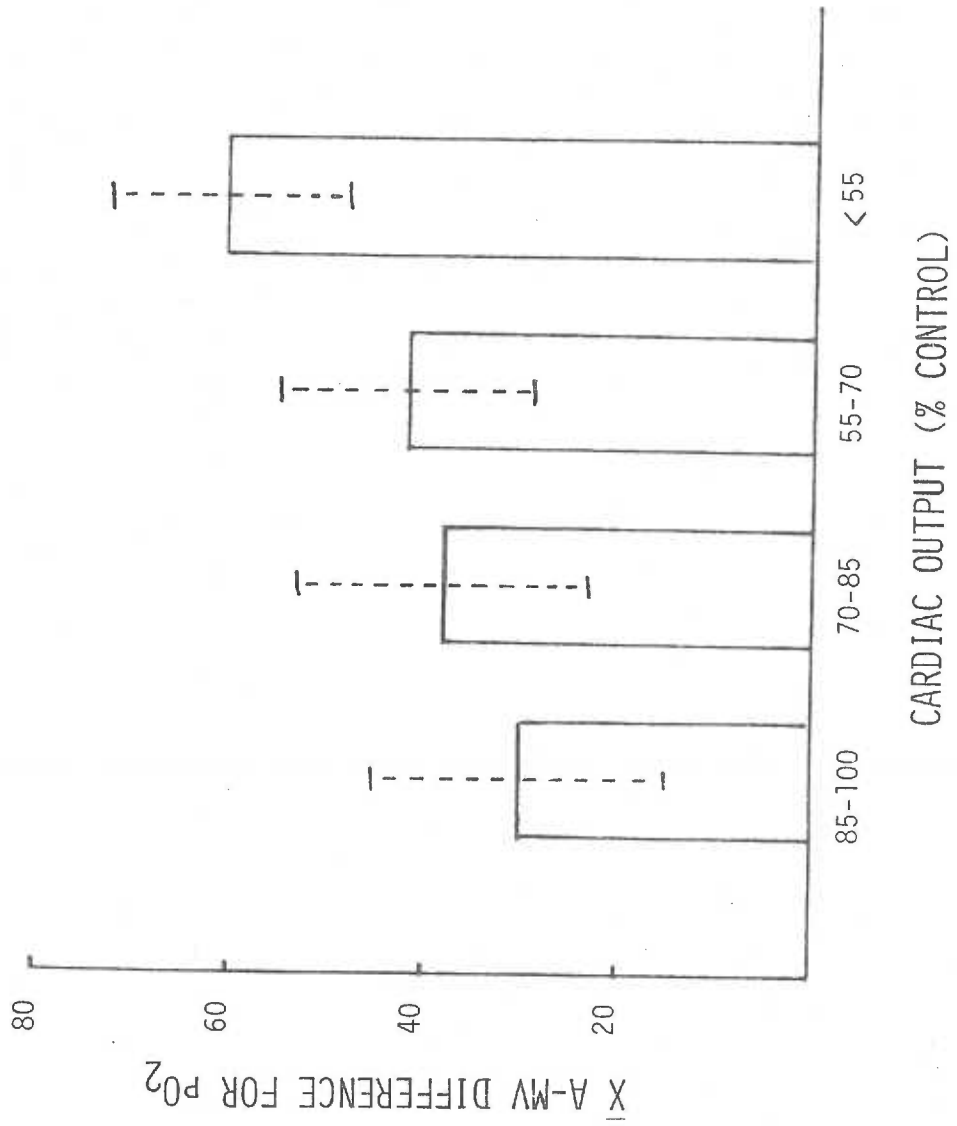

X A-MV DIFFERENCE FOR PO_2
80
60
40
20
CARDIAC OUTPUT (% CONTROL)
< 55
55-70
70-85
85-100

Figure 13.

Bar graph of mean arterial-mixed venous (HCO_3^-) differences as a function of percent of control cardiac output

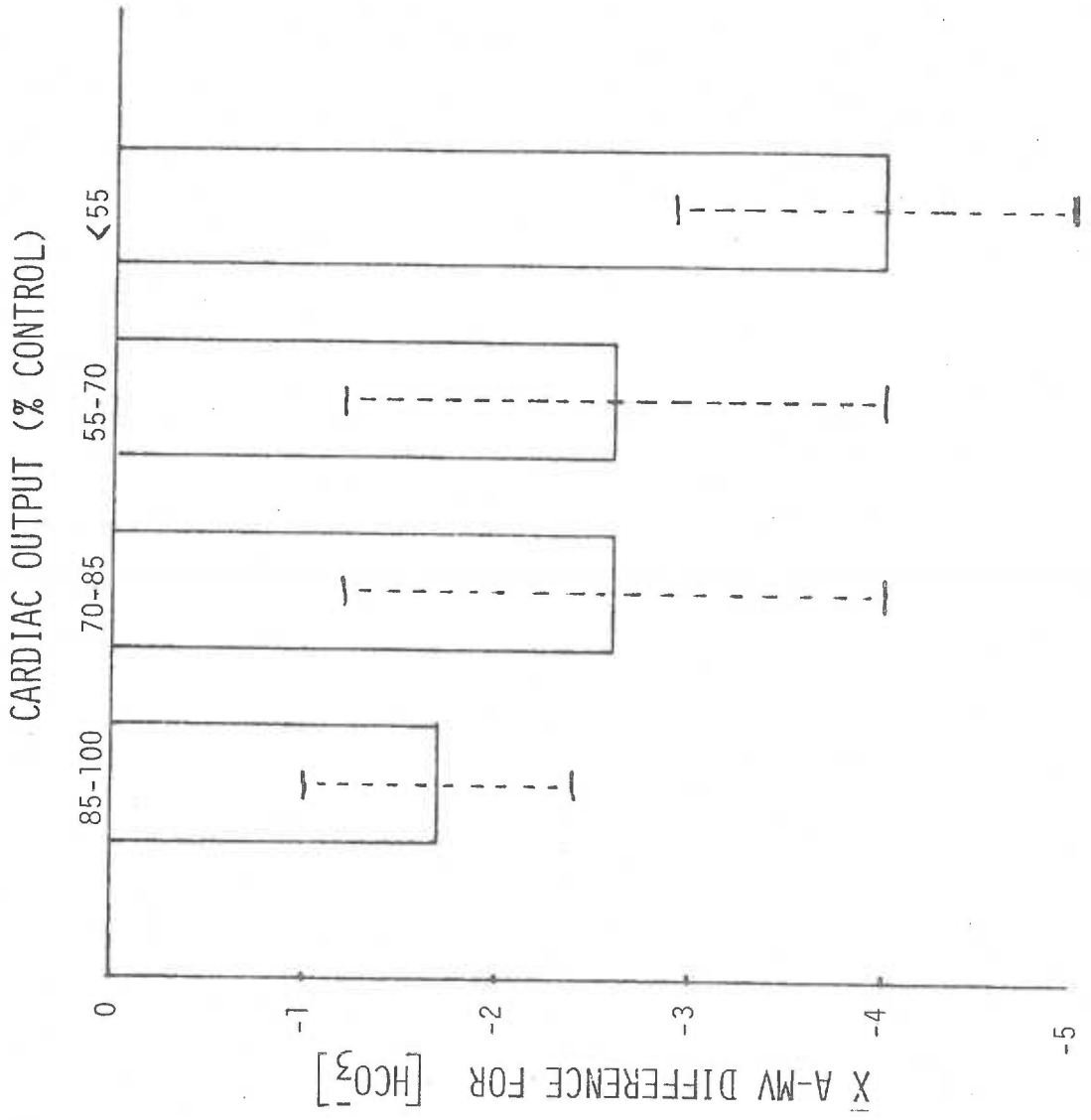
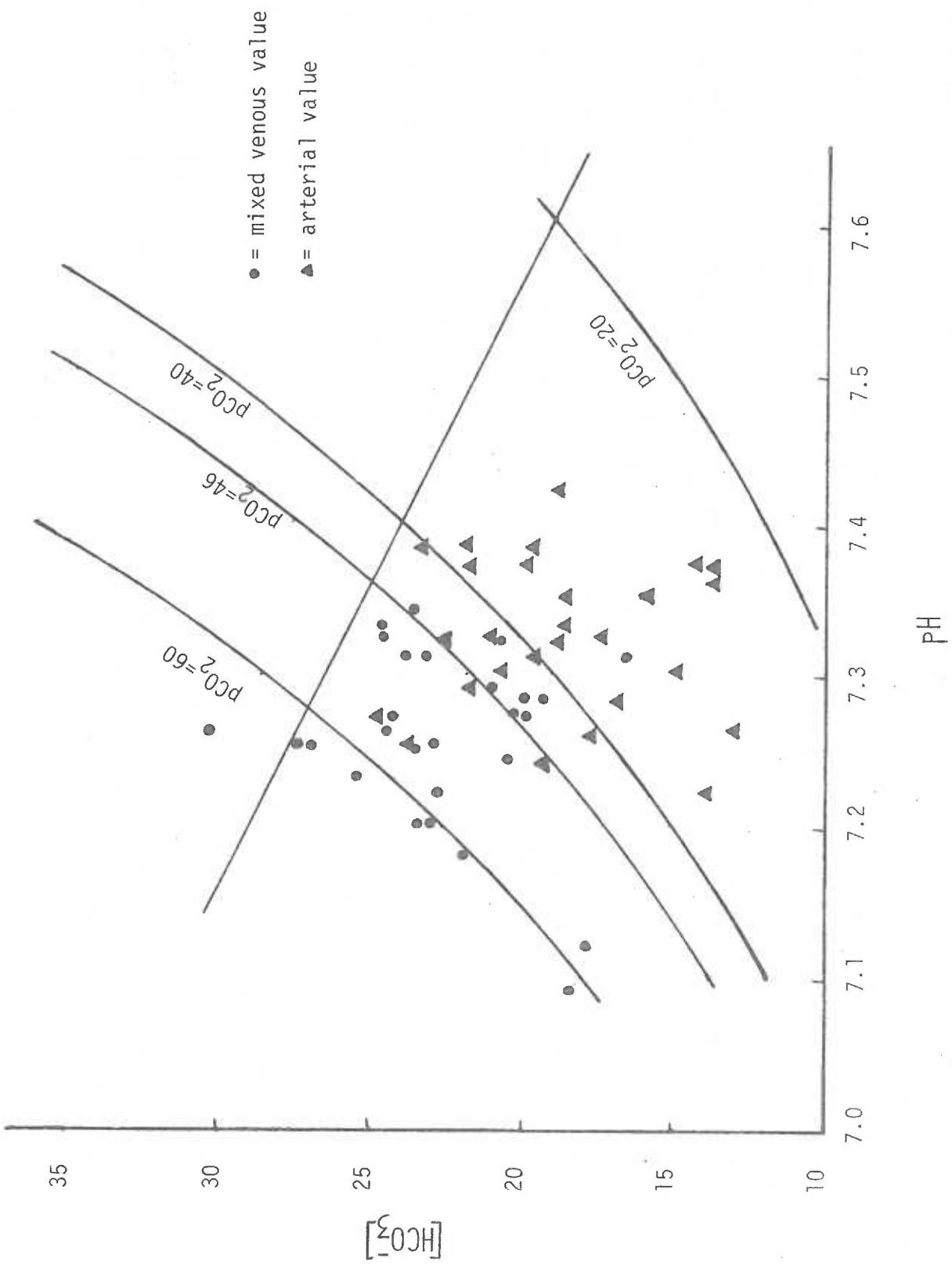

CARDIAC OUTPUT (% CONTROL)
<55
55-70
70-85
85-100
0
-1
-2
-3
-4
-5
X A-MV DIFFERENCE FOR [HCO3-]

Figure 14.

The last 3 valves of arterial and mixed venous blood—gas parameters for dogs 2-10 plotted on a pH/(HCO_3^-) diagram


● = mixed venous value
▲ = arterial value
PCO_2=60
PCO_2=40
PCO_2=20
PCO_2=46
$[HCO_3^-]$
35
30
25
20
15
10
7.0
7.1
7.2
7.3
7.4
7.5
7.6
pH

CHAPTER IV

DISCUSSION

The discussion is organized under four major headings:

1) How does arterial blood-gas composition compare to mixed venous blood-gas composition in states of decreasing cardiac output?
2) Does mixed venous blood-gas composition follow a predictable pattern in states of decreasing cardiac output?
3) Possible complications resulting from repeated sampling of mixed venous blood.
4) Implications for nursing practice.

How does arterial blood-gas composition compare to mixed venous blood-gas composition in states of decreasing cardiac output?

In the review of the literature it was established that the buffer slope of mixed venous blood represented the true in vivo buffer slope of the body. In addition it was suggested that the blood-gas values obtained from mixed venous blood represent the true status of the tissues regarding oxygenation and acid-base balance.

In this research, arterial and mixed venous blood-gas compositions were compared during stepwise decrements in cardiac output. Each blood-gas parameter is discussed separately in order to more clearly delineate the differences in arterial and mixed venous blood.

pH-

The mean initial pH for mixed venous blood was less than that for arterial blood. This difference can be attributed to the addition of acids from metabolic activity of tissue cells to capillary blood which

flows into veins.

After reduction of cardiac output the mean final value for pH decreased in both arterial and mixed venous blood but the decrement was more precipitous for mixed venous blood. The more pronounced decrease in pH of mixed venous blood can be explained by both a decreased oxygen delivery due to reduced cardiac output and a continued CO_2 production by tissue cells. A decreased O_2 delivery leads to tissue hypoxia and anaerobic metabolism with increased production of lactic acid. This acid decreases the pH of venous blood. In addition, low blood flow allows the CO_2 produced by cell metabolism to accumulate and shifts equation 1 to the right increasing the $\{H^+\}$. The arterial pH decreased because of the metabolic acidosis from anaerobic metabolism but this decrease is moderated by respiratory compensation. The increased $\{H^+\}$ and decreased pressure in arterial blood stimulates ventilation and the resultant decreased arterial pCO_2 moderates the fall in pH (equation 1).

$\underline{pCO_2}$ -

The mean arterial pCO_2 decreased from a control value of 47.8 to 31.9 torr as a result of the hemorrhage. This can again be explained by the effect of the increased alveolar ventilation rate.

The mean mixed venous pCO_2 was essentially unchanged from control to final values. This is somewhat contrary to findings of Tung et al. (1976) who found an increase in mixed venous pCO_2 after hemorrhage. The discrepancy can be explained by looking at what processes are involved in determining the mixed venous pCO_2. From equation 2 it can be seen that mixed venous pCO_2 is a function of cardiac output ($\dot{Q}$), arterial $\{CO_2\}$, metabolic CO_2 production and the fraction of CO_2 produced that is transported as physically dissolved CO_2. Since there was no reason

to suppose there was a change in metabolic production of CO_2, the mixed venous pCO_2 is a reflection of two processes. One is the systemic delivery to the capillary bed ($\dot{Q}\{CO_2\}_a$), and the second is the reduced blood flow due to the decreased cardiac output. Since both the cardiac output and the arterial pCO_2 decreased, there was a decreased delivery to the capillary bed. This decreased delivery offset the increased accumulation on the venous side due to the low blood flow such that there was no net change in mixed venous pCO_2.

$\underline{pO_2}$ -

The mean arterial pO_2 increased from a control value of 76.2 torr (>95% saturation) to a final value of 93.5 torr (>99% saturation). The change in oxygen saturation caused by this increase is minimal. This increased pO_2 is due to the increased alveolar ventilation rate caused by the increased $\{H^+\}$ and the reduced blood pressure.

The mean mixed venous pO_2 decreased from a control value of 50.3 (~80% saturation to 27.4 torr (~50% saturation) (Figure 5, p. 31). At low pO_2 values the oxygen dissociation curve is more linear so each decrement in pO_2 has a more marked effect on oxygen saturation. This finding is in agreement with those of Tung, et al. (1976) and represents a state of acute tissue hypoxia even though arterial pO_2 is within normal limits or as in these experiments greater than control values.

$\underline{HCO_3^-}$ -

Mixed venous $\{HCO_3^-\}$ was always greater than arterial $\{HCO_3^-\}$. The $\{HCO_3^-\}$ decreased in both arterial and mixed venous blood with hemorrhage; however, the fall was more precipitous in the arterial blood. Thus, the A-V differences for $\{HCO_3^-\}$ increased.

Arterial $\{HCO_3^-\}$ decreased by 44% while mixed venous $\{HCO_3^-\}$ decreased by only 34%. These findings are as predicted and were also reported by Tung, et al. (1976).

The more precipitous drop in arterial $\{HCO_3^-\}$ can be explained by again examining equation 1. As ventilation is stimulated by increased $\{H^+\}$, carbon dioxide is expired and the reaction shown in equation 1 shifts to the left. This shift reduces the $\{HCO_3^-\}$ in the arterial blood. In the venous circulation, the low blood flow from decreased cardiac output tends to allow accumulation of CO_2 which increases $\{HCO_3^-\}$ and partly counteracts the decrease due to buffering of lactic acid. Thus, both arterial and mixed venous $\{HCO_3^-\}$ decreased due to buffering of fixed acids produced during the metabolic acidosis from tissue hypoxia.

Does mixed venous blood-gas composition follow a predictable pattern in states of decreased cardiac output?

It has been shown in the previous section and in the results that the A-V differences increased for all blood-gas parameters when cardiac output was reduced. This can be seen in Figures 6-13. Thus, one can argue that increased arteriovenous differences constitute a pattern.

From a physiological point of view it can be expected that reduced cardiac output can lead to increased anaerobic metabolism in systemic tissues. The lactic acid would enter the blood in systemic capillaries and decrease the pH and $\{HCO_3^-\}$. In addition to the baroreceptor response to decreased blood pressure, the increased $\{H^+\}$ would stimulate peripheral (and possibly central) chemoreceptors thereby increasing alveolar ventilation rate which in turn decreases alveolar and thus arterial pCO_2. These processes would cause the pH, pCO_2, and $\{HCO_3^-\}$ to decrease while the arterial pO_2 would increase. These changes in arterial blood result-

ing from the above processes can be displayed on the pH/$[HCO_3^-]$ diagram (Figure 15, Area A).

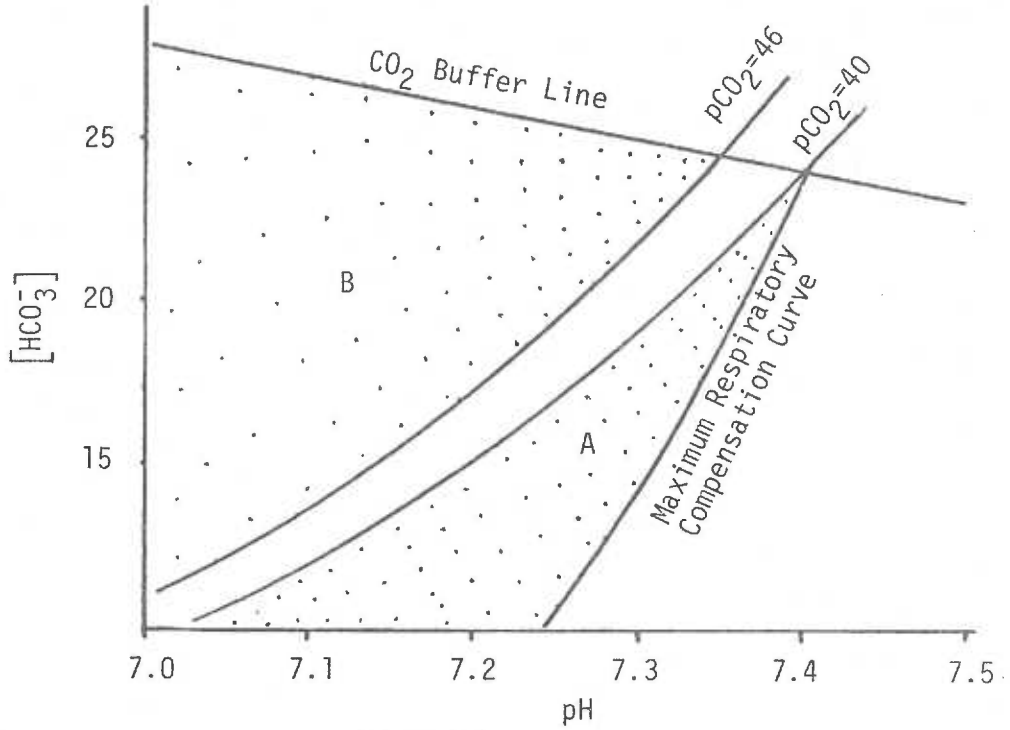


Figure 15

pH/$[HCO_3^-]$ diagram showing areas of compensated metabolic acidosis (Area A) and combined metabolic and respiratory acidosis (Area B).

Normal mixed venous blood-gas values are slightly different from arterial. The pCO_2 is usually about 46 torr. The increased pCO_2 in venous blood results in a slightly lower pH because of the reaction seen in equation 1. This reaction will also result in a slightly higher $[HCO_3^-]$ in mixed venous blood. The normal pO_2 in mixed venous blood is about 40 torr.

Reducing cardiac output as a result of hemorrhage can be expected to cause a decreased pH due to anaerobic metabolism and accumulated lactic acid. Increased pCO_2 results from continued tissue production despite low blood flow with resultant accumulation in the venous blood.

The $\{HCO_3^-\}$ will be greater than that in arterial blood but lower than normal. The mixed venous values resulting from this reduced cardiac output will fall within the shaded area (B) in Figure 15.

Assessing acid-base status based on arterial and mixed venous blood, one would arrive at different interpretations. Arterial blood-gas analysis would lead to the diagnosis of compensated metabolic acidosis whereas mixed venous blood would indicate a combined (mixed) acidosis with both metabolic and respiratory components. (It should be emphasized that the respiratory acidosis in mixed venous blood is recognized by a pCO_2 greater than 46 torr).

Figure 14 depicts that the blood-gas values of arterial and mixed venous blood reflect these predictions. Furthermore, since mixed venous blood represents a flow weighted average of venous blood and represents output from the tissues it can be argued that the acid-base assessment from the mixed venous blood is the more accurate regarding tissue status. Furthermore, arterial blood when used for acid-base assessment may give misleading information regarding the tissues. The conclusion reached from the review of the literature and the results of this research is that mixed venous blood represents the most accurate sample for determining the acid-base status of the tissues, especially in instances of reduced cardiac output.

Possible complications resulting from repeated sampling of mixed venous blood.

Throughout this study, use of mixed venous blood obtained from the pulmonary artery has been suggested for use in assessment of acid-base status. It is pertinent at this time to comment on the pulmonary artery catheter and point out that catheterization of the pulmonary artery is

not a totally innocuous procedure. In addition, repeated blood sampling from the catheter may pose an added threat with respect to infection and possible introduction of air.

Size, Hollingsworth, Brimm, Peters, Vergilio and Shackford (1981) did a prospective study in 219 critically ill patients to assess the complication rate of insertion and maintenance of flow-directed pulmonary artery catheters.

All patients had the catheter inserted by housestaff using a gowned sterile technique. Insertion sites were either pre-existing central venous catheter sites or the subclavian, internal jugular, cephalic or femoral veins. All patients had a separate intravenous infusion maintained prior to insertion or the PA catheter and continued throughout the period of pulmonary artery catheter insertion.

There was a 3% (N=10) occurrence of major complications (9 during catheter insertion and 1 during catheter maintenance). These major complications included pneumothorax, arrhythmias requiring treatment and subclavian venous thrombosis.

Minor complications included arterial puncture, venous bleeding and infection. Cellulitis occurred at the insertion site in 16% of the patients with a mean duration of catheterization of 108 $\pm$ 9 hours. Catheter related sepsis was seen in 8% of the patients. Mean catheterization in this group was 103 $\pm$ 9 hours. The increased rate of infection was directly related to duration of catheterization. A final category of minor complications were arrythmias not requiring treatment. The rate of this complication was 10%.

The authors concluded that pulmonary artery catheterization was associated with morbidity but the benefits of the procedure in critically

ill patients often outweighed the risk. To control possible complications the following factors should be recognized:

1) Risks of sepsis were rare prior to 72 hours but increased significantly after this time. Thus, it was suggested catheters should be replaced after 72 hours.
2) Scrupulous sterile technique must be observed.
3) The insertion and maintenance of a separate intravenous infusion allowed prompt treatment of arrythmias and decreased the mortality of this complication.

Puri, Carlson, Bander, and Weil (1980) did a prospective study on the complications of vascular catheterizations. They investigated central venous, pulmonary artery, and arterial catheterizations. All patients were critically ill patients and catheters were inserted by six postgraduate fellows in critical care medicine.

Pulmonary artery catheterization had a complication rate of 10%. These complications included bleeding, transient ectopic heart beats, ventricular tachycardia and catheter related sepsis.

These authors concluded that complications of PA catheters are more frequent than anticipated. Because the PA catheters were associated with complications of sepsis, it was speculated there might be an increase in catheter related sepsis and right heart endocarditis with prolonged use. They also concluded PA catheters were especially susceptible to contamination not only due to the central placement but also due to repeated breaks in the closed system to obtain cardiac output measurements. (It can be expected that increased sampling for blood-gas assessment might further increase this complication).

It is interesting to note that in this prospective study, arterial catheterization had the highest incidence of complications. These complications included critically reduced arterial flow, bleeding and hematoma, emboli, and one instance of hemorrhage requiring blood transfusions.

Implications for nursing practice.

In the previous section it has been stated that mixed venous blood represents the preferred sampling site for acid-base assessment. In addition it was established that PA catheterization is not without risk of complications for the patient. In this section the implications of these two conclusions will be discussed in regard to the practice of professional nursing.

Nurses who care for critically ill patients are in a unique situation for monitoring the patient. In addition their ability to gather all data regarding the patient allows them an opportunity for total assessment and optimal management. Some nursing practice implications are as follows:

1) If a patient already has a PA catheter in place, the nurse can be an advocate by suggesting use of mixed venous blood for assessment of acid-base status. As seen by the work of Bieber (1979) and Griffith (1980) mixed venous blood-gas values are closely correlated to arterial blood-gas values over wide ranges of acid-base disturbances. In addition, if cardiac output is decreased, mixed venous blood is the site of choice for sampling and finally the complication rate of PA catheters has been found to be less than that of indwelling arterial catheters. Therefore, the nurse might use this data to encourage use of mixed venous blood when a PA catheter is already in place. (It must be re-

membered that if pulmonary function is to be assessed, arterial blood is the site of choice).

2) The nurse must be aware of the possible complications from PA catheterizations and sampling. Breaks in the system for cardiac output determinations or sampling for blood-gas analysis must be done judiciously based on careful assessment. Scrupulous attention to sterile technique must be maintained. The nurse must monitor both her own technique and that of other personnel to insure adequacy of sampling and safety of technique.

3) If arterial blood is being used for acid-base assessment, the nurse must be careful in her assessment to include parameters of cardiac output assessment. If the patient does indeed have decreased cardiac output her interpretation of the results of the blood-gas analysis must reflect this fact.

4) Since it is not feasible that every patient would have a central line in place for sampling of mixed venous blood, it would be of interest and usefulness for nurses to be involved in research which seeks to find alternate sources of blood which could be used for acid-base assessment. Possibilities for these sites include peripheral venous blood, arterialized peripheral venous blood, or femoral venous blood. Involvement in clinical research would also be important in corroborating these research findings in the clinical setting.

5) Finally, the nurse can use her knowledge to encourage others involved in patient care to make the proper judgements regarding assessment of acid-base balance and proper site selection for information needed.

Limitations of the study.

The obvious limitation to this research is that it is based on a

mammalian model involving small numbers. In addition the problems of initial respiratory acidosis in some animals and widely varying cardiac outputs made comparisons more difficult. However, despite these problems, there is no doubt that based on the theoretical model, the predictions, and the results, the findings are sound regarding both acid-base physiology and the accurate assessment of tissue acid-base status.

Chapter V

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary and Conclusions

Currently arterial blood is used for assessment of acid-base status. This research investigated the use of mixed venous blood as an alternate site for assessment of acid-base status in states of reduced cardiac output.

Ten, mongrel dogs were used in the experiments. Stepwise decrements in cardiac output were accomplished by periodic bleeding from the femoral artery. Cardiac output determinations and simultaneous arterial and mixed venous blood samples were obtained for blood-gas analysis.

Results showed that arterial and mixed venous blood-gas analysis provides different information regarding acid-base status in decreased states of cardiac output. A-V differences for all parameters (pH, pCO_2, $\{HCO_3^-\}$ and pO_2) were increased as a result of the hemorrhage. In addition, mixed venous blood showed a pattern of mixed (combined) metabolic and respiratory acidosis, while arterial blood-gas analysis showed a compensated respiratory acidosis.

Based on these results it can be concluded that arterial and mixed venous blood show different patterns of acid-base status in states of decreased cardiac output. Furthermore, because mixed venous blood represents output of the tissues, it can be concluded that mixed venous blood is the preferred site for sampling blood to assess acid-base status of interstial fluid.

Recommendations for Further Study

Because this research was based on a mammalian model and because it has been shown that PA catheterization can have complications for the patient there are several obvious recommendations for further research. These recommendations are as follows:

1) Research in clinical settings comparing mixed venous blood-gas composition and arterial blood-gas composition during states of reduced cardiac output.

2) Research conducted investigating other sources of venous blood that might be used for assessment of acid-base status that may be less of a risk to the patient.

3) Research conducted in states of reduced cardiac output due to other shock states - i.e. cardiogenic, septic, etc. to investigate relationships between arterial and mixed venous blood-gas analysis in these instances.

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APPENDIX A

Raw data from 10 Experimental Animals Showing Blood-Gas Parameters Obtained During Induced States of Decreased Cardiac Output.

DOG 1
41# (18.6 kg)
2/13/81

	PH $\bar{X}$	S.D.	pCO_2 $\bar{X}$	S.D.	pO_2 $\bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}$ $\bar{X}$
Control									
Arterial	7.3780	.0010	40.3		77.3333	.0577	2.6133	0.2483	23.0076
Mixed Venous	7.367	.0010	44.1		50.1667	0.2082	100%		24.5474
Sample									
Arterial	7.3953	.0021	37.2333	0.0577	84.6333	0.1528	2.230	0.2352	22.1207
Mixed Venous	7.373	.0015	43.5667	0.0577	48.1333	0.1528	(85.3%)		24.5879
Sample 3									
Arterial	7.424	.0091	33.3333	.0577	87.6000	0.5292	1.6533	.0493	21.1565
Mixed Venous	7.3980	.0010	36.557	0.1528	43.5667	0.2082	(63.3%)		21.8543
Sample 4									
Arterial	7.3000	.0010	39.4		84.600	0.1000			18.7959
Mixed Venous	7.4357	.0023	23.6		77.2333	0.1155	1.51		15.3879
Sample 5									
Arterial	7.3283	0.0015	37.2		91.733	0.2887	1.31		18.9413
Mixed Venous	7.4880	0.0017	19.1667	0.1155	102.0333	0.1528	(50.1%)	0.0513	14.0966
Sample 6									
Arterial	7.2950	.0010	32.5000	0.1000	90.1000	0.1000	0.9575	0.0435	15.3267
No Mixed Venous Sample							(36.6%)		

DOG 2
28# (12.7 kg)
2/20/81

	PH $\bar{X}$	S.D.	pCO_2 $\bar{X}$	S.D.	pO_2 $\bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}$ $\bar{X}$
Control									
Arterial	7.3520	.0026	46.2333	0.0577	83.0000	0.6000	1.5333	0.1234	24.8612
Mixed Venous	7.3227	.0021	50.8000	0.2000	41.7000	0.4359	(100%)		25.5347
Sample 2									
Arterial	7.3123	0.0025	47.6333	0.0577	85.2667	0.3055	1.2000	0.0141	23.3764
Mixed Venous	7.2817	.0029	54.2000	0.1000	40.3667	0.0577	(78.2%)		24.7894
Sample 3									
Arterial	7.3010	.0017	43.0		91.4333	0.4509	1.0967	0.0252	20.5606
Mixed Venous	7.2503	0.0025	54.8667	0.0577	37.4000	0.1732	(71.5%)		23.3440
Sample 4									
Arterial	7.2627	.0021	40.6333	0.1155	98.2667	0.3055	0.6300	0.0100	17.7889
Mixed Venous	7.1843	0.0025	59.4333	0.0577	29.0667	0.5508	(41.1%)		21.7218
Sample 5									
Arterial	7.2183	0.0012	34.6000	0.1000	107.3333	0.6110	0.5133	0.0153	13.6755
Mixed Venous	7.0910	.0020	61.9000	0.1000	24.0333	0.3512	(33.5%)		18.2498

DOG 3
29# (13.2 kg)
2/27/81

	$pH\ \bar{X}$	S.D.	$pCO_2\ \bar{X}$	S.D.	$pO_2\ \bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}\ \bar{X}$
Control									
Arterial	7.3317	0.0025	42.3333	0.0577	87.2333	0.5132	1.845	0.0212	21.7244
Mixed Venous	7.2963	0.0021	49.2		53.7333	0.7638	(100%)		23.2719
Sample 2									
Arterial	7.36	0.00	37.57	0.06	93.33	0.12	1.4650	0.0071	20.5782
Mixed Venous	7.2880	0.0017	51.4	0.00	49.5000	0.4359	(79.4%)		23.8523
Sample 3									
Arterial	7.3123	0.0025	40.2333	0.0577	91.2667	0.0577	1.0033	0.0379	19.7448
Mixed Venous	7.271	0.0000	50.0667	0.1155	45.7333	0.3215	(54.4%)		22.3417
Sample 4									
Arterial	7.3340	0.0020	35.1000	0.1000	92.1333	0.1155	0.9740	0.1006	18.1081
Mixed Venous	7.2853	0.0006	44.8333	0.1528	41.3667	0.0577	(52.8%)		20.6760
Sample 5									
Arterial	7.3517	0.0029	29.5333	0.0577	98.3333	0.1528	1.0900	0.0975	15.8701
Mixed Venous	7.2783	0.0012	43.2000	0.1000	37.2000	0.2646	(59.1%)		19.6043
Sample 6									
Arterial	7.3667	0.0023	24.4000	0.1000	94.3000	0.1732	0.6667	0.0929	13.5724
Mixed Venous	7.3057	.0025	34.0	0.0000	44.4000	0.1732	(36.1%)		16.4341

DOG 4
42# (19.1 kg)
3/6/81

	$pH\ \bar{X}$	S.D.	$pCO_2\ \bar{X}$	S.D.	$pO_2\ \bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}$
Control									
Arterial	7.370	.0021	38.9	.0577	73.2	.0577	3.25		21.8030
Mixed Venous	7.359	.0012	43.8	0	47.3	.1	(100%)		23.9354
Sample 2									
Arterial	7.264	0.002	52.8	0.0577	56.4	.2887	1.84		23.1846
Mixed Venous	7.252	.0006	55.5	0.1528	34.1	.5000	(57%)		23.7061
Sample 3									
Arterial	7.421	0.0017	29.4	0.1155	85.6	0.5568	1.25		18.5316
Mixed Venous	7.308	.0	47.2	.0577	24.8	0.2646	(38%)		22.9355
Sample 4									
Arterial	7.362	.001	24.8	0	93.57	0.51	0.93		13.47
Mixed Venous	7.27	0.00	44.43	0.12	22.60	0.30	(29%)		19.67
Sample 5									
Arterial	7.26		23.83	0.06	96.87	0.47	0.667		12.92
Mixed Venous	7.12	0.00	55.53	0.31	18.30	0.20	(21%)		17.48

DOG 5
35# (15.9 kg)
3/13/81

	pH $\bar{X}$	S.D.	pCO_2 $\bar{X}$	S.D.	pO_2 $\bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}\bar{X}$
Control									
Arterial	7.242	0.0012	57.7	0.1	86.4	0.2887	1.86		24.0848
Mixed Venous	7.244	0.0020	62.7	0.1732	54.3	0.4163	(100%)		26.2926
Sample 2									
Arterial	7.355	0.0025	39.6	0	115.2	0.2082	1.74		21.4418
Mixed Venous	7.305	0.002	51.1	0	48.9	0.4933	(93.5%)		24.6597
Sample 3									
Arterial	7.324	0.0006	41.3	0.0577	100.1	0.1155	.97		20.8217
Mixed Venous	7.264	0.0021	55.6	.0577	43.2	.4509	(52.5%)		24.414
Sample 4									
Arterial	7.238	.0021	46.1	0	91	.4359	.89		19.0663
Mixed Venous	7.116	.0021	65.9	.1155	37.8	.3512	(47.8%)		23.0915
Sample 5									
Arterial	7.279	.0012	37.0	.0577	95.5	.3464	.87		16.8178
Mixed Venous	7.196	.0020	60.6	.0577	27.3	.0577	(46.8%)		22.7530

DOG 6

42# (19.1 kg)

3/20/81

	$pH\ \bar{X}$	S.D.	$pCO_2\ \bar{X}$	S.D.	$pO_2\ \bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}\ \bar{X}$
Control									
Arterial	7.3573	0.0015	43.4667	0.0577	51.4667	0.2517	3.1033	0.0058	23.6605
Mixed Venous	7.3807	0.0006	43.8	0.0000	44.8667	0.2082	(100%)		25.1617
Sample 2									
Arterial	7.3750	0.0017	41.0	0.0000	58.0667	0.1155	2.2633	0.0833	23.2461
Mixed Venous	7.3270	0.0017	48.3333	0.1155	41.8000	0.1000	(72.9%)		24.5365
Sample 3									
Arterial	7.3830	0.0017	37.7667	0.0577	68.4333	0.3215	1.7525	0.0538	21.8110
Mixed Venous	7.3437	0.0015	44.4333	0.0577	36.8000	0.1000	(56.5%)		23.4409
Sample 4									
Arterial	7.3033	0.0021	30.8667	0.0577	78.5333	0.1528	0.7567	0.1150	14.8374
Mixed Venous	7.2363	0.0015	48.6667	0.1528	19.4333	0.4041	(24.4%)		20.0493

DOG 7
45# (20.5 kg)
4/4/81

	$pH\ \bar{X}$	S.D.	$pCO_2\ \bar{X}$	S.D.	$pO_2\ \bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}\ \bar{X}$
Control									
Arterial	7.269	.002	50.1	.2	64.2	.1528	3.12		22.2538
Mixed Venous	7.260	.002	53.8	.2646	48.8	.0577	(100%)		23.4072
Sample 2									
Arterial	7.285	.0015	43.4	.4509	71.9	.3512	2.47		20.0012
Mixed Venous	7.289	.0015	45.8	.3786	47.7	.2646	(79.2%)		21.3026
Sample 3									
Arterial	7.347	.0006	34.5	.1155	91.8	.1528	1.86		18.3394
Mixed Venous	7.317	.0006	42.2	.2082	44.5	.2082	(59.6%)		20.9353
Sample 4									
Arterial	7.321	.0026	34.5	.3512	94.6	.1732	.99		17.2737
Mixed Venous	7.273	.001	45.2	.2646	38.7	.4726	(31.7%)		20.2631
Sample 5									
Arterial	7.365	.0006	25.4	0	97.5	.1528	.87		14.0734
Mixed Venous	7.276	.0006	42	.2082	30.1	.4509	(27.9%)		18.9590

DOG 8

34# (15.5 kg)

4/10/81

	$pH\ \bar{X}$	S.D.	$pCO_2\ \bar{X}$	S.D.	$pO_2\ \bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}\bar{X}$
Control									
Arterial	7.2720	0.0010	59.0	0.0000	74.7333	0.0577	2.0000	0.1086	26.3887
Mixed Venous	7.2513	0.0021	65.4	0.0000	49.8000	0.1732	(100%)		27.8897
Sample 2									
Arterial	7.3147	.0021	50.3	0.0000	98.7667	0.1155	1.4475	0.0780	24.8219
Mixed Venous	7.2647	0.0025	62.9333	0.1155	44.9667	0.2881	(72.4%)		27.6788
Sample 3									
Arterial	7.2520	0.0026	55.5333	0.1155	85.4000	0.1000	1.2225	0.0877	23.7203
Mixed Venous	7.2487	0.0012	62.7667	0.2517	30.2333	0.1528	(61.1%)		26.6070
Sample 4									
Arterial	7.2900	0.0017	46.3667	0.2082	98.6333	0.4509	0.8933	0.0321	21.6159
Mixed Venous	7.2307	0.0006	61.5667	0.0577	32.8000	0.5000	(44.7%)		25.0387
Sample 5									
Arterial	7.3233	0.0015	37.2667	0.0577	103.5667	0.0577	0.7267	0.0115	18.7580
Mixed Venous	7.2157	0.0015	57.4000	0.2000	24.6000	0.3000	(36.3%)		22.5517

DOG 9
35# (15.9 kg)
4/17/81

	$pH\ \bar{X}$	S.D.	$CO_2\ \bar{X}$	S.D.	$O_2\ \bar{X}$	S.D.	C.O.	S.D.	$\{HCO_3^-\}$
Control									
Arterial	7.367	0.0015	49	.1155	83	.3512	2.95		27.2749
Mixed Venous	7.341	.0006	55.2	.1	50.5	.3786	(100%)		28.9405
Sample 2									
Arterial	7.287	.0015	57.4	.1	78.3	.2082	2.63		26.5753
Mixed Venous	7.253	.0017	66.9	0	45.7	.2	(89.2%)		28.6413
Sample 3									
Arterial	7.274	.0015	55.3	.2517	74.1	.1528	2.29		24.8480
Mixed Venous	7.263	0	68.7	.1	42.8	.1732	(77.6%)		30.0970
Sample 4									
Arterial	7.316	.0015	45.3	.1732	86.5	.1528	1.63		22.4215
Mixed Venous	7.254	.0021	63.4	.0577	38.4	.4509	(55.3%)		27.2054
Sample 5									
Arterial	7.382	.0015	33.9	0	94.5	.1528	1.36		19.5329
Mixed Venous	7.265	.0015	55.4	.1	32.2	0	(46.1%)		24.3824

DOG 10
50# (22.7 kg)
4/24/81

	$pH\ \bar{X}$	S.D.	$pCO_2\ \bar{X}$	S.D.	$pO_2\ \bar{X}$	S.D.	C.O. $\bar{X}$	S.D.	$\{HCO_3^-\}\bar{X}$
Control									
Arterial	7.3450	.0017	43.3333	0.2082	82.4667	0.4509	3.6633	0.2608	22.9292
Mixed Venous	7.3337	0.0021	46.7667	0.0577	61.8	0.000	(100%)		24.1103
Sample 2									
Arterial	7.3583	0.0021	40.8000	0.1000	86.0667	0.0577	2.5400	0.0900	22.2601
Mixed Venous	7.3200	0.0026	48.6667	0.1528	50.7667	0.0577	(69%)		24.3108
Sample 3									
Arterial	7.3710	0.0010	38.8333	0.0577	89.5557	0.4619	1.9960	0.3414	21.8158
Mixed Venous	7.3237	0.0023	48.6333	0.0577	47.5000	0.5292	(54%)		24.5019
Sample 4									
Arterial	7.3673	0.0006	35.6667	0.1155	78.6333	0.5508	1.57	0.4209	19.8669
Mixed Venous	7.3063	0.0023	48.2667	0.3215	35.5000	0.1732	(43%)		23.58
Sample 5									
Arterial	7.3113	0.0006	39.8	0.0000	73.2667	0.2517	1.2175	0.1808	19.4872
Mixed Venous	7.2467	0.0012	53.6667	0.0577	26.5000	0.1000	(33%)		22.6450

AN ABSTRACT OF THE THESIS OF

JAN MURPHY

For the MASTER OF NURSING

Title: THE USE OF MIXED VENOUS BLOOD IN ASSESSMENT OF ACID-BASE STATUS IN DECREASED STATES OF CARDIAC OUTPUT.

Approved: [redacted]
Jack L. Keyes, Ph.D., Thesis Advisor

Currently arterial blood is used in the assessment of acid-base status. Theory based on acid-base physiology and some clinical research suggest that arterial blood may not give the accurate information regarding acid-base status of the tissues. A model adapted from Griffith (1980) suggests mixed venous blood as the site of choice for assessment of tissue acid-base status. The questions asked in this study were:

1) How does arterial blood-gas composition compare to mixed venous blood-gas composition in states of decreasing cardiac output?

2) Does mixed venous blood-gas composition follow a predictable pattern in states of decreasing cardiac output?

Ten, mongrel dogs of both sexes were used in this study. They were anesthetized, intubated and breathed room air spontaneously throughout the experiments. Cardiac output was decreased by periodic bleedings from the femoral artery. Cardiac output was determined from a flow directed pulmonary artery catheter using the thermodilution technique. Simultaneous arterial and mixed venous blood samples were obtained anaerobically in glass syringes and pH, pCO_2 and pO_2 determined. The $\{HCO_3^-\}$ was determined from the Henderson-Hasselbalch equation.

Results showed that arterial and mixed venous blood-gas analysis show different patterns in states of reduced cardiac output. Arteriovenous differences for all parameters increased as cardiac output decreased. Arterial blood-gas analysis showed a pattern of compensated metabolic acidosis while mixed venous blood-gas analysis showed a combined (mixed) metabolic and respiratory acidosis.

From the results it was concluded that mixed venous blood does follow a predictable pattern in decreased states of cardiac output and that this pattern differs from the acid-base pattern seen in arterial blood. Furthermore, it is concluded that mixed venous blood provides the most accurate source for assessment of tissue acid-base status.