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

by

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CHAPTER 1

INTRODUCTION

Blood-gas analysis is a valuable tool in the diagnosis and management of critically ill patients. Nurses are involved not only in the process of drawing the blood samples, but in the assessment and intervention based on the results obtained from the laboratory.

Arterial blood has been the traditional source for obtaining blood for blood-gas analysis. Blood in the arterial circulation represents the output of heart and lungs and is of uniform composition. Therefore, cardiopulmonary function, as well as acid-base status, can be assessed by analyzing the blood gas composition of blood from any artery. Fifteen years ago it was proposed on theoretical grounds that knowledge of mixed venous blood-gas composition may be valuable in assessment of acid-base status (Roos & Thomas, 1967; Michel, 1968). More recent investigations have shown that in certain conditions mixed venous blood gives a more accurate picture of systemic acid-base status than does arterial blood (Tung, Bettice, Wang, & Brown, 1976; Griffith, McKenzie, Keyes, & Peterson, 1982; Murphy, 1982). One condition in which knowledge of mixed venous blood-gas composition has been helpful is in the management of hemorrhagic shock (Kazarian & Del Guercio, 1980).

Samples of mixed venous blood can be obtained once a flow-directed (Swan-Ganz) catheter has been inserted into the pulmonary artery. Unfortunately, the insertion of a Swan-Ganz catheter itself and the subsequent breaks in the system required to obtain blood samples are not without risk to the patient. At greatest risk are pediatric patients less than one year of age and adults over the age of sixty (Kennedy, 1982). Some of the major complications that have been reported include myocardial infarct, cardiac arrhythmias, pulmonary emboli, perforation of the heart or a major vessel, and focal neurologic damage (Gwost, Stoebe, Chesler, & Weir, 1982; Kennedy, 1982).

In critically ill patients, it is often necessary to accept the risks of a procedure if the information obtained is vital in diagnosis and/or management of that patient's disease. In many cases, the condition of the patient that warrants frequent monitoring of blood-gases may also warrant monitoring of pressures within the heart or pulmonary artery via a Swan-Ganz catheter. But what if a patient does not have a Swan-Ganz catheter in place and knowledge of mixed venous blood gas composition would be helpful? Should catheterization be risked to obtain a blood sample?

A solution to the problem may be peripheral venous sampling. Peripheral veins have the advantage of being more accessible and further, venipuncture is associated with fewer risks and complications than pulmonary artery catheterization. However. blood flow in peripheral veins is affected by local tissue conditions. When cardiac output is decreased, as in shock, peripheral vasoconstriction occurs resulting in reduced flow to the extremities. Studies have been conducted in dogs to evaluate the reliability of using peripheral venous blood for blood-gas analysis over wide ranges of respiratory and metabolic acid-base disturbances (Schriver, 1981; Carveth, 1979). Schriver(1981) found a close correlation between changes in the blood-gas composition of peripheral venous blood and those of mixed venous blood during respiratory and acid-base disturbances. In a study where cardiac output was gradually reduced via hemorrhage, Feldon (1982) found that peripheral venous blood-gas composition could be used to assess systemic acid-base status. However, at low cardiac outputs it was often difficult to obtain samples because of the markedly reduced peripheral blood flow.

What is needed is an accessible vein which is large enough not to be markedly affected by local temperature, has adequate blood flow during shock, and receives blood

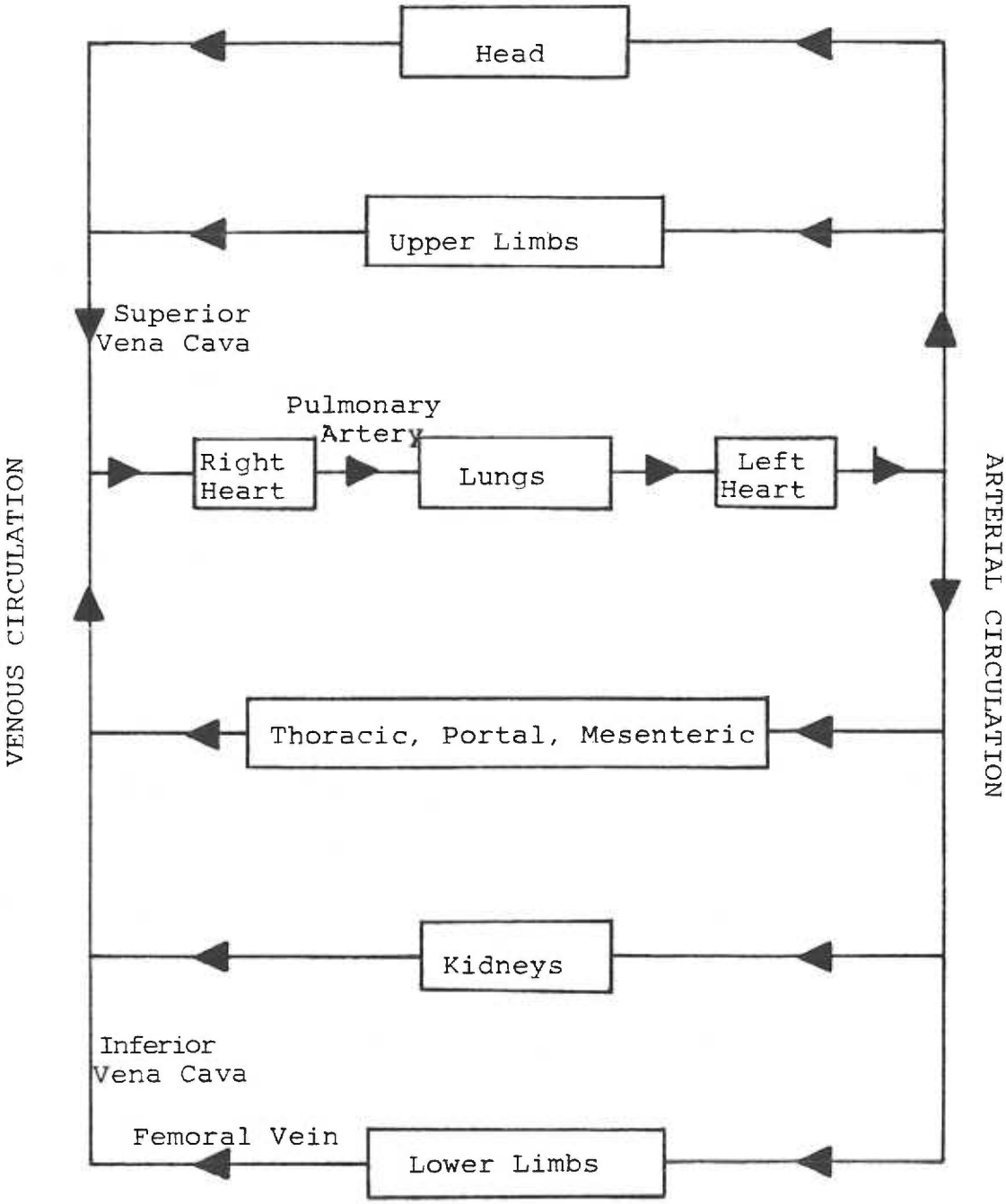
from a large enough systemic tissue bed to be representative of systemic tissue status. Such a site may be the femoral vein.

It is the overall purpose of this study to determine how well blood-gas composition of femoral venous blood correlates with that of mixed venous blood when cardiac output is reduced via hemmorhage.

Theoretical Framework

Before the rationale for using femoral venous blood can be presented, it is first necessary to establish the premise that mixed venous blood gas composition gives a more accurate picture of acid-base status of the tissues than does arterial blood, particularly when cardiac output is decreased. First, a physiological model will be presented to illustrate the relationship between arterial, femoral venous, and mixed venous blood. Next, the theoretical grounds for using mixed venous blood-gas composition in acid-base assessment will be discussed. Finally, the rationale for using femoral venous blood when mixed venous blood is unobtainable will be presented.

The model in Figure 1 illustrates the direction of blood flow through the systemic circulation. In the lungs, gas exchange occurs between pulmonary capillaries and the alveoli. Blood flows from pulmonary capillaries



The Mammalian Circulatory System

Figure 1. Arrows depict the direction of blood flow through arterial and venous circulations. Arterial circulation represents the output of heart and lungs. The venous circulation represents the output of separate but parallel circuits through systemic tissue beds and organs. The femoral vein drains the circuit perfusing the lower limbs. Blood in the pulmonary artery is a flow weighted average of all circuits.

into the left ventricle and then is pumped into systemic circulation. The blood-gas composition of arterial blood is a function of the balance of pulmonary blood flow and alveolar ventilation. In health, there is an overall matching of ventilation with perfusion such that gas exchange can take place with the environment to maintain homeostasis (Slonim & Hamilton, 1976, p. 103). Any condition which disrupts either function will be reflected by a change in arterial blood-gas composition. Thus, arterial blood-gas analysis is a sensitive tool for assessing cardio-pulmonary function.

It can be seen from the model that blood leaving the arterial circulation flows through the capillary beds of organs and tissues via separate but parallel circuits. The blood in systemic capillaries equilibrates with interstitial fluid (ISF) surrounding the cells. Oxygen diffuses into the ISF while CO_2 and fixed acids are taken up and buffered by capillary blood. Since blood equilibrates with ISF while flowing through systemic capillaries, venous blood-gas composition should reflect that equilibrium.

The blood-gas composition of venous blood is a function of tissue perfusion and metabolic activity. Since systemic tissues differ in terms of blood supply and metabolic activity, the pH and gas composition of

blood draining the separate circuits in the model will not necessarily be the same.

As venous blood flows toward the heart, blood from the separate venous circuits combines in increasingly larger veins. This composition of systemic blood is thoroughly mixed in the right ventricle of the heart, flows into the pulmonary artery and once again returns to the lungs. Blood in the pulmonary artery represents a true mixture of venous blood. However, the blood-gas composition is weighted more heavily by tissues and organs that have a higher rate of flow. Mixed venous blood-gas composition will reflect the average gas composition of the interstitial fluid. Therefore, mixed venous blood-gas analysis should be a reliable tool for assessing the acid-base status of systemic tissues.

Theoretical Justification for Using Mixed Venous Blood in Acid-Base Assessment

In 1967, Roos and Thomas presented a mathematical model to analyze *in vitro* and *in vivo* carbon dioxide dissociation curves of true plasama. Using data available in the literature describing the composition of mixed venous and arterial blood, mathematical formulae were derived to calculate carbon dioxide dissociation curves. *In vitro* and *in vivo* curves were constructed for a variety of physiological conditions, among them the

normal state and a state of decreased cardiac output. They concluded that mixed venous blood was a more accurate reflection of an in vivo CO_2 titration curve.

Before the implications of their study can be discussed, it is necessary to clarify the physiological differences between in vitro and in vivo titration (buffer) curves.

In vitro CO_2 titration curves are obtained by first removing a sample of blood from the body. The sample is titrated by equilibrating the blood with varying concentrations of carbon dioxide. The reaction which occurs is described by the following equation:

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

*where HB represents the conjugate acids, (plasma proteins and hemoglobin), and B^- the conjugate bases, (HB^- and Pr^-).

When carbon dioxide is added to the blood, buffering occurs. In an in vitro sample, the buffering capacity is determined by the concentration of hemoglobin and plasma protein. With the addition of CO_2, these buffers bind with hydrogen ions dissociated from carbonic acid. With buffering, the reaction in equation 1 shifts to the right resulting in an increase in the bicarbonate

concentration [HCO_3^-]. The [H^+] increases and thus pH is also reduced. With the increased [H^+], the blood buffers (B^-) form more HB (vertical reaction) and hence causes more HCO_3^- to be produced (horizontal reaction). The greater the concentration of blood buffers, the less the change in pH and the greater the increase in [HCO_3] as CO_2 is added. All of the HCO_3 produced in the <u>in vitro</u> titration reaction is confined to the blood itself.

With <u>in vivo</u> tritration, equilibration with CO_2 takes place in the body before the blood sample is removed. A change in CO_2 is accomplished by either decreasing alveolar ventilation or increasing the fractional concentration of inspired CO_2 (F_{Ico_2}). However, the added CO_2 is not just confined to the blood as occurs under <u>in vitro</u> conditions, but also equilibrates with the large volume of ISF (Figure 2).

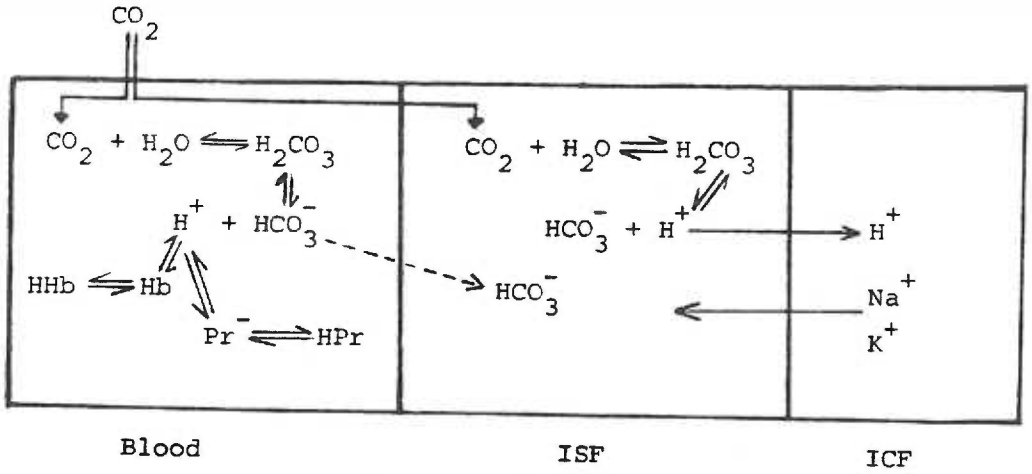


Figure 2. The effects of adding CO_2 to the blood. With <u>in-vitro</u> titration, reaction is confined to the blood alone. With <u>in-vivo</u> titration, CO_2 and HCO_3^- diffuse into the ISF.

Interstitial fluid has a very low concentration of protein and no hemoglobin and therefore has a low buffer capacity for carbonic acid. Added CO_2 quickly diffuses from the blood into the ISF thereby reducing the plasma bicarbonate concentration. With <u>in vivo</u> titration there will be a smaller change in $[HCO_3^-]$ and a larger change in pH for the same amount of CO_2 added than would be obtained with <u>in vitro</u> titration.

As can be seen by Fig. 3, the buffer value of

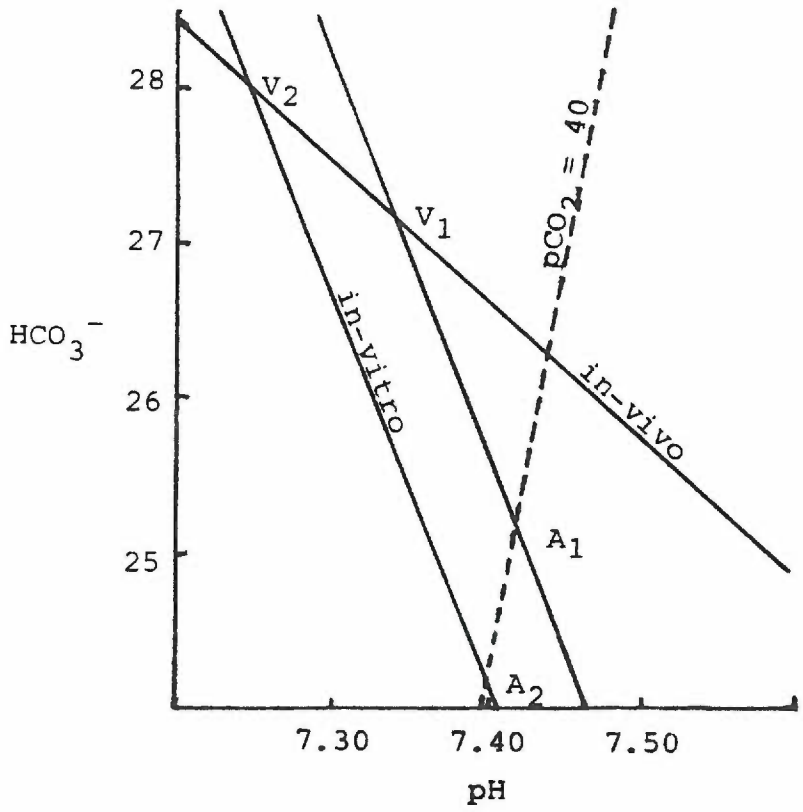


Figure 3. "Normal <u>in vivo</u> CO_2 titration curve of true oxygenated mixed venous plasma (V_1V_2). A_1 and V_1 represent plasma composition of, respectively, arterial and mixed venous blood at control conditions; A_2 and V_2 represent plasma composition after reduction of cardiac output to half normal". Roos and Thomas, 1967, p. 1051.

in vitro blood is expressed by a steeper slope of a line relating [HCO_3] (ordinate) to pH (abscissa). Again, the difference in the slope is due to the greater concentration of buffers, hemoglobin, and proteins, in the blood alone (*in vitro*) than in blood which is in equilibrium with ISF (*in vivo*).

In a steady state, there is no net change over time in tissue metablolism. There is also no net change over time in the composition of interstitial fluid. Since ISF is equilibrated to the steady state carbon dioxide tension, ISF is not a factor in buffering the CO_2 produced at a constant rate by tissues. Therefore, blood that is exposed to CO_2 as it passes through the systemic capillaries acts in an identical way to that of an *in vitro* sample exposed to an identical CO_2 tension. In a steady state, mixed venous blood, V_1 and arterial blood, A_1, are related in terms of an *in vitro* slope (Fig. 3).

Roos and Thomas calculated the effects of reducing the cardiac output while maintaining constant CO_2 production and arterial CO_2 tension. Mixed venous blood and ISF will titrate to a higher CO_2 tension along an *in vivo* slope to a new steady state, V_2. Mixed venous and arterial blood will again be related in terms of an *in vitro* slope once a new steady state is reached. Since arterial CO_2 tension was assumed to be constant, the new

arterial point will fall on the pCO_2 40 torr isobar where it is intersected by the new mixed venous *in vitro* buffer curve. It can be seen in Fig. 3 that the effect of reducing cardiac output produced a decrease in both arterial $[HCO_3]$ and pH even though it was assumed there was no addition of acid to the arterial blood.

The analysis of Roos and Thomas shows that in a steady state, the blood-gas composition of arterial and mixed venous blood are related in terms of an *in vitro* CO_2 titration slope. However, when the steady state is disrupted, the change in blood-gas composition is reflected in mixed venous blood first. Mixed venous blood will titrate along an *in vivo* slope to a new steady state. Therefore, arterial blood-gas composition can only be predicted in terms of the mixed venous value.

One year following publication of the model described by Roos and Thomas, Michel (1968) presented a theory of the buffering behavior of blood which supports the argument that the CO_2 buffer curve of mixed venous blood is the true slope of an *in vivo* titration curve. Michel considered how the Haldane effect alters arterial and mixed venous blood-gas composition during normal respiratory exchange and during hypoxemia.

The Haldane effect facilitates the uptake of CO_2 from the tissues and its release in the lungs. As hemoglobin is deoxygenated in the tissues, blood is able

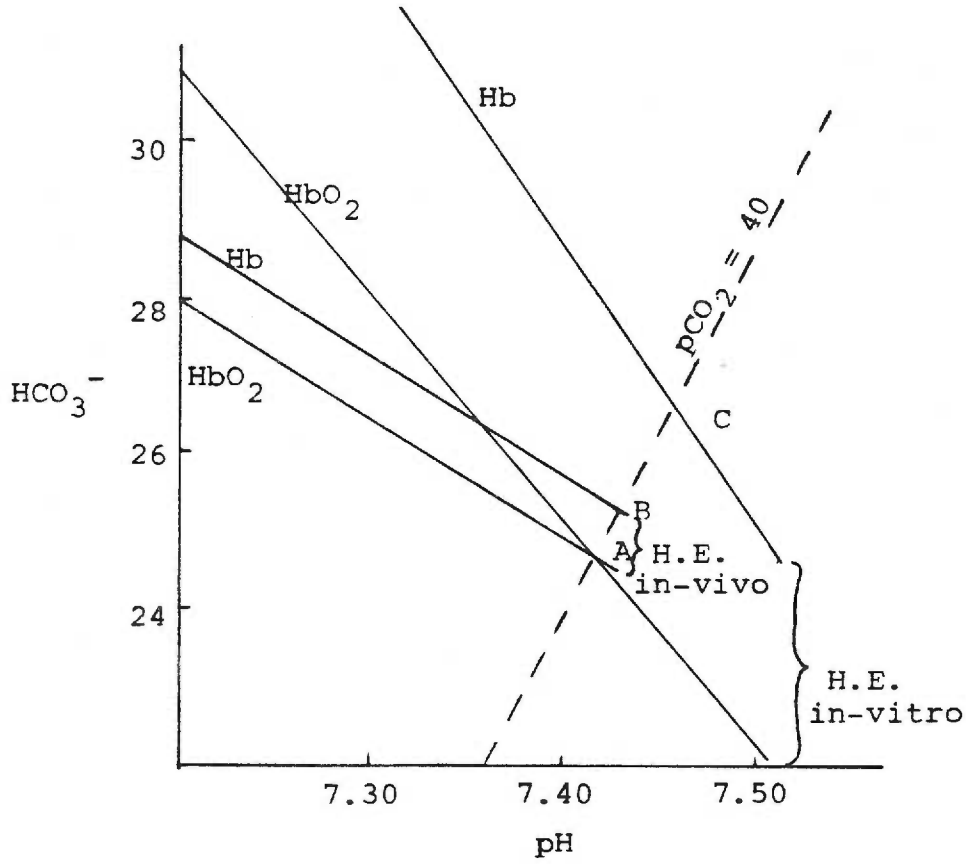


Figure 4. Showing the Haldane Effect (H.E.), in-vitro and in-vivo, at constant pCO_2. Modified from Michel, 1968, p. 285.

to buffer and take up more CO_2. In the lungs, oxygenating the blood drives out carbon dioxide.

In Fig. 4, the in vivo and in vitro response of the Haldane effect are compared. Point A represents completely oxygenated blood at a pCO_2 of 40 torr. Deoxygenation makes hemoglobin a weaker acid. As H^+ are removed from solution the reaction in equation 1 (p. 8) shifts to the right. More CO_2 enters the blood at constant pCO_2 and is converted to HCO_3^- resulting in an increase in $[HCO_3^-]$ and pH (Haldane effect). The in vitro Haldane effect results in a much greater increase

in $[HCO_3^-]$, point C, since all the bicarbonate is confined to the blood alone. When deoxygenation occurs *in vivo*, point B, some of the bicarbonate ions diffuse from the blood and equilibrate with ISF resulting in less increase in plasma $[HCO_3^-]$ and pH. It should be noted that Michel's model did not account for intracellular buffering.

Michel considered the Haldane effect in relation to the normal respiratory cycle in a steady state. For purposes of discussion, gas exchange is considered in distinct steps. Blood leaving the left ventricle is assumed to be fully oxygenated, Ao in Fig. 5. As oxygen diffuses out of the systemic capillaries, the Haldane effect causes the shift from Ao to A'. Carbon dioxide diffuses into the blood and is buffered along an *in vitro* titration slope (Roos & Thomas, 1967) to a higher pCO_2 (point Vo). Point Vo represents mixed venous blood at a normal pCO_2 of 46 torr. In the lungs only CO_2 and O_2 are exchanged. There is evidence that bicarbonate ions are confined to the capillaries in the lungs and do not equilibrate with the pulmonary ISF (Chinard, Enno & Nolan, 1954). Therefore, the Haldane effect in the lungs would be that of *in vitro* CO_2 equilibration (Fig. 4). In the pulmonary capillary, blood is first oxygenated, V', then CO_2 is dissociated along an *in vitro* slope to the original arterial point, Ao. Thus, in a steady state,

the magnitude of the Haldane effect in systemic tissues and lung tissues is the same. It is partly because of this relationship that acid-base assessment based on *in vitro* blood analysis has been useful.

Michel next considered the change that would occur when the steady state was disrupted. When an event occurs to alter the steady state, the composition of blood and ISF changes. Venous blood will reflect the change first. Figure 5 depicts what would occur if the event altering the steady state were a doubling of the arterial-venous (A-V) difference such as occurs with reduced cardiac output.

Assume that the pO_2 and pCO_2 of the arterial blood is constant. Ao represents the control value of arterial blood at a pCO_2 of 40 torr and saturation of oxygen (SO_2) of 100%. Vo represents the control venous value of pCO_2 46 torr and SO_2 70% (Fig. 5). If the A-V difference were doubled, the oxygen desaturation of hemoglobin in the venous blood would also double. The *in vivo* Haldane effect resulting from this would initially displace the venous point upward along the pCO_2 46 isobar to C. In addition, pCO_2 will increase as a result of decreased cardiac output. The rise in pCO_2 also causes an increase in $[HCO_3]$. Equilibration of HCO_3 occurs in the ISF, hence, pH decreases and $[HCO_3]$ increases along the *in vivo* titration curve (C, V_f). The new venous blood-gas

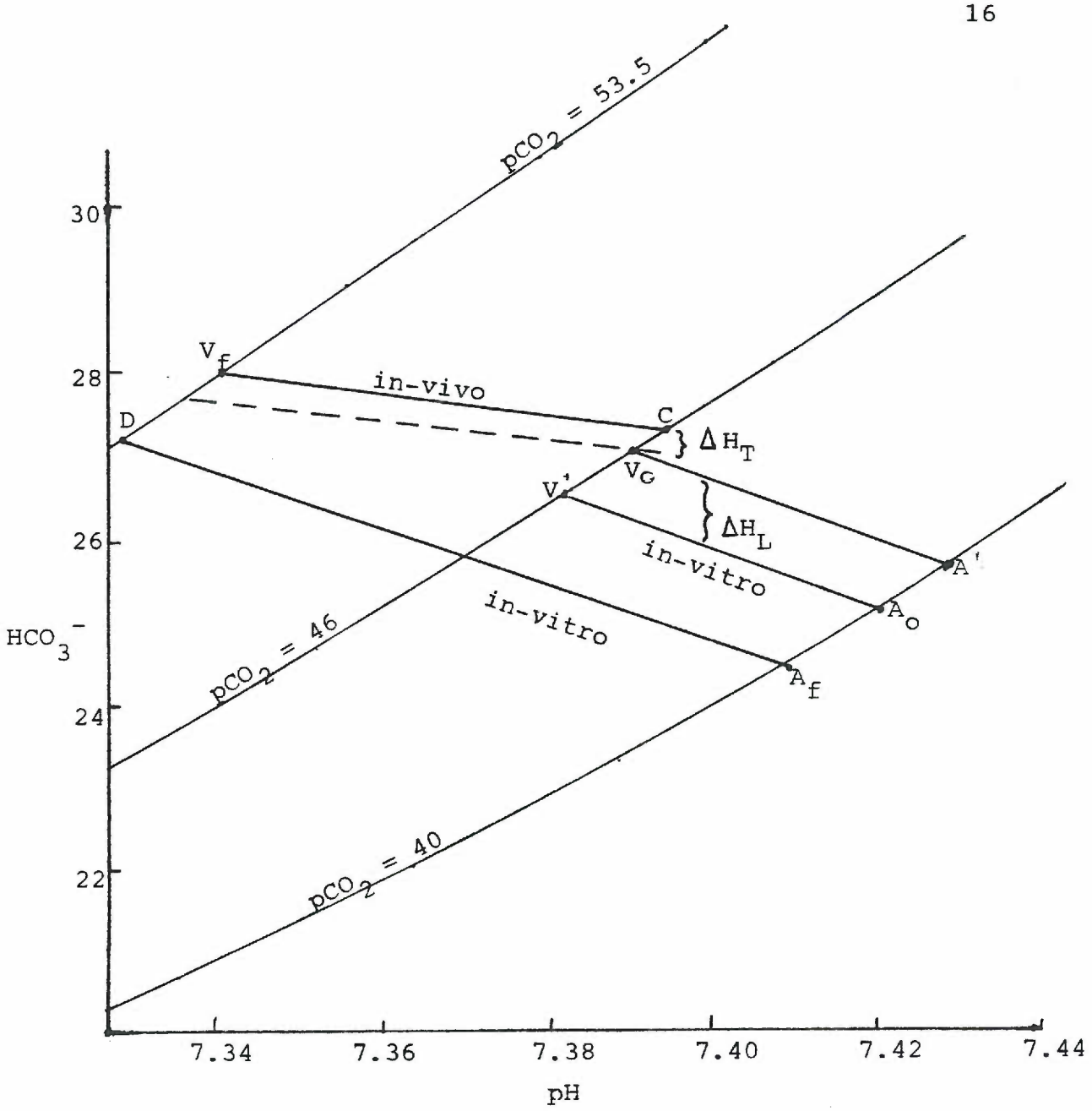


Figure 5. A steady state and the effect of doubling the A-V difference for oxygen saturation between arterial and mixed venous blood at a constant $_{a}pCO_2$. Ao and Vo represent initial steady state arterial and mixed venous values, respectively. A' represents deoxygenation of blood in the systemic capillary and V' oxygenation in the pulmonary capillary depicted here as the first component of the Haldane effect in the tissue and lung respectively. A_f and V_f represent the final arterial and mixed venous values after A-V difference is doubled. ΔH_L is the magnitude of the Haldane effect in the lungs and ΔH_T the Haldane effect in the tissues for a ΔSO_2 of 30%. Modified from Michel, 1968, p. 288 and Murphy, 1982.

value is represented by point V_f at a pCO_2 of 53.5 torr. In the lungs, the Haldane effect retains its full value ($\Sigma \Delta HL + \Delta H_T$) as blood is resaturated with oxygen (SO_2=100%), point D. Since the CO_2 buffer line in the lungs follow an *in vitro* slope and since it was assumed that the arterial pCO_2 was kept constant, the new arterial value, A_f, will be located on the *in vitro* buffer line passing through point D and the pCO_2 40 isobar. The effect of increasing the A-V difference for oxygen saturation on arterial blood would be a decrease in pH but with no change in pCO_2. By contrast, in mixed venous blood the decrease in pH is twice as great as in arterial blood and is asssociated with an increase in both $[HCO_3^-]$ and pCO_2. Michel concluded that examination of the arterial blood-gas alone might erroneously suggest a metabolic acidosis.

In summary, work by Michel and Roos and Thomas provides a justification for considering the use of mixed venous blood in acid-base assessment on theoretical grounds. The *in vivo* CO_2 dissociation curve of blood is the true curve of mixed venous blood. "Arterial blood is a transformation of the mixed venous blood according to the *in vitro* dissociation curves." (Michel, 1968, p. 290). In a steady state, arterial and mixed venous blood-gas composition are related through *in vitro*

dissociation curves. But following disruption of a steady state, it is mixed venous blood that reflects the true picture of intracellular fluid. Due to the Haldane effect in the lungs, arterial blood will not reflect the acid-base status of interstitial fluid. It should be noted that the effects of whole body bufferings were not calculated in the models of either Michel or that of Roos and Thomas. Clinical investigations which will be reviewed have shown that intracellular buffering does change the slope of the in vivo dissociation curve predicted by these mathematical models.

Rationale for Using Femoral Venous Blood When Mixed Venous is Unobtainable.

Ideally, mixed venous blood-gas composition should be used in making systemic acid-base assessments when cardiac output is decreased. If, however, blood from the pulmonary artery is unobtainable, femoral venous blood may be a reliable substitute.

The femoral vein drains the large muscle mass and connective tissue of the lower limbs. Blood flows from the femoral vein into the common iliac vein deep in the groin and then into the inferior vena cava. The femoral vein provides a site for obtaining blood draining a major tissue circuit (Fig. 1) that would have an adequate blood flow in shock and is also easily accessible. In fact,

the femoral vein is a clinically accepted site for obtaining peripheral venous blood samples in both pediatric and adult patients.

Compared to pulmonary artery catheterization, the risks associated with femoral venipuncture are minimal. There is some chance of entering the femoral artery which lies lateral to the vein. In children, there is risk of osteomyelitis if the needle is inserted too deeply and enters the head of the femur. With careful attention to technique, however, femoral venous blood samples can be safely and easily obtained. (Custer and Steinhoff, 1978, p. 1953).

Review of the Literature

The focus of the proposed study is how the blood-gas composition of femoral venous blood responds when cardiac output is reduced and if that pattern of change mimics that of mixed venous blood. Currently, venous blood-gas analysis is not a widely used method of assessing acid-base status. Before the clinical significance of using femoral venous blood-gas composition to predict that of mixed venous blood can be established, experimental evidence must first support the concept that mixed-venous blood is a reliable means of assessing systemic acid-base status over a wide range of acid-base disturbances. In the following review,

relevant studies regarding the use of mixed venous, peripheral venous and femoral venous blood-gas composition in assessment of acid-base status are reported.

The review of the literature is organized in the following way:

1) The use of mixed venous blood-gas composition in acid-base disturbances.
2) The use of peripheral venous blood in assessing acid-base disturbances.
3) The effects of decreased cardiac output on the blood-gas composition of arterial, mixed venous, and femoral venous blood.

The Use of Mixed Venous Blood-Gas Composition in Acid-Base Disturbances

Samet, Linhart, Barold, and Hildner (1969) investigated the reliability of using mixed venous blood in place of arterial blood for measuring the blood-gas parameters, pH, pCO_2, pO_2, and base excess.

Fifty non-acutely ill patients undergoing cardiac catheterization were studied. Samples of mixed venous and systemic arterial blood were obtained anaerobically and simultaneously. Determination of pH, pCO_2, and pO_2 were accomplished by microelectrode technique. Base excess was determined from a nomogram.

Samet, et al., found significant correlation (+0.77, $p<0.01$) when parameters obtained from pulmonary artery (abscissa) were plotted against those obtained from systemic arterial blood (ordinate). However, when the values from mixed venous blood (abscissa) were plotted against the difference obtained from pulmonary and systemic arterial blood (ordinate), a low correlation was shown to exist (+0.29, $p=0.05$).

The investigators concluded that there were general trends in a relationship between mixed venous and arterial blood for pH,pCO_2, and pO_2 and base excess. However, because of the low correlation between the difference in composition between systemic and pulmonary arterial samples and the values of the pulmonary arterial sample, they concluded mixed venous blood was an unreliable substitute for arterial blood.

A more critical look at the relationship of linearly related variables cast some doubt on their conclusions. In critical reviews of Samet, et al., Griffith (1980) and Murphy (1982) argued that the rejection of mixed venous blood was unjustified. An example presented by Griffith (p. 69) illustrates their argument.

Assume that two variables, x and y are linearly related. Plotting y values on the ordinate against x

values on the abscissa will yield a straight line. The relationship is described by the following equation:

$$y = a + bx$$

where a = the y intercept (2)

b = the slope

Three different values for the above relationship will be considered (Table 1). To simplify discussion, "a" is always assumed to be zero. However, the conclusions reached in this discussion would also hold, if the values of "a" were different from zero.

Table 1

Examples of slope y-x vs y computed for three different values of b.

	y	x	y-x
I. If b=0.9, then:	1	1.11	0.11
a=0	2	2.22	0.22
y=0.9x	3	3.33	0.33
slope of y-x vs y=0.11			
II. If b-1.0, then:	1	1	0
a=0	2	2	0
slope of y-x vs y=0			
III. If b=2, then:	1	.5	0.5
a=0	2	1.0	1.0
y=2x	3	1.5	1.5
slope of y-x vs y=0.5			

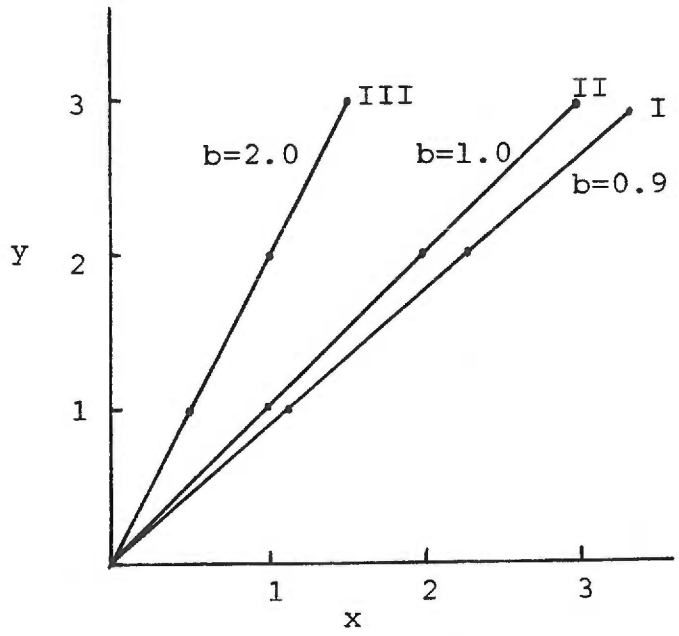


Figure 6A

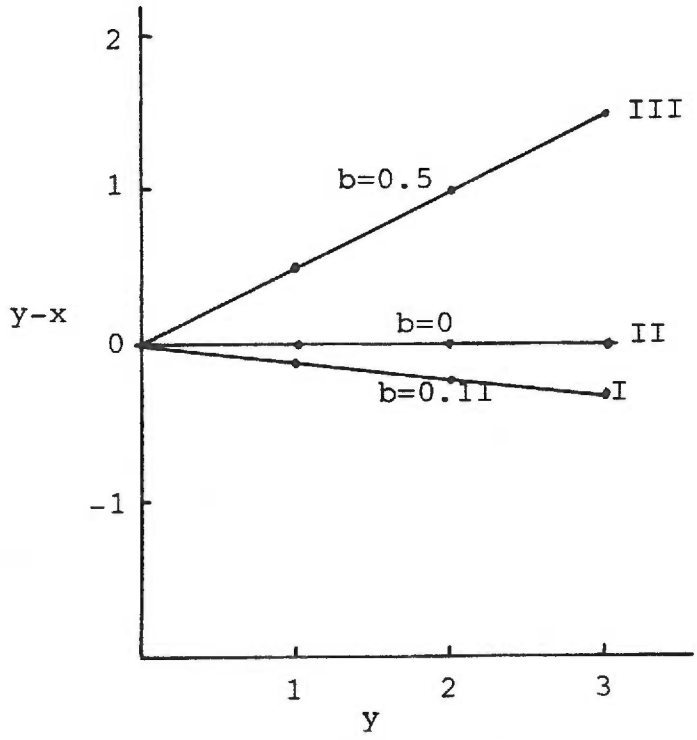


Figure 6B

Figure 6. The relationship of y vs x (6A) and y-x vs y (6B) for y=bx when b (slope) = 0.9, b = 1.0, and b = 2.0. Values taken from Table 1. Modified from Griffith (1980).

Plotting y (ordinate) against x (abscissa) yields three straight lines with varying slopes (Fig. 6A). Variables which are perfectly correlated produce a straight line with a slope of 1.0 (b=1.0). When this relationship is plotted as y-x (ordinate) vs y (abscissa) (Fig. 6B), a straight line is yielded but with a slope of zero. If the slope of x vs y is 0.9 then a plot of y-x vs y yields a slope of -0.11. And finally, if the slope of x vs y is 2 then a plot of y-x vs y will yield a slope of 0.5. It can be clearly seen that as the slope of the relationship y vs x approaches the value of 1.0 then the slope of y-x vs y will approach zero. In other words, a slope of zero can be expected on a plot of x-y vs y if there is a perfect correlation between these values in a plot of y vs x.

If Samet's data is now analyzed considering this relationship, it is apparent that the low correlation of 0.29 between mixed venous values and pulmonary arterial minus systemic arterial values, was misinterpreted. In fact, a low correlation coefficient with a slope approaching zero would be expected for two variables which are positively correlated. Samet's data actually support the reliability of using mixed venous blood in acid-base assessment.

Kazarian and Del Guercio (1980) studied the use of

mixed venous blood-gases to monitor patients in traumatic shock. The subjects of the study were ten patients in profound hypovolemic shock at onset and required resuscitation, multiple blood transfusions, and surgical control of hemorrhage. Either a central venous pressure catheter or a Swan-Ganz catheter were inserted to monitor pressures and mixed venous blood-gas composition. Paired samples of arterial and mixed venous blood were analyzed during resuscitation and surgery.

Resuscitation and control of hemorrhage was complete within 45 minutes of arrival in the emergency department. Four of the 10 patients survived. The authors claim the degree of trauma in survivors and non-survivors was comparable. It was found that arterial oxygen tension (PaO_2) for all patients was well above 100 mmHg with arterial oxygen saturation (SaO_2) over 90 percent. This was attributed to the fact that all patients were intubated and received 100% oxygen as the inspired gas.

The mixed venous oxygen saturation (S_VO_2) of survivors averaged 40% while non-survivors averaged 25 percent. Survivors used 52% of available oxygen in blood, whereas non-survivors used an average of 69% (normal: 20-25%). This increase in oxygen extraction was said to indicate a more severe oxygen deprivation in the

tissues of non-survivors as a result of continued bleeding and/or low cardiac output.

From the data reported, I calculated the A-V differences for pH and pCO_2. For pH, the A-V difference was 0.002 pH units in survivors and 0.107 in non-survivors. The A-V differences for pCO_2 was 13 torr in survivors and 2 in those who died. These data suggest that the tissues of non-survivors suffered a more severe combined acidosis, that is respiratory plus metabolic, whereas the tissues of survivors exhibited respiratory compensation of metabolic acidosis.

Kazarian and Del Guercio stated, "although arterial blood-gases are probably more frequently used, mixed venous blood-gases may more accurately indicate the progress and ultimate survival of the patient and monitor the effects of treatment", (p. 180). They contended that mixed venous blood-gas values gives an indication of the adequacy of circulation and reflects a balance between the amount of oxygen delivered to the tissues and the amount of oxygen consumed. An S_VO_2 of 60% or less implies poor tissue perfusion with increased oxygen extraction and requires immediate correction. The S_VO_2 of 5 non-survivors remained below 40% through the resuscitative and operative periods, while all the survivors showed improvement of S_VO_2 (>60%) during this

time. The authors concluded that S_VO_2 values were a valuable means of monitoring the adequacy of circulation and predicting survival.

There were two letters to the editor in response to this article. Lipton (1980) questioned the similarity of the survivor and non-survivor groups. He asserted that the very low initial pH and S_VO_2 values in non-survivors indicated either much greater blood loss or of a longer duration. Lipton suggested that initial pulse and blood pressure may be just as valuable in determining the extent of hemorrhage. Lipton also believed valuable time would be lost in inserting and positioning catheters, thereby delaying definitive treatment. He suggested that measurement of urine output was as good, and less expensive a means of monitoring a patient's response to fluid therapy than S_VO_2. Finally, Lipton criticized the authors' contention that S_VO_2 values were valuable predictors of survival stating, "in critical trauma patients a predictor of survival may be reliable but it is seldom valuable" (p. 597).

In reply, Kazarian and Del Guercio (1980) maintained that mixed venous blood-gas values give more sensitive information of patients who present in a moribund state with unobtainable blood pressures. They

stated that resuscitation and control of hemorrhage was the immediate response, that no time was lost repositioning catheters, and that initial venous samples were obtained from whatever central lines were in place. Further, during the post-operative period, S_VO_2 would reflect hemodynamic changes long before they would be reflected in hourly urine output measurements.

In a second letter, Piantodosi and Bradley (1980) criticized Kazarian and Del Guercio's article on several statistical grounds. 1) No data were reported to demonstrate that the survivor and non-survivor groups were homogeneous with regard to variables which may affect survivability such as sex and age. 2) That further analysis of the data using correlation coefficient, stepwise regression model, and discriminant analysis identified $PaCO_2$, PaO_2, P_VCO_2, and venous pH as better indicators of survival than S_VO_2. 3) Since the sample size was so small, further investigation was necessary to test these conclusions.

In reply, Kazarian and Del Guercio stated that all 10 patients were male, 19 years to 38 years old with one survivor 63 years old. All were resuscitated, intubated, and given ventilatory support at high oxygen concentrations. They argued that due to the profound effect of resuscitative measures on the arterial

blood-gas values, a statistical analysis of $Pa0_2$, $PaCO_2$, and $Sa0_2$ is less meaningful than mixed venous oxygen saturation in assessing the balance of oxygen delivered to and oxygen consumed by the tissues. They stated that no attempt was made to claim statistical significance from their small sample and agreed that further study was needed on large groups of patients.

Griffith, McKenzie, Peterson, and Keyes (1982) studied the blood-gas composition of mixed venous blood over a wide range of acid-base disturbances. Metabolic acid-base disturbances were induced in healthy anesthetized dogs. Metabolic acidosis was achieved by infusion of 0.3M NH_4Cl (Baker's Analyzed Reagent). Metabolic alkalosis was produced in 4 dogs by infusion of $NaHCO_3$. Paired samples of arterial and mixed venous blood were drawn at 30 minute intervals during infusion. Respiratory acid-base disturbances were induced in 9 dogs. A tracheostomy was performed and ventilation was controlled via a mechanical respirator. A respiratory acidosis was induced in 4 dogs by increasing the fractional concentration of CO_2 in steps from 0 (room air) to 3%, 5%, and finally 10% CO_2 in 0_2. Respiratory alkalosis was produced in 5 dogs by hyperventilation using room air as the inspired gas mixture. Tidal volume was increased by 150 ml increments up to 750 ml. Mixed

venous and arterial samples were drawn 60 minutes following each change in tidal volume.

Results showed that changes in pH, pCO_2, and $[HCO_3]$ of mixed venous blood mimicked those found in arterial blood in both respiratory and metabolic acid-base disturbances. These results held over a wide pH range (6.69-7.70). During changes in pCO_2 the average slope of the CO_2 buffer line was slightly less for mixed venous blood than that for arterial blood. This is in agreement with the predictions made by Roos and Thomas (1967) that the true in vivo buffer curve for CO_2 is that of mixed venous blood. However, Roos and Thomas predicted that the arterial CO_2 buffer curve would be steeper than was obtained by Griffith, et al., (1982). This discrepancy can be explained by the fact that intracellular buffering was not included in the Roos and Thomas model. It is likely that intracellular buffering did have an effect on the slope of the pH/HCO_3 curve for mixed venous blood obtained by Griffith, et al.

The changes in pO_2 values in mixed venous blood did not always mimic those of arterial blood. In general, the pO_2 increased in both arterial and mixed venous blood during metabolic acidosis and decreased in metabolic alkalosis. This pattern was thought to be related to the respiratory response to the metabolic acid-base state,

hyperventilation in metabolic acidosis and hypoventilation during metabolic alkalosis. In respiratory acidosis, both arterial and mixed venous pO_2 increased due to the high fractional concentration of oxygen. During respiratory alkalosis arterial pO_2 increased slightly while mixed venous pO_2 decreased significantly.

In summary, it was found that there is a predictable change in mixed venous pH, pCO_2, and $[HCO_3]$ which mimics the changes in the arterial parameters over a wide range of respiratory and metabolic acid-base disturbances. Although mixed venous pO_2 changes were not consistent with changes in arterial pO_2, mixed venous blood may in fact be providing more accurate information on the acid-base and oxygenation status of systemic tissues. Griffith, et al., concluded that the blood-gas composition of mixed venous blood can be used to accurately assess acid-base status.

Summary of the Use of Mixed Venous Blood-Gas Composition in Acid-Base Disturbances

There has been very little clinical or laboratory research studying the blood-gas composition of mixed venous blood. Summarizing the knowledge of this topic:

1) There is some controversy in whether mixed venous blood-gas composition can be a reliable substitute for that of arterial blood based on interpretation of statistical methods.
2) When cardiac output is reduced due to hemorrhagic shock, mixed venous oxygen saturation was a better indicator of tissue oxygenation and clinical improvement than arterial oxygen saturation.
3) Changes in pH, pCO_2 and $[HCO_3]$ of mixed venous blood mimicked that of arterial blood in both respiratory and metabolic acid-base disturbances. Changes in arterial and mixed venous pO_2 values were less consistent.

The Use of Peripheral Venous Blood in Assessing Acid-Base Disturbances

The majority of research conducted in the use of peripheral venous blood for acid-base assessment evaluates how well the pH, pCO_2 and pO_2 of peripheral venous blood correlates with that of arterial blood.

This investigator could find no published reports of human research comparing peripheral venous blood to that of mixed venous blood.

Schriver (1981) examined the relationship of arterial and venous blood in respiratory acid-base disturbances in dogs where the pH varied from 6.87 to 7.74. The values of pH, pCO_2, and $[HCO_3]$ of peripheral venous blood, both warmed (arterialized) and unwarmed, were compared with these variables in arterial and mixed venous blood.

Ten healthy mongrel dogs were anesthetized with Sodium Pentobarbital (30mg/kg). The trachea was cannulated and the animal was mechanically ventilated using a Harvard Animal Respiratory (Model 3).

Catheters were placed in the femoral and pulmonary arteries for obtaining arterial and mixed venous blood samples, respectively. A vein in each forepaw was catheterized for obtaining peripheral venous samples. Thermometers were placed under the skin near the tip of each catheter. To obtain arterialized venous blood, one paw was warmed with a 100 watt bulb to a temperature of 38-42°C.

Respiratory acidosis was induced in five dogs by increasing the concentration of CO_2 in the inspired gas mixture in three steps. Concentrations were 3%, 5%, and

10% CO_2 in O_2. Samples of warmed and unwarmed peripheral venous blood, mixed venous blood and arterial blood were drawn at 20 and 60 minutes following a change in the inspired gas mixture.

Respiratory alkalosis was induced in 5 dogs by increasing the tidal volume of the respirator by 150 ml increments in three stages. Blood samples were drawn as described for the first group following a change in the tidal volume.

Mean rectal temperature was 37.0°C ∓ 0.3. Temperature of the warmed paw at the sampling site ranged from 38.0°C to 43.0°C. Temperature of the unwarmed paw ranged from 28.0°C to 38.0°C.

It was found that the values of pH, pCO_2, and $[HCO_3]$ of peripheral venous blood (warmed and unwarmed) correlated closely with those of arterial blood. Correlation coefficients (Pearson's $\underline{r}$) were 0.84 or greater for $[HCO_3]$ and 0.92 or greater for pH and pCO_2 in both the hypercapnia and hyperventilation groups. The pO_2 of the venous samples (warmed and unwarmed) did not correlate well with arterial pO_2. In hypercapnia, Pearson's $\underline{r}$ was equal to or greater than 0.67, while during hypocapnia $\underline{r}$ varied from -0.53 to +0.61.

In general, there were no differences between values obtained from warmed and unwarmed venous blood.

These findings differ from that of Carveth (1979), who compared the blood-gas parameters of arterial blood to those of warmed and unwarmed peripheral venous blood during controlled metabolic acid-base disturbances. Carveth found that warmed peripheral venous blood more closely correlated with arterial blood than did blood obtained from an unwarmed venous site. Carveth used superficial veins draining the skin of the forepaw while Schriver used somewhat deeper veins. Warming would have a greater effect on increasing flow to a superficial vein. Flow in deeper forepaw veins is less likely to be affected as greatly by changes in ambient paw temperature. Blood flow in the femoral vein draining the leg is likely to have a pattern of response to warming similar to that of deep forepaw veins.

Peripheral venous values for pH and pCO_2 were highly correlated with those same variables in mixed venous blood ($r > 0.97$). For $[HCO_3]$, the correlation was equal to or greater than 0.87 during hyperventilation and 0.73 or greater during hypercapnia. For pO_2, values for peripheral venous blood (warmed and unwarmed) were correlated more closely with mixed venous blood than with arterial blood. There was a higher correlation when mixed venous pO_2 values were less than 50mm Hg than when pO_2 was greater than 50 torr. Further, there was a

slightly greater correlation between mixed venous pO_2 and unwarmed peripheral venous blood. In general, mixed venous pO_2 values were lower than peripheral venous pO_2 values. Schriver attributes the lower metabolic activity and lower O_2 consumption of the cells in the paw as the reason for high peripheral pO_2 values.

Schriver concluded that pH, pCO_2, and $[HCO_3^-]$ of free-flowing peripheral venous blood was a reliable indicator of respiratory acid-base status and could be used in lieu of arterial blood in acid-base assessment. Peripheral venous blood was not a reliable predictor of arterial pO_2 but might be useful in predicting the direction of pO_2 change in mixed venous blood.

Felden (1982) evaluated the reliability of using peripheral venous blood to assess systemic acid-base status when cardiac output was reduced. The pH, pCO_2, pO_2, and $[HCO_3]$ of peripheral venous blood (arterialized and non-arterialized) were compared to the same variables in arterial and mixed venous blood.

Cardiac output was progressively reduced in 10 healthy mongrel dogs by controlled hemorrhage. Cardiac output was determined by thermodilution technique. Respiration was not controlled. Arterialized blood was obtained by warming the paw with a 100 watt bulb to a subcutaneous temperature of 38-42°C just prior to

obtaining the blood sample. The other paw, not warmed, provided non-arterialized blood. Samples of mixed venous and arterial blood were obtained from catheters placed in the pulmonary and femoral artery respectively.

Arterial, mixed venous, and arterialized and non-arterialized peripheral blood samples were drawn prior to (control) and 45 minutes following each of 3 reductions in cardiac output. It was found that in both arterialized and non-arterialized blood there was little change in mean A-V differences for all parameters when cardiac output was 50% of control or greater. However, when cardiac output was less than 50% of control, the mean A-V difference increased markedly for all variables. The magnitude of the A-V difference was found to be slightly more constant in arterialized peripheral blood than for non-arterialized blood, when cardiac output was greater than 50% of control. These findings were explained by the markedly reduced blood flow to peripheral veins following blood loss. When cardiac output was greater than 50% of control, warming the paw, and hence increasing the blood flow, offset some of the vasocontriction in peripheral veins. When blood volume was reduced such that cardiac output was equal to or less than 50% of control, arterialization was ineffective in

increasing peripheral circulation.

Felden also noted that blood-gas parameters of peripheral venous blood did not all change in the same direction as those of arterial blood when cardiac output was reduced. There was a decrease in pH, and $[HCO_3]$ in both arterial and peripheral venous blood with reduced cardiac output. However, pCO_2 increased in peripheral venous blood and decreased in arterial blood with blood loss. The pO_2 increased in arterial and decreased in peripheral venous blood. The blood gas parameters of arterial blood indicated compensated acidosis while those of peripheral venous blood indicated the presence of a combined acidosis.

Felden next compared the relationship between peripheral venous parameters with that of mixed-venous blood. As with A-V differences, mean mixed venous minus peripheral venous (MV-PV) values were relatively constant until cardiac output was 50% of control or less. For pH, pCO_2, and $[HCO_3]$, the magnitude of MV-PV differences was considerably less than mean A-V differences. The pH, pCO_2, and $[HCO_3]$ of peripheral venous and mixed venous blood all changed in the same direction indicating the same acid-base status, combined acidosis, as cardiac output was decreased. Peripheral venous pO_2 values did not correlate closely with mixed venous pO_2. Generally,

peripheral venous values were higher than those of mixed venous. This would indicate that metabolic activity and, hence, oxygen consumption of tissues in the paw are lower than 0_2 consumption of other tissues and organs during shock. The mean pO_2 difference (MV-PV) was more constant in non-arterialized peripheral venous blood than for arterialized peripheral venous.

Data obtained by Felden when cardiac output was greater than 50% of control were in agreement with data presented by Schriver (1981). It is likely that cardiac output was decreased somewhat in the mechanically ventilated dogs in Schriver's experiment. However, since high correlations were found between arterial blood-gas composition and that of both peripheral and mixed venous blood, the decrease in cardiac output must have been less than 50% of control.

Felden concluded that when cardiac output was 50% of control or greater, the pH, pCO_2, and $[HCO_3]$ of peripheral venous blood can be used to assess systemic acid-base status. Peripheral venous pO_2 cannot be used to predict arterial pO_2 but may reflect the pO_2 of mixed venous blood. When cardiac output was less than 50% of control it became difficult to obtain peripheral venous blood samples.

Summary of the Use of Peripheral Venous Blood

1) The pH, pCO_2, and $[HCO_3]$ of peripheral venous blood correlates well with those parameters in arterial and mixed venous blood over a wide range of acid-base disturbances (pH 6.87 to 7.74) and when cardiac output is not severely reduced.
2) When cardiac output is reduced 50% of control or greater, the pH, pCO_2 and $[HCO_3^-]$ of peripheral venous and mixed venous blood show the same pattern of change. Changes in blood-gas composition of arterial blood did not correlate well with either peripheral or mixed venous blood.
3) When cardiac output is less than 50% of control, peripheral venous blood-gas composition does not correlate well with either that of arterial or mixed venous blood.

The Effects of Decreased Cardiac Output on the Blood-Gas Composition of Arterial, Mixed Venous and Femoral Venous Blood

In 1967, Brown, Kim, and Moorhead studied the effects of metabolic acidosis on intracellular pH. Acidosis was produced by five different methods in dogs. The method of pertinence to this review was hemorrhagic

shock. Eight dogs were anesthetized and nephrectomized. A marker dye, DMO, was injected for determination of intracellular pH and allowed to equilibrate. The animal was bled from the carotid artery until a mean arterial pressure of 40mm Hg was reached. An automatic leveling device and blood reservoir were used to maintain hypotension. Following stabilization, arterial and femoral venous blood was analyzed for pH and pCO_2. Bicarbonate concentration was calculated using the Henderson-Hasselbalch equation. A skeletal muscle sample was obtained to determine intracellular pH.

Comparison of mean values obtained from arterial and femoral venous blood revealed a significant increase in the A-V difference for pH and pCO_2 following hemorrhage. Arterial pH and pCO_2 decreased significantly presenting a picture of metabolic acidosis with respiratory compensation. Femoral venous blood-gas parameters showed a severe acidosis (pH 7.06, pCO_2 59mm Hg, $[HCO_3]$ 16.5mEq/L.) as a result of reduced tissue perfusion.

Intracellular acidosis was also severe. Mean intracellular $[H^+]$ increased significantly from 126 to 177 nM/L. There was no significant change in intracellular $[HCO_3^-]$. It is probable that the increase in pCO_2 produced an increase in intracellular $[HCO_3^-]$

that was nearly equal to the decrease resulting from the buffering of fixed acids or loss of [HCO_3^-] from intracellular fluid. Intracellular pH decreased from a mean of 6.91 to 6.75. By contrast, mean arterial pH was 7.29 during shock.

Brown et al. (1967) concluded that arterial blood did not reflect the acid-base changes occurring at the cellular level. They state, "...these findings point out the importance of using venous rather than arterial blood pH in calculation of intracellular pH." (p. 598). Their stated conclusions are very relevant to the present study and have clinical significance as well. In assessing acid-base conditions at the cellular level, venous blood which has equilibrated with those cells, will yield more accurate information than arterial blood which represents the outflow of heart and lungs. Brown et al. found femoral venous blood to accurately reflect the intracellular acid-base changes of skeletal muscle.

Tung, Bettice, Wang, and Brown (1976) investigated intracellular and extracellular acid-base changes during hemorrhagic shock. Samples of arterial, mixed venous, and femoral venous blood were analyzed to determine the extracellular response. Skeletal muscle samples from the hind limb were analyzed to determine intracellular response. Twenty-two mongrel dogs were anesthetized and

intubated. An intracellular marker, DMO, was injected into the animal and allowed to equilibrate for two hours. This marker was used to determine intracellular pH. After control samples were obtained, the animals were bled to a mean carotid arterial pressure of 50mm Hg. This pressure was maintained throughout the experiment by retransfusing or bleeding as needed. Arterial and mixed venous blood samples were collected at 30, 60, 90, and 120 minutes following hemorrhage. A second sample of skeletal muscle and femoral venous blood was taken at 120 minutes.

The values of pH, pCO_2, and $[HCO_3]$ are shown in Figure 7. In both arterial and mixed venous blood the greatest change for all parameters occurred within the first 45 minutes after hemorrhage. There was a greater difference between values obtained from arterial and mixed venous blood than the difference between values from mixed venous and femoral venous blood.

Bicarbonate concentration decreased in all three blood sources. While femoral and mixed venous values were nearly equal after 2 hours the A-V difference for $[HCO_3]$ had increased.

The pCO_2 of both femoral and mixed venous blood increased following hemorrhage. The 2-hour femoral venous value, however was greater than that of mixed

venous blood suggesting that there are tissues which are being better perfused during shock than that of the hind limb. Arterial pCO_2 decreased initially and then remained fairly constant. Thus there was a marked increase in the A-V difference for pCO_2. These results can be explained by the decrease in cardiac output produced by hemorrhage. Oxygen delivery to the tissues is reduced resulting in anaerobic metabolism and metabolic acidosis. Respiration is stimulated by the decrease in pH and blood pressure. As ventilation increased, the arterial pCO_2 is reduced and partially compensates for the metabolic acidosis. In venous blood, CO_2 produced by cellular metabolism accumulates due to reduced blood flow through systemic capillaries. Thus, pCO_2 in mixed venous and femoral venous blood increased.

Arterial pH decreased gradually from 7.36 before hemorrhage to 7.21 after 2 hours. In mixed venous blood the decline in pH was more precipitous during the first 45 minutes, then continued to decline slowly. Again there was a widening of the A-V difference for pH (Figure 7).

There were profound differences between arterial and mixed venous pO_2 and oxygen saturation of hemoglobin. Arterial pO_2 increased 14 torr as a result of the increased ventilation during metabolic acidosis.

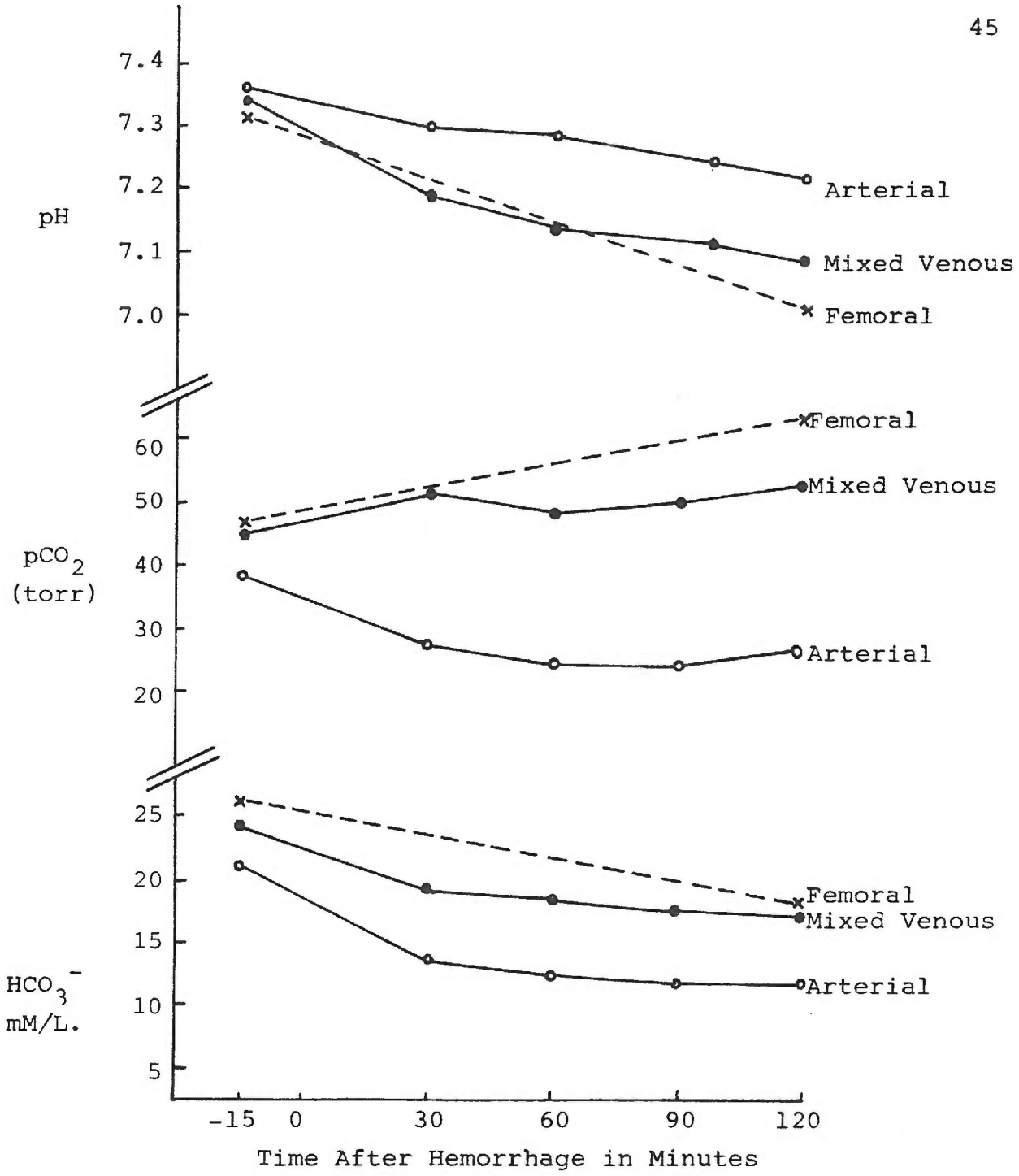


Figure 7. Acid-base parameters in arterial, mixed venous, and femoral venous blood during hemorrhagic shock. Zero time indicates the end of hemorrhage. Femoral venous values were extracted from Table 1, p. 234. Modified from Tung, et al. 1976, p. 232.

The increase in arterial pO_2 produced only a minimal increase in oxygen saturation. Mixed venous pO_2, by contrast, decreased 20 torr. The effect of this decrease on mixed venous oxygen saturation is quite dramatic. This is because these pO_2 values are in the lower end of the oxyhemoglobin dissocation curve where reducing pO_2 produces a marked reduction in oxygen saturation. The A-V difference for oxygen saturation was 81% representing a significant increase in oxygen extraction in the shock state. Despite the normal arterial pO_2, an acute state of hypoxia was present in the tissues and is reflected in the venous samples.

Tung et al. (1976) compared the intracellular changes of skeletal muscle tissue during hemorrhagic shock to those of femoral venous blood. The unstated but underlying assumption was that femoral venous blood reflected the interstitial fluid of skeletal muscle. The intracellular and femoral venous pCO_2 values were identical, both in control and in shock states. This is explained by the fact that CO_2 diffuses readily across the cell membrane and equilibrates. There was only a slight decrease in mean intracellular pH with an insignificant change in mean intracellular $[HCO_3^-]$ ($p>0.05$). It was surprising that there was so little change in intracellular pH and $[HCO_3^-]$ in light of the

severe combined metabolic and respiratory acidosis in extracellular fluid.

To summarize, the blood-gas composition of arterial and venous blood (femoral and mixed venous) react in different ways to a state of decreased cardiac output in hemorrhagic shock. The arterial parameters presented a picture of respiratory compensated metabolic acidosis (a decreased pH, pCO_2, and $[HCO_3^-]$. One might interpret the venous blood-gas values (decreased pH, and HCO_3^- with increased pCO_2) as a respiratory acidosis, superimposed on a metabolic acidosis. Tung et al. (1967) point out the problem in terminology when using acid-base definitions which are based on arterial samples, to describe data from a venous source. The elevated pCO_2 in venous blood does not reflect a pulmonary event. Unless the term "respiratory" is broadened to include tissue perfusion, another term must be found. However, it is evident that when cardiac output is decreased, arterial pCO_2 reflects a pulmonary response and sheds little light on the status of the tissues.

While Tung et al. did not directly compare the blood-gas composition of femoral venous blood to that of mixed venous blood, a visual comparison can be made by plotting his data from femoral blood on a graph with data from arterial and mixed venous blood, as was done in

Figure 7. It can be seen that for the values of pH, pCO_2, and $[HCO_3^-]$, the pattern of change in femoral venous blood mimics that of mixed venous blood in hemorrhagic shock. However, it would be useful to know the femoral venous values at 30, 60, and 90 minutes after hemorrhage.

Murphy (1982) investigated the effects of decreased cardiac output on the blood-gas composition of arterial and mixed venous blood. Ten anesthetized mongrel dogs were intubated and allowed to breath room air spontaneously throughout the experiment. A flow-directed (Swan-Ganz) catheter was inserted into the pulmonary artery (PA). The catheter was connected to a pressure transducer to monitor PA pressures which were recorded as wave changes on a polygraph recorder (Grass Model 7C). Another catheter was placed in the femoral artery. Cardiac output was reduced in stages by controlled bleeding from the femoral artery. Cardiac output was determined using a thermodilution technique. Forty minutes following each bleeding episode, simultaneous anaerobic blood samples of arterial and mixed venous blood were obtained and analyzed for pH, pCO_2, and pO_2. Bicarbonate concentration was calculated from the Henderson-Hasselbalch equation.

Results showed that for each blood-gas parameter

there was a widening of the arterial-venous difference when cardiac output was reduced. The pH of both arterial and mixed venous blood decreased following hemorrhage, but the decrease was more precipitious in mixed venous blood. For pCO_2, the mean arterial value decreased while the mean mixed venous value was essentially unchanged. This finding was contrary to data obtained by Tung et al. (1976), where mixed venous pCO_2 was found to increase after hemorrhage. Murphy explained this descrepancy by looking at what determines mixed venous pCO_2 using the following equation:

$$\dot{Q}\ [CO_2]_{mv} = \dot{Q}\ [CO_2]_a + \dot{V}CO_2 \cdot f \qquad (3)$$

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 is transported as physically dissolved CO_2

From equation 3 it can be seen cardiac output (Q), arterial $[CO_2]$, metabolic CO_2 production and the fraction of CO_2 produced that is transported as physically dissolved CO_2, all affect the $[CO_2]$ of mixed venous

blood. In Murphy's experiments, the only factors which varied were cardiac output and arterial pCO_2. Both cardiac output and arterial pCO_2 decreased resulting in a decreased delivery to the capillary bed. It is probable that the decreased delivery counterbalanced the increased accumulation of CO_2 in the capillaries due to reduced blood flow such that there was no net change in mixed venous pCO_2.

Mean bicarbonate concentration was always greater in mixed venous blood than in arterial. Following hemorrhage, $[HCO_3]$ decreased in both arterial and mixed venous blood, but the decrement was greater in the arterial samples.

Mean arterial pO_2 increased by 17 torr in shock accompanied by a small rise in oxygen saturation of hemoglobin (95 to 99%). For mixed venous blood the pO_2 decreased by 23 torr while oxygen saturation decreased by 30%. These findings are similar to those of Tung et al. (1976). Mixed venous blood gave evidence of the severe state of tissue hypoxia while arterial pO_2 was within normal limits.

Murphy concluded that mixed venous blood follows a predictable pattern during states of decreased cardiac output that is different from arterial blood. Further, that mixed venous blood should be the source of choice in

assessing the acid-base status of the tissues, especially in states of decreased cardiac output.

Murphy's study presents valuable information concerning the behavior of mixed venous blood during hemorrhagic shock. However, it was found that one-half of the dogs were in respiratory acidosis during the control period. This was attributed to the depressant effects of general anesthesia on medullary respiratory centers. Had the animals been mechanically ventilated there probably would not have been such a variance in control values, allowing better comparison of acid-base changes among dogs following hemorrhage.

Summary of the Effects of Decreased Cardiac Output on Arterial and Venous Blood-Gas Composition

1) When cardiac output is reduced, the pattern of change in blood-gas parameters of arterial blood is different than the pattern of change in femoral and mixed venous blood.
2) When cardiac output is reduced the blood-gas parameters of venous blood more accurately reflects intracellular acid-base changes than those parameters in arterial blood.
3) When cardiac output is reduced, the pattern of change in blood-gas parameters of femoral venous blood mimics that of mixed venous blood.

Problem Statement

In this study, the effects of reduced cardiac output on the blood-gas composition of arterial, mixed venous, and femoral venous blood were investigated. In the review of the literature, only two studies were found that investigate the blood-gas composition of femoral and mixed venous blood during states of decreased cardiac output, (Brown, et al., 1967; Tung, et al., 1976). In fact, in these studies, femoral venous blood was analyzed only as it related to intracellular acid-base changes and was not directly compared to mixed venous blood. It is possible, however, by extrapolating from their data, to make some predictions on how the blood-gas composition of femoral venous and mixed venous blood will respond in my study. The following questions were addressed:

1) How does the blood-gas composition of femoral venous and mixed venous blood compare with that of arterial blood when cardiac output is reduced?
2) Will the blood-gas composition of femoral venous blood mimic that of mixed venous blood as cardiac output is reduced?

Implications for Nursing Practice

The practice of professional nursing encompasses a wide range of settings, roles, and services. Depending on the area of specialization, the type of nursing care provided will differ. For example, a psychiatric nurse in a crisis center, a nurse administrator in an HMO, and a critical care nurse in a hospital ICU, would all be performing a variety of nursing services and operating from differing bases of knowledge and expertise. The common focus in their practices would be to assist their patients in achieving their maximum health potential.

For nurses practicing in critical care settings, the knowledge base must necessarily include a grasp of acid-base physiology in order to make the nursing assessments crucial to their patients' recovery. In the last few decades, nurses have acquired greater expertise and assumed greater responsibility in assessment of the patient's condition and implementing nursing intervention. The quality of care nurses provide their patients is dependent, in part, upon their skill in assessing acid-base status through monitoring of fluid balance and vital signs, observation of color and mental status, obtaining blood for blood-gas analysis and interpreting the results.

Hand-in-hand with the expanding role of the nurse

goes the responsibility of keeping abreast of new knowledge in nursing and contributing to that knowledge through research. This proposed research was instigated because recent investigations have shown that mixed venous blood may provide valuable information for acid-base assessment which is not provided by arterial blood. Presently, mixed venous sampling is possible only via placement of a catheter in the pulmonary artery. Pulmonary arterial catheterization is an expensive and painful procedure associated with significant risks. Studies have shown that very young children and older adults are at greatest risk from this procedure (Gwost, et al., 1980). Risk of infection increases each time the system is opened to obtain blood. Further, the small lumen of pediatric-sized catheters increases the chance of blood clotting in the catheter during sampling requiring additional cost and risk in replacement. Obviously, patients would benefit from a less hazardous method of venous sampling.

This study will evaluate the use of femoral venous blood as an alternative to that of mixed venous blood when cardiac output is reduced. An animal is used as a first step in testing the hypothesis. If further testing on human subjects establishes a predictable and reliable relationship between mixed venous and femoral venous

blood, this information will affect how nurses assess patients' acid-base status. For assessment of tissue oxygenation in patients with reduced cardiac output, such as cardiac decompensation following cardiac surgery, or in hemorrhagic shock, venous blood-gas analysis would be needed. The nurse must be cognizant of the risks of pulmonary arterial sampling, as well as the degree to which cardiac output is reduced, when determining if femoral venous blood may be an acceptable alternative to that of mixed venous blood.

By engaging in research of this kind, nurses contribute to new knowledge which will benefit their patients in two ways: 1) it will increase the nurse's ability to make accurate acid-base assessments and initiate appropriate intervention and 2) it will reduce patients' risks associated with mixed venous sampling.

CHAPTER II

METHODS

Statement of the Variables

The independent variable was the change in cardiac output achieved by hemorrhaging the animal. At least three separate phlebotomies were done on each animal during the experiment.

The dependent variables were pH, pCO_2, pO_2, and $[HCO_3]$ of arterial, mixed venous, and femoral venous blood. Prior to phlebotomy, control values for independent and dependent variables were obtained from each animal to serve as baseline data. Following each successive hemorrhage, cardiac output was measured and samples of arterial, mixed venous, and femoral venous blood was obtained.

Design

The design of this study is experimental. An animal model was used. Each animal served as its own control.

Procedure

Ten healthy mongrel dogs were anesthetized with an intravenous injection of sodium pentabarbital (30 mg/Kg). Anesthesia was maintained throughout the experiment with 30-45 mg dose administered intravenously every 1-2 hours as needed. The experimental protocol is summarized in Table 2.

Table 2

Experimental Protocol

Time	Procedure	Stabilization Period
9:00	Surgery: tracheostomy insertion of catheters. Begin mechanical respiration.	60 min.
11:00	Measure cardiac output, obtain control blood samples Set 1 (arterial, M.V., F.V., Hct, plasma proteins).	
11:30	First hemorrhage Analysis of blood-gas composition of control samples.	40 min.
12:30	Measure cardiac output, obtain blood samples, Set 2.	
1:00	Second hemorrhage Analyze Set 2 blood samples.	40 min.
2:00	Measure cardiac output obtain blood samples, Set 3.	
2:30	Third hemorrhage Analyze Set 3 blood samples	40 min.
3:30	Measure cardiac output, obtain blood samples, Set 4.	
4:00	Analyze Set 4 blood samples.	30 min.
4:30	Retransfuse all blood previously removed.	
5:00	Measure cardiac output, obtain blood samples, Set 5.	
5:30	Analyze Set 5 blood samples.	

Once the animal was anesthetized, the surgical procedures were performed. The trachea was cannulated and the cannula attached to a volume respirator. A Swan-Ganz flow-directed thermodilution catheter (7 French) was inserted into the pulmonary artery via the right external jugular vein to obtain mixed venous samples and measure cardiac output. The catheter was connected to a pressure transducer. Progression and placement of the catheter into the pulmonary artery was monitored by wave form and pressure changes recorded on a polygraphrecorder (Grass Model 7C). The left carotid artery was cannulated to obtain arterial blood samples and monitor arterial blood pressure. A femoral vein was cannulated for obtaining femoral venous samples.

The animal was allowed to stabilize for about one hour following the surgical procedures. A baseline cardiac output was obtained and control samples of arterial, mixed venous and femoral venous blood were drawn. Other baseline data collected include heart rate, respiratory rate, blood pressure, rectal temperature, hematocrit and plasma protein concentration.

The animal was then bled via the carotid artery to reduce blood volume and cardiac output. The actual volume of blood removed was approximately 7% of total body weight. On the average, about 16 ml/Kg was removed

with each hemorrhage. The animal was then allowed to stabilize. Cardiac output was again measured following stabilization. Arterial, mixed venous and femoral venous samples were then drawn simultaneously. The animal was hemorrhaged at least two more times, followed by a measure of cardiac output and withdrawal of blood samples as outlined above.

The animal was then transfused with all the blood previously removed in successive hemorrhages. Following stabilization, cardiac output was measured and a final set of blood samples were drawn and analyzed. Blood pressure, heart and respiratory rate, and rectal temperature were monitored throughout the experiment. Body temperature was maintained with a heat lamp.

Once the experiment was completed, the animal was euthenized with an injection of phenobarbital. A post mortem examination confirmed the location of the Swan-Ganz catheter.

Measurements and Reliability of Measurements

Cardiac Output. Cardiac output was determined using thermodilution technique. Syringes containing 3 ml volumes of 5% glucose in water, for injectate, were chilled to 0-5°C and maintained at this temperature in an ice bath. An Edwards Laboratories Cardiac Output computer (Model 9520A) was used to measure cardiac output. This

computer has an accuracy of ∓ 3%+0.02 L/min. and a repeatability of better than ∓ 2%. The computer was connected to an Edwards Laboratories Strip Chart Reacorder (Model 9810) to record thermodilution curves. At least five successive measurements were made each time cardiac output was determined. The three closest values obtained with these measurements were averaged to provide the final values accepted for cardiac output.

Blood Sampling Technique. Blood samples were collected in 1 ml matched glass syringes. To prevent air leakage from contaminating the blood gases, the plungers and barrels were lubricated with silicone stopcock grease. In addition, a small bead of mercury was drawn into the syringe to provide a seal when the syringe was uncapped and to permit gentle mixing of the blood sample just prior to analysis. Heparin was added to the dead space of the syringe to prevent clotting of the blood sample. Syringes were color-coded with a small piece of tape to identify its source: red for arterial, blue for mixed venous and white for femoral venous.

All blood samples were drawn simultaneously and anaerobically using the following procedure: First, a volume of flush solution was removed from the catheter which was equal to twice the catheter deadspace. Blood

was withdrawn slowly, over a period of one minute, into the prepared syringe. Slow withdrawal helps assure that blood from upstream will not be drawn into the syringe. It also decreases the likelihood of drawing in air bubbles from around the hub of the catheter. Once 1 ml of blood was withdrawn, the syringe was held hub down to allow the mercury to seal the blood until the syringe was capped. The syringes were then placed in an ice bath until analyzed. If air contamination was present or suspected, the sample was discarded. A separate blood sample was collected to determine hematocrit and plasma protein concentration.

Analysis of Blood Samples. The blood samples were analyzed within 15 minutes of withdrawal. A Radiometer BGA3 Mark II blood-gas analyzer was used to measure pH, pCO_2, and pO_2. This analyzer has a reproducibility of $\mp$ 0.001 pH units, $\mp$ 0.5 mm Hg pCO_2 and $\mp$ 1.0 mm Hg pO_2. Prior to the analysis of each series of blood samples, the pH, pCO_2, and pO_2 electrodes were calibrated according to the procedure described in the BGA3 Instrument Manual. Samples were analyzed in random order. Repeated readings were made on each sample until 3 readings agreed within 0.005 pH units, or within 1.0 mg Hg for pCO_2 and pO_2.

CHAPTER III

RESULTS

General Description

Ten dogs of mixed breed ranging in weight from 17.7-27.3 Kg were subjects in this study. Each animal was mechanically ventilated at a rate of 12-15/min and a tidal volume of 14 ml/kg body weight. Rectal temperature was monitored throughout the experiment and averaged 38°C ∓ 1.5 in control periods and 37.6°C ∓ 1.5 after hemorrhage.

Hematocrit and serum protein concentrations were measured each time blood samples were obtained. Serum protein concentration ranged from 5.2-7.0 Gm% initially and 4.8-6.1 Gm% when cardiac output was at its lowest. The initial and final mean value for hematocrit remained at 0.47 despite a blood loss great enough to reduce cardiac output by at least 50% of control values (Table 3). Previous investigators have also noted this compensatory response to hemorrhage in dogs (Murphy 1982, Feldon, 1982). This finding is attributed to an infusion of red blood cells into circulation through splenic contraction in response to hemorrhage (Smith & Hamlin, 1970).

Control cardiac output measurements ranged from 2.01-5.60 L/min (Table 3). Cardiac output was reduced in

2, 3, or 4 stages until approximately 45% of the estimated blood volume was removed. Since cardiac output is dependent on body size and the weight of the experimental animals varied so greatly, the post hemorrhage cardiac output values are expressed in terms of percent of control to allow comparison between animals.

Table 4 contains a complete summary of blood-gas values and the corresponding cardiac output for all dogs. The data from Dog 8 are included in Tables 3 and 4 for inspection. However, cardiac output measurements from Dog 8 were suspected to be inaccurate because of 1) failure of deflation of the balloon at the tip of the Swan Ganz catheter resulted in inaccurate cardiac output measurements during control measurements and 2) an episode of unmeasurable bleeding around a blood sampling catheter during the course of the experiment. Since accurate control data from Dog 8 were not obtained further inferences derived from this individual experiment could not be made with any degree of confidence. Therefore, data from Dog 8 were not included in subsequent analyses.

Comparison of Mixed Venous and Femoral Venous Blood-Gas Composition When Cardiac Output is Reduced.

pH The relationship between femoral and mixed venous pH values is shown in Figure 8. Data from

control, hemorrhage and post-transfusion periods are included. Pearson's product moment (r) for the data was 0.96 over the entire range of cardiac output. It is apparent that there is a close linear relationship between femoral and mixed venous pH although nearly all the points fall below the identity line.

pCO_2 Figure 9 shows the relationship between femoral venous and mixed venous pCO_2 values for control, hemorrhage and transfusion periods. There appears to be greater scattering of points above the identity line, particularly when pCO_2 is greater than 55 torr. Eight of 10 points (80%) in this region of high pCO_2 represent cardiac output of 50% of control of less. An r of 0.74 was calculated for the relation between femoral and mixed venous pCO_2 when the entire range of cardiac output was included.

$[HCO_3^-]$ Figure 10 shows the relationship of $[HCO_3^-]$ between femoral and mixed venous blood for control, transfusion and reduced cardiac output. Points appear to be equally distributed on both sides of the identity line. The data yielded an r of 0.81.

pO_2 The relationship between femoral venous and mixed venous pO_2 is shown in Figure 11. Although points are not clustered closely along the identity line, they appear to be linearly related over a range from 16 to 62

torr. Pearson's r was 0.79 when pO_2 data from all ranges of cardiac output were included.

Table 5 shows the results of paired t tests between mixed venous and femoral venous values determined for control, final hemorrhage and transfusion periods. Note that only two values were significantly different at the 0.01 level for a two tailed test. These values were for pH and pCO_2 at final hemorrhage when mean cardiac output was 38 $_w$ 9% of control.

Comparison of Arterial Blood-Gas Composition to that of Femoral and Mixed Venous When Cardiac Output is Reduced

Table 7 shows mean arterial, mixed venous and femoral venous values for pH, pCO_2, $[HCO_3^-]$ and pO_2 for specific ranges of cardiac output. These data are displayed graphically in Figures 12, 13, 14, and 15.

pH The effect of reduced cardiac output and retransfusion on the pH of arterial, mixed venous and femoral venous blood is shown in Figure 12. Arterial pH remained relatively stable throughout the experiment. Femoral and mixed venous pH followed the same pattern, decreasing gradually until cardiac output was approximately 50% of control. However, with further decrements in cardiac output, both decreased more precipitously. With transfusion, the pH of all three

blood sources returned to values which were only slightly more acidic than initial values.

$\underline{pCO_2}$ A comparison of changes in arterial, mixed venous and femoral venous pCO_2 as a function of cardiac output is shown in Figure 13. Mean arterial pCO_2 decreased only slightly as cardiac output decreased (Table 7). Mixed venous and femoral venous pCO_2 decreased in the same general pattern as cardiac output was reduced. However, once cardiac output was reduced to values less than 50% of control, the difference between femoral venous and mixed venous pCO_2 increased (Table 5). With transfusion, arterial and venous pCO_2 values returned to nearly control values.

$\underline{[HCO_3^-]}$ Decreased cardiac output had less effect on plasma bicarbonate concentration than on other blood-gas parameters. Visual inspection of Figure 14 reveals a similar pattern of change for $[HCO_3^-]$ in femoral venous and mixed venous blood, particularly when cardiac output was greater than 50% of control. There was an increase in the arterial-venous difference for $[HCO_3^-]$ in both femoral and mixed venous blood. The $[HCO_3^-]$ returned to slightly lower values in all three samples with transfusion.

$\underline{pO_2}$ From Table 4 it can be seen that for Dogs 3, 5, and 7 control arterial pO_2 was less than 70 torr.

Note that as cardiac output decreased mean arterial pO_2 did not change significantly. However, pO_2 decreased significantly ($p<0.01$) in both femoral and mixed venous blood (Table 6, Figure 15). There is a remarkably similar pattern between changes in mixed venous and femoral venous pO_2 with decreased cardiac output and transfusion. As would be expected there is an increase in the arterial-venous difference for pO_2 when cardiac output decreased. With transfusion mixed venous and femoral venous pO_2 increased markedly, and in an identical pattern, while the increase in arterial pO_2 was negligible.

Comparison of the pH/$[HCO_3^-]$ Relationship in Arterial, Mixed Venous and Femoral Venous Blood

The relationship between pH and $[HCO_3^-]$ as determined from blood-gas analysis of arterial, mixed venous and femoral venous blood is shown in Figure 16. Isobars are shown for mean control arterial pCO_2 (39 torr) and mean control femoral and mixed venous pCO_2 (43 torr). Only values obtained during hemorrhage are included.

Arterial points appear to be equally distributed along the 39 torr pCO_2 isobar in Figure 16. Eighteen of 30 arterial values (60%) fall in the region of compensated metabolic acidosis. Eleven arterial values

(37%) occupy the area between the 39 and 43 torr pCO_2 isobar. One point (3%) is located above the 43 torr isobar.

Only three mixed venous values fell below the 43 torr isobar (control pCO_2 isobar for femoral and mixed venous blood.) Eighty-eight percent of all venous values occupy the region of combined metabolic and respiratory acidosis. Note that metabolic acidosis in venous blood is recognized by a pCO_2 greater than 46 torr. Ten percent of the mixed venous points are located between the pCO_2 39 and 43 torr isobars which is the region for compensated metabolic acidosis for venous blood. All of the 8 femoral venous values that lie above the pCO_2 60 torr isobar are those blood-gas data obtained when cardiac output was less than 50% of control.

Table 3

Summary of Control (C) and Final Hemorrhage (H) values for Cardiac Output, Temperature, Hematocrit, and Plasma Protein

Dog #	Body Wt (Kg)	Total Blood Removed(ml)	Cardiac Output L/min		Heart Rate		Rectal Temperature ° Celcius		Hematocrit		Plasma Protein Concentration GM%	
			C	H	C	H	C	H	C	H	C	H
1	17.7	605	2.33	1.02	132	135	35	36	51	55	6.0	5.8
2	18.2	835	2.99	1.00	177	174	37.5	37.5	41	45	6.8	5.6
3	20.5	900	3.56	0.99	204	-	39	-	48	49	7.0	6.0
4	20.5	825	3.24	1.25	171	144	38	37	47.5	50	6.4	5.2
5	17.7	500	3.77	1.22	186	-	38	-	38	35	5.2	4.8
6	20	500	5.60	1.38	195	165	40	39	34	30	5.2	4.8
7	19.1	500	2.53	1.0	189	177	39	-	42	45	5.2	5.0
8	27.3	800	5.03	1.90	180	188	40	40	51	45	6.2	5.4
9	23.6	650	2.01	1.01	186	180	37.5	36.1	65	59	7.2	6.1
10	24.1	500	3.43	1.64	-	146	38	37.5	48	53	6.0	5.9
X	20.6	646	3.27	1.17	180	163	38.2	37.6	46.6	46.6	6.1	5.5
S.D	3.2	166	1.05	0.23	21	20	1.5	1.5	8.6	8.8	0.7	0.5

Table 4

Summary of Blood-Gas Values and Corresponding Cardiac Output for Dogs 1 - 10

	Cardiac Output		pH			pCO_2 mmHg			$[HCO_3^-]$ mEq/L			pO_2 mmHg		
	$\bar{x}$	%control	A	MV	FV	A	MV	FV	A	MV	FV	A	MV	FV
Dog 1	2.33	100	7.308	7.282	7.276	39.5	46.2	46.7	19.1	21.1	21.0	104.5	46.7	45.9
	1.73	74	7.271	7.257	7.240	42.9	54.4	54.8	19.1	23.5	22.7	97.0	44.5	37.0
	1.32	57	7.261	7.243	7.244	41.2	48.1	50.2	17.9	20.1	21.0	98.3	43.2	44.1
	1.02	44	7.232	7.204	7.153	40.4	52.9	64.1	16.4	20.2	21.8	92.5	36.1	28.6
	2.71	116	T7.289	7.273	7.251	33.1	37.0	39.9	15.4	16.6	17.0	113.3	56.6	45.6
Dog 2	2.99	100	7.348	7.350	7.349	45.1	48.1	47.5	24.0	25.8	25.4	81.6	50.4	40.3
	1.70	57	7.346	7.321	7.321	47.0	48.7	44.8	22.3	24.3	22.4	83.5	47.7	38.7
	1.48	49	7.355	7.333	7.310	41.8	50.1	54.9	22.6	25.8	26.8	85.4	43.5	38.3
	1.32	44	7.378	7.296	7.251	35.4	51.1	66.2	20.2	24.2	28.2	95.6	35.3	34.3
	1.00	33	7.304	7.211	7.116	33.3	51.3	71.0	16.0	20.0	22.2	89.5	30.6	20.6
	3.10	104	T7.307	7.291	7.280	42.4	46.2	48.3	20.6	21.6	22.0	96.6	52.6	53.9
Dog 3	3.56	100	7.338	7.333	7.332	48.0	46.0	47.3	25.0	23.5	24.3	66.6	53.7	57.0
	2.07	58	7.323	7.303	7.308	44.8	47.8	44.8	22.5	23.0	21.8	66.7	56.5	44.3
	1.61	45	7.362	7.320	7.301	41.3	48.5	49.8	22.7	24.2	23.8	79.1	53.3	40.0
	1.53	43	7.373	7.323	7.294	38.3	49.4	52.2	21.6	24.9	24.6	89.4	46.1	38.0
	0.99	28	7.370	7.283	7.248	35.5	51.0	56.3	19.9	23.4	28.8	92.0	45.2	28.3
	4.68	131	T7.378	7.354	7.362	40.4	44.0	41.9	23.1	23.8	23.1	90.1	64.4	56.2
Dog 4	3.24	100	7.429	7.415	7.385	35.3	37.0	43.7	22.7	23.0	25.4	90.3	50.6	42.0
	1.65	51	7.413	7.390	7.370	36.3	39.3	44.2	22.5	23.1	24.8	83.4	40.8	30.2
	1.65	51	7.398	7.350	7.306	33.6	43.4	51.4	20.1	23.2	24.9	80.0	35.3	32.1
	1.55	48	7.368	7.302	7.272	34.5	44.6	55.1	19.3	21.4	24.6	93.9	37.4	35.8
	1.25	39	7.369	7.285	7.243	33.7	48.7	58.3	18.9	22.4	24.4	88.2	31.2	31.7
	1.89	58	T7.371	7.330	7.302	36.9	45.8	50.7	20.7	23.4	24.3	93.9	38.8	41.2
	2.80	86	T7.399	7.385	7.382	38.5	39.6	42.9	23.1	23.0	24.8	91.2	43.7	52.6
Dog 5	3.77	100	7.317	7.293	7.290	46.4	50.5	54.3	23.0	23.7	25.3	59.6	33.0	33.6
	2.27	60	7.325	7.284	7.254	42.3	50.6	58.5	21.4	23.3	25.1	68.2	25.9	22.7
	1.85	49	7.327	7.268	7.212	41.1	50.3	63.1	20.9	22.3	24.6	79.3	22.1	19.2
	1.22	32	7.286	7.236	7.193	41.7	54.5	62.8	19.3	22.4	23.4	79.6	16.3	22.6
	2.00	53	T7.327	7.293	7.249	40.4	47.3	55.7	20.5	22.2	23.6	83.2	30.7	34.4
	3.50	93	T7.337	7.321	7.303	43.4	45.9	49.6	22.6	23.0	23.8	78.6	37.8	41.4
Dog 6	5.60	100	7.376	7.346	7.338	38.2	43.0	40.9	21.7	22.8	21.3	70.5	42.4	43.0
	3.39	61	7.337	7.309	7.286	39.9	43.4	43.2	20.7	21.1	20.0	66.3	35.7	33.3
	1.38	25	7.200	7.135	7.074	38.8	50.4	53.6	14.7	16.4	15.2	79.1	28.5	22.2
	5.12	91	T7.186	7.181	7.205	42.3	44.8	42.6	15.5	16.3	16.3	74.7	50.3	42.3

Table 4 (Continued)

Dog 7	2.53	100	7.397	7.365	7.372	35.3	41.7	39.0	21.1	23.1	22.0	96.9	46.2	41.6
	1.55	61	7.395	7.350	7.334	35.4	43.3	44.1	21.0	23.2	22.8	93.3	39.9	40.4
	1.0	40	7.334	7.264	7.228	36.2	48.9	51.1	18.7	21.5	20.7	94.3	31.5	27.7
	2.50	99	T7.335	7.313	7.298	37.5	42.6	43.1	19.4	20.9	20.5	87.3	48.6	47.5
Dog 8	5.03	100	7.344	7.329	7.333	36.1	37.3	38.3	19.1	19.1	19.7	89.1	62.5	65.9
	2.57	51	7.358	7.307	7.276	35.8	42.5	48.6	19.5	20.6	21.9	93.1	44.7	38.1
	1.90	38	7.353	7.308	7.253	37.7	46.1	53.7	20.3	22.4	23.0	92.5	38.5	33.1
	2.72	54	T7.393	7.369	7.356	35.5	39.1	39.0	21.0	21.9	21.2	101.3	53.0	49.5
Dog 9	2.01	100	7.373	7.354	7.333	29.9	32.4	36.1	16.9	17.5	18.6	91.9	51.9	48.2
	7.78	89	7.327	7.306	7.284	35.3	40.0	47.8	17.9	19.4	22.0	79.4	46.3	29.3
	1.32	66	7.308	7.274	7.219	34.5	42.9	57.5	16.8	19.3	22.8	80.5	41.3	22.9
	1.01	50	7.272	7.217	7.144	35.4	50.6	64.8	15.8	19.9	21.6	83.5	33.2	25.3
	1.87	93	T7.305	7.295	7.234	35.7	38.8	51.8	17.2	18.3	21.2	88.4	44.8	37.5
Dog 10	3.43	100	7.447	7.427	7.436	33.3	37.3	36.3	22.3	23.8	23.7	90.4	44.0	37.8
	2.16	63	7.408	7.373	7.363	36.1	42.8	45.5	22.1	24.2	25.1	89.5	39.6	31.4
	1.64	48	7.387	7.331	7.353	35.5	47.5	44.5	20.7	24.3	24.0	87.1	26.8	36.2
	3.60	105	T7.398	7.385	7.381	38.2	42.9	41.2	22.8	24.9	23.7	91.8	52.6	49.1

Key: A = Arterial Blood
MV = Mixed Venous Blood
FV = Femoral Venous Blood

Table 5
Results of Paired t Test Between Mixed Venous and Femoral Venous Blood-Gas Parameters for Control, Final Hemorrhage and Transfusion Periods*

			Mixed Venous	Femoral Venous	Paired t
pH	Control	$\bar{X}$	7.352	7.346	1.435
			+7.400	+7.394	
		SD	-7.304	-7.298	
	Final Hemorrhage	$\bar{X}$	7.237	7.188	4.2973†
		SD	+8.108	+7.277	
			-7.182	-7.113	
	Transfusion	$\bar{X}$	7.306	7.297	.9964
			+7.379	+7.367	
		SD	-7.244	-7.237	
pCO_2	Control	$\bar{X}$	42.5	43.5	1.0263
		SD	5.9	6.0	
	Final Hemorrhage	$\bar{X}$	50.6	58.5	3.4513†
		SD	2.2	8.1	
	Transfusion	$\bar{X}$	42.4	44.6	1.3837
		SD	3.3	4.2	
$[HCO_3]$	Control	$\bar{X}$	22.7	23.0	0.706
		SD	2.3	2.4	
	Final Hemorrhage	$\bar{X}$	21.2	22.5	1.9434
		SD	2.4	3.6	
	Transfusion	$\bar{X}$	20.9	21.4	1.0491
		SD	3.2	3.0	
pO_2	Control	$\bar{X}$	46.5	43.3	2.1664
		SD	6.3	6.7	
	Final Hemorrhage	$\bar{X}$	31.0	27.0	1.4672
		SD	7.7	5.0	
	Transfusion	$\bar{X}$	50.2	47.3	1.2903
		SD	7.8	6.3	

*Dog 8 excluded
†Significantly different $p<0.01$

Table 6

Results of paired t test for arterial, mixed venous and femoral venous blood-gas parameters between control vs final hemorrhage periods and final hemorrhage vs transfusion periods. Degrees of freedom = 8.*

		Control vs final Hemorrhage	Final Hemorrhage vs Transfusion
Arterial	pH	3.4668†	2.4941
	pCO_2	1.0968	1.5733
	HCO_3^-	4.9909†	3.4407†
	pO_2	0.8782	1.0681
Mixed Venous	pH	6.6814†	11.7685†
	pCO_2	5.2754†	6.7260†
	HCO_3^-	1.6285	0.4518
	pO_2	11.7882†	12.3602†
Femoral Venous	pH	6.9610†	7.8523†
	pCO_2	6.3180†	6.3744†
	HCO_3^-	0.5244	1.3349
	pO_2	6.0678†	9.0768†

*Dog 8 omitted

†Significantly different p=0.01

Table 7
Mean Blood-Gas Values for Five Ranges of Cardiac Output and Post Transfusion*

Range Cardiac Output % Control			pH			pCO_2			$[HCO_3^-]$			pO_2		
			Art	MV	FV	Art	MV	FV	Art	MV	FV	Art	MV	FV
71-100	N=11	$\bar{X}$	7.354	7.336	7.327	39.0	43.3	45.0	21.2	22.5	22.9	85.3	46.3	41.4
		SD	+0.056	+0.055	+0.059	5.9	6.5	6.4	2.6	2.3	2.2	7.0	5.7	7.4
			-0.049	-0.049	-0.052									
61-70	N=4	$\bar{X}$	7.360	7.324	7.297	36.5	43.1	47.6	20.2	22.0	22.6	82.4	39.1	32.0
		SD	+0.050	+0.042	+0.050	2.4	0.3	6.7	2.3	2.2	2.1	12.0	2.4	7.2
			-0.046	-0.047	-0.060									
51-60	N=6	$\bar{X}$	7.342	7.312	7.299	40.1	46.3	48.9	21.1	22.8	23.4	79.2	41.8	35.6
		SD	+0.016	+0.055	+0.048	4.2	4.2	5.6	1.8	1.4	1.8	10.1	10.5	8.5
			-0.017	-0.048	-0.025									
41-50	N=9	$\bar{X}$	7.337	7.286	7.249	38.2	49.4	57.2	20.0	23.0	24.4	87.3	37.1	32.9
		SD	+0.060	+0.053	+0.081	3.0	2.4	7.7	2.5	2.1	2.1	6.1	9.6	7.0
			-0.054	-0.048	-0.068									
<40	N=6	$\bar{X}$	7.301	7.227	7.179	36.6	51.2	58.9	18.1	21.1	22.6	85.7	30.4	25.5
		SD	+0.080	+0.063	+0.083	3.6	2.1	7.2	2.6	3.0	4.5	5.9	10.3	4.4
			-0.067	-0.067	-0.070									
Post-transfusion	$\bar{X}$		7.321	7.306	7.297	39.1	42.4	44.6	20.0	20.9	21.4	90.2	50.2	47.3
N=9	SD		+0.078	+0.073	+0.070	3.4	3.3	4.2	3.2	3.2	3.0	11.0	7.8	6.3
			-0.067	-0.062	-0.060									

*Dog 8 excluded
**Since the pH scale is exponential, the mean pH values were determined by first converting pH to $[H^+]$ and then reconverted back to pH
Note: N refers to number of blood-gas samples included in each grouping.

Figure 8. The identity relationship is shown between mixed venous and femoral venous pH values obtained during control, hemorrhage and transfusion periods. Each symbol represents one pair of values. The identity line shows a slope and correlation coefficient of 1.0. Linear regression analysis for the data were: intercept -1.457, slope 1.196, and r 0.96.

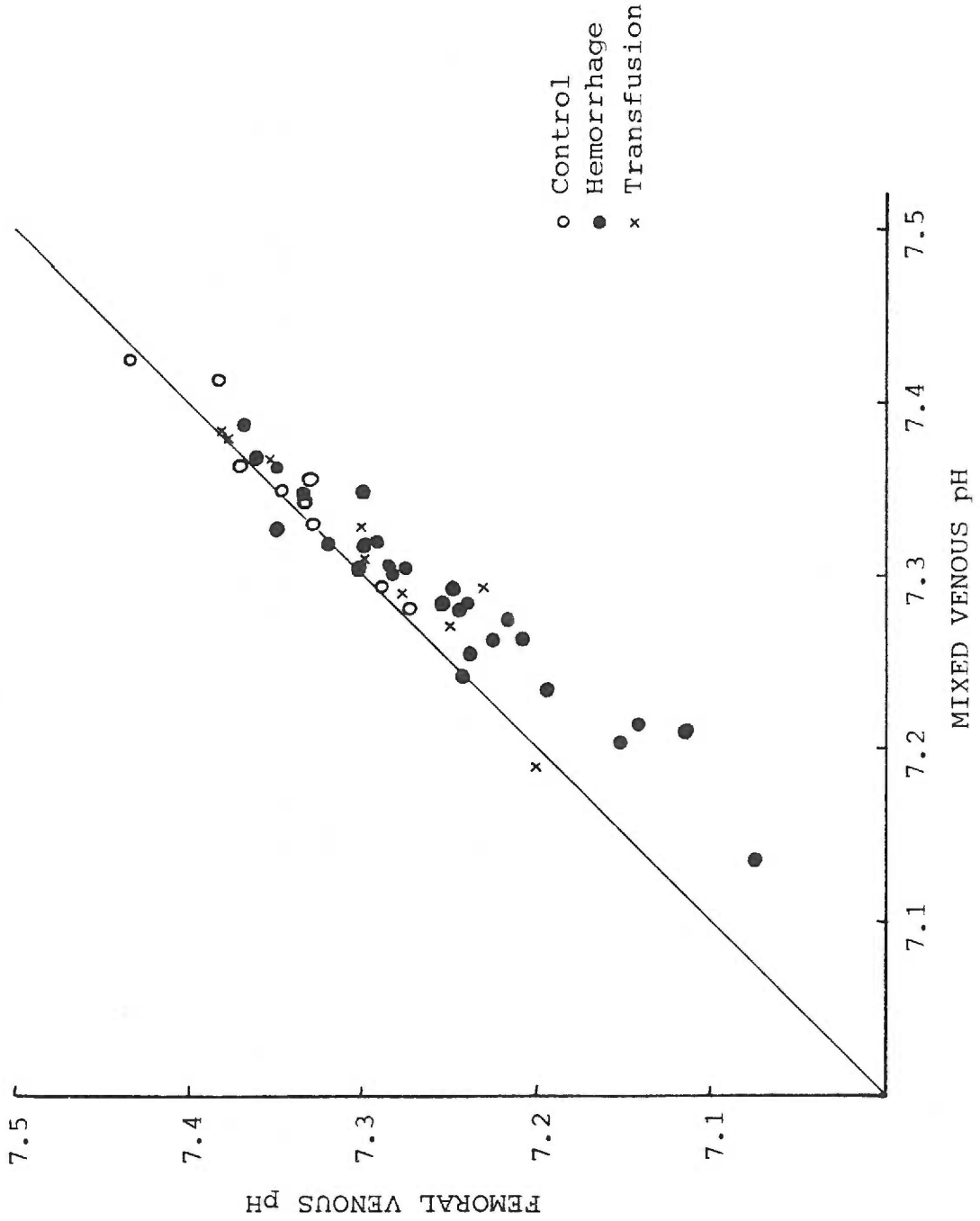

o Control
● Hemorrhage
× Transfusion
FEMORAL VENOUS pH
MIXED VENOUS pH
7.1
7.2
7.3
7.4
7.5

Figure 8

Figure 9. The identity relationship is shown between mixed venous and femoral venous pCO_2 values obtained during control, hemorrhage and transfusion periods. Each symbol represents one pair of values. The identity line shows a slope and correlation coefficient of 1.0. Linear regression analysis for the data were: intercept -6.28, slope 1.23 and r 0.74.

Figure 9

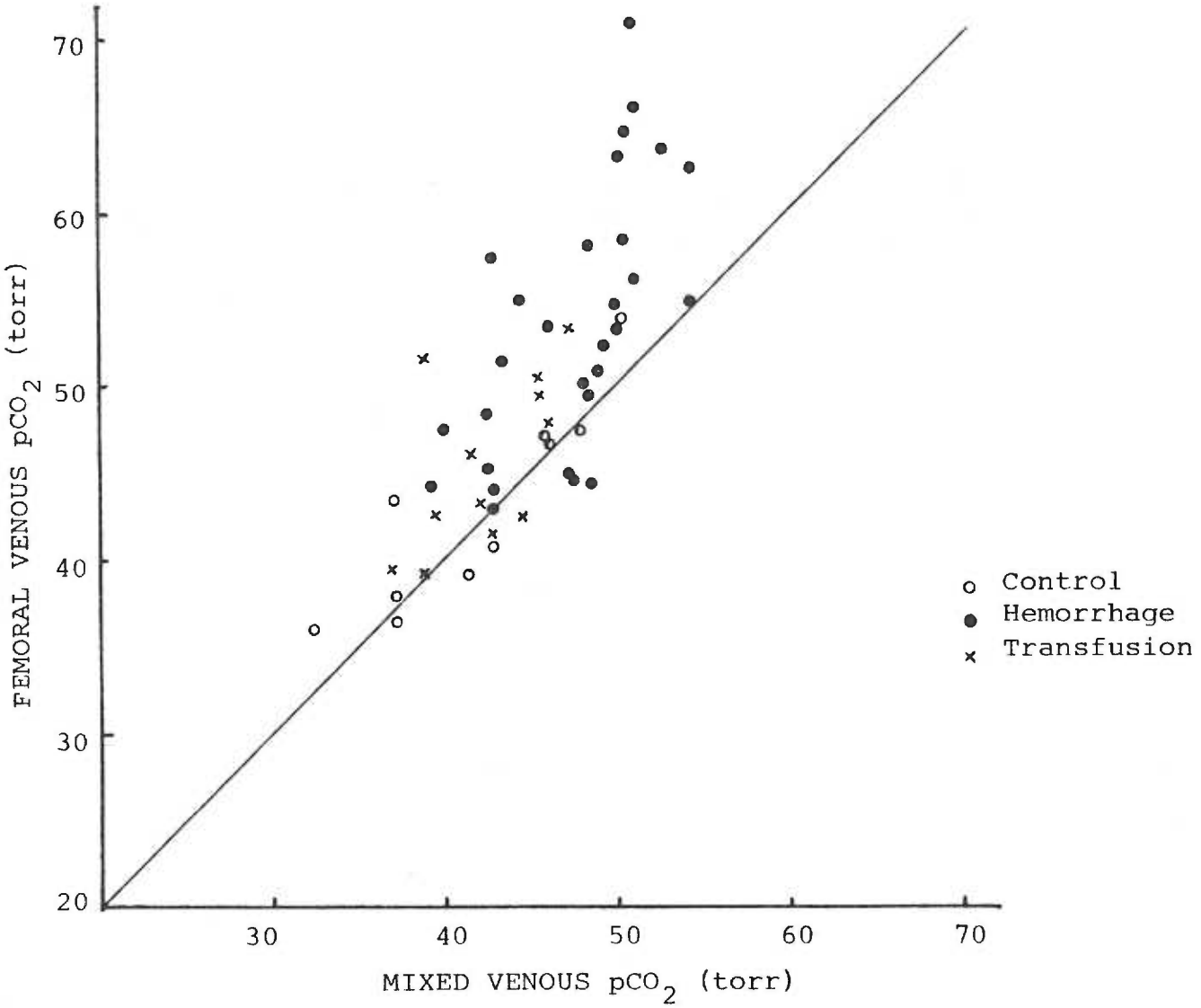

70
60
50
40
30
20
30
40
50
60
70
FEMORAL VENOUS pCO_2 (torr)
MIXED VENOUS pCO_2 (torr)
Control
Hemorrhage
Transfusion

Figure 10. The identity relationship is shown between mixed venous and femoral venous [HCO_3^-] values obtained during control, hemorrhage and transfusion periods. Each symbol represents one pair of values. The identity line shows a slope and correlation coefficient of 1.0. Linear regression analysis for the data were: intercept -2.71, slope 0.91 and r 0.81.

Figure 10

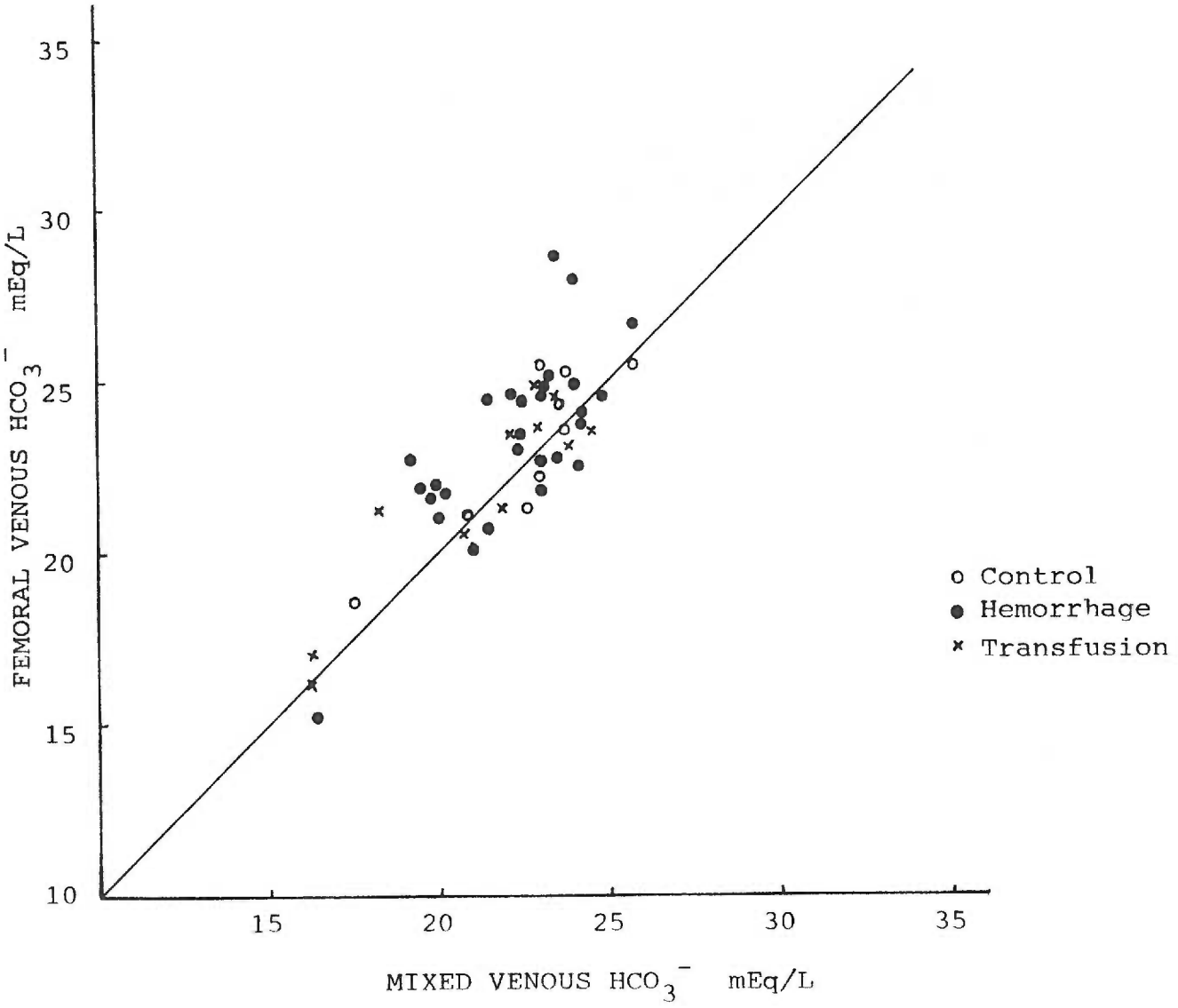

35
30
25
20
15
10
FEMORAL VENOUS HCO_3^- mEq/L
15
20
25
30
35
MIXED VENOUS HCO_3^- mEq/L
o Control
● Hemorrhage
× Transfusion

Figure 11. The identity relationship is shown between mixed venous and femoral venous pO_2 values obtained during control, hemorrhage and transfusion periods. Each symbol represents one pair of values. The identity line shows a slope and correlation coefficient of 1.0. Linear regression analysis for the data were: intercept 5.90, slope 0.75 and r 0.79.

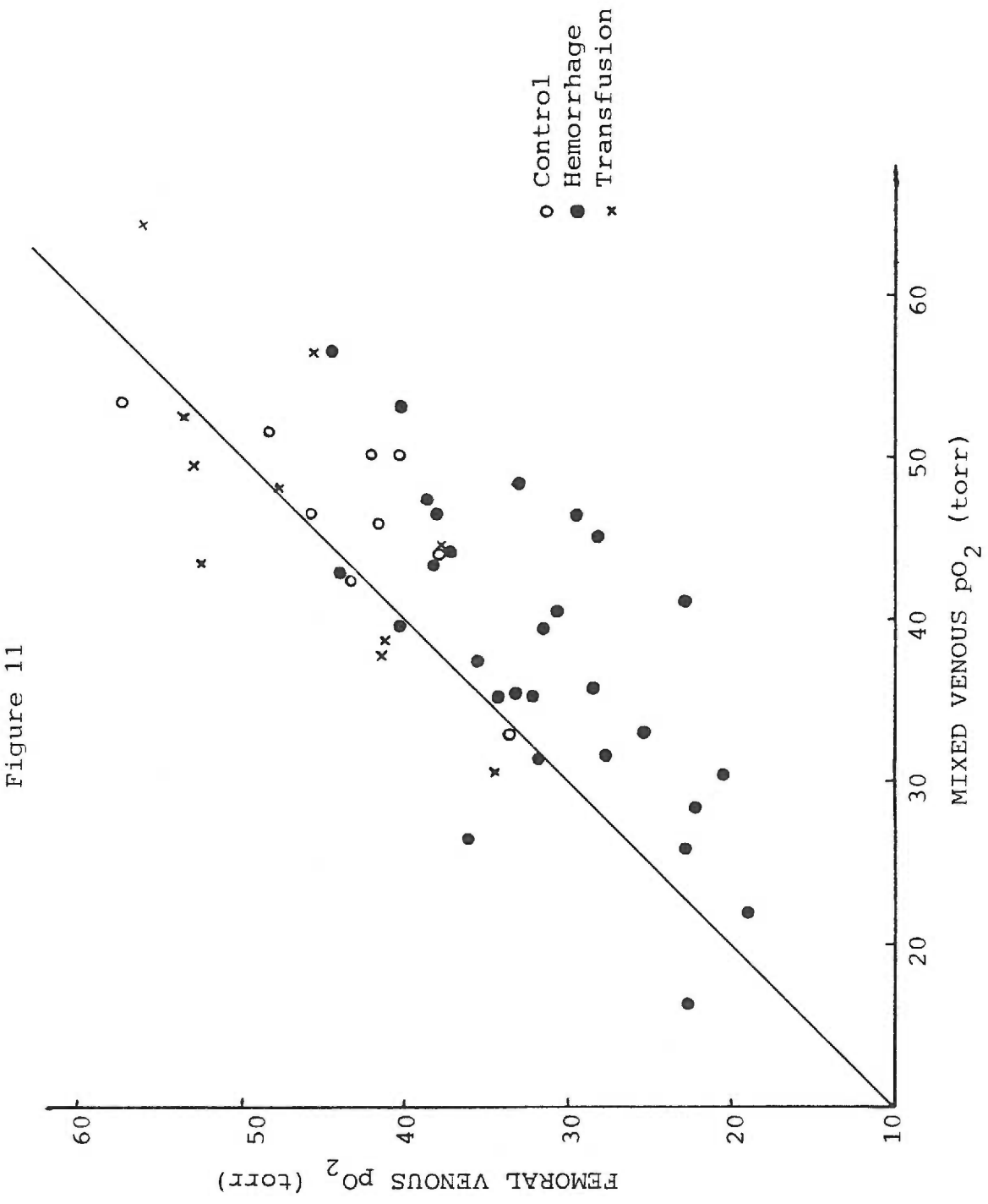

o Control
● Hemorrhage
× Transfusion
FEMORAL VENOUS pO_2 (torr)
MIXED VENOUS pO_2 (torr)
10
20
30
40
50
60

Figure 11

Figure 12. A comparison of pH values in femoral venous, mixed venous and arterial blood at varying reductions in cardiac output from control, and after transfusion. ∘ are femoral venous values, • are mixed venous values and x are arterial values.

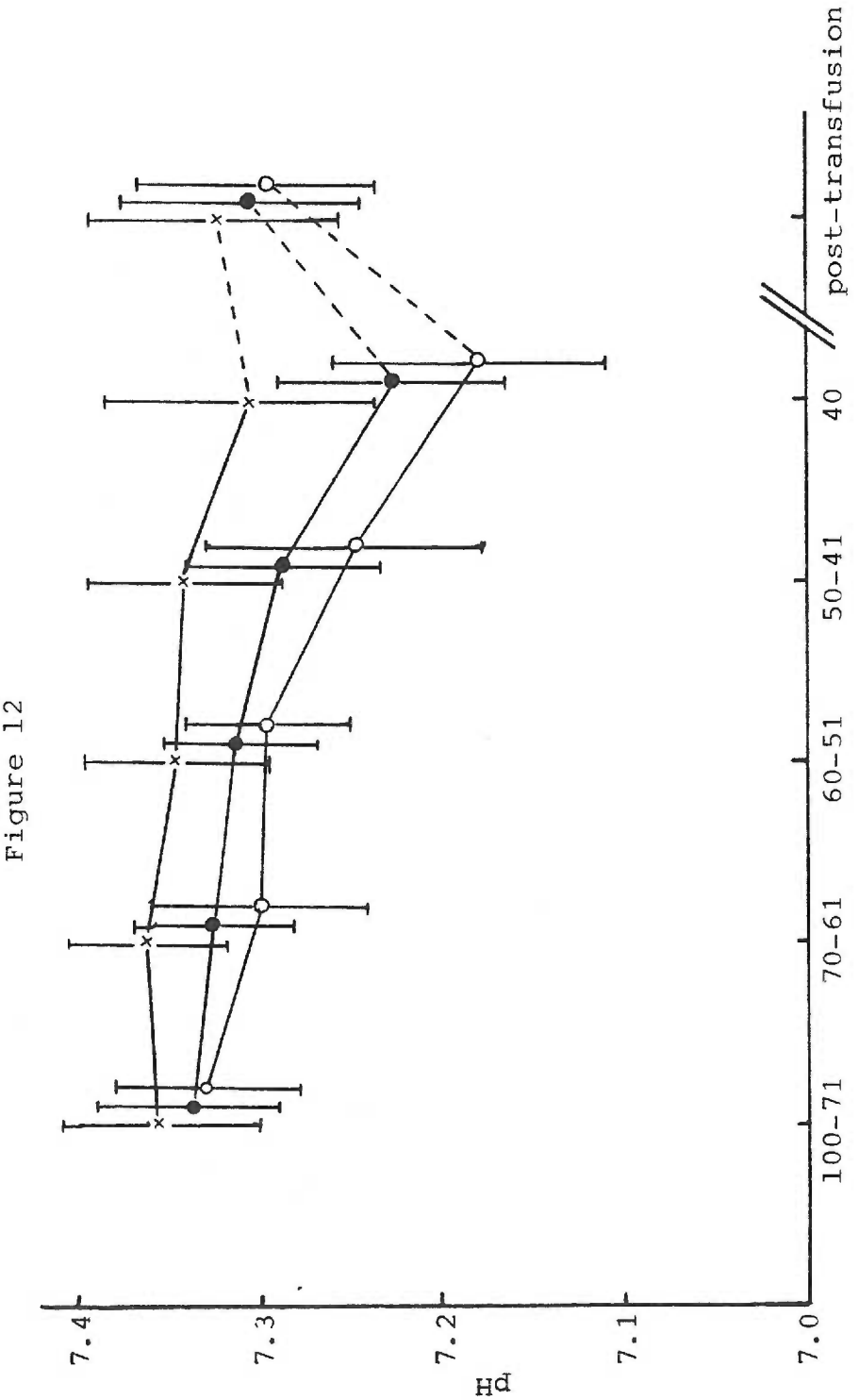

7.4
7.3
7.2
7.1
7.0
pH
100-71
70-61
60-51
50-41
40
post-transfusion
CARDIAC OUTPUT (% CONTROL)

Figure 12

Figure 13. A comparison of pCO_2 values in femoral venous, mixed venous and arterial blood at varying reductions in cardiac output from control, and after transfusion. o are femoral venous values, ● are mixed venous values and x are arterial values.

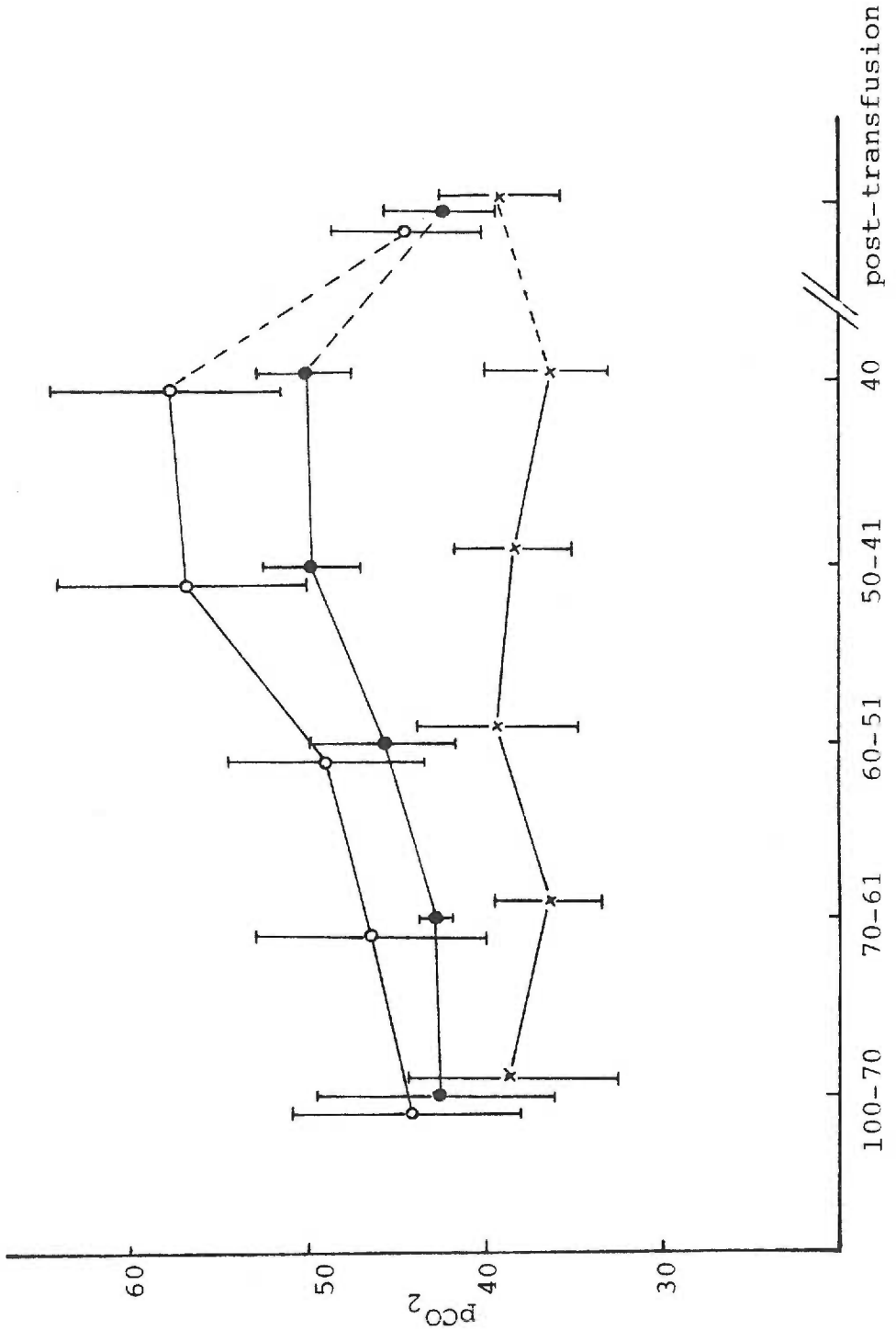

60
50
40
30
pCO_2
100-70
70-61
60-51
50-41
40
post-transfusion
CARDIAC OUTPUT (% CONTROL)

Figure 13

Figure 14. A comparison of $[HCO_3^-]$ values in femoral venous, mixed venous and arterial blood at varying reductions in cardiac output from control, and after transfusion. O are femoral venous values, ● are mixed venous values and x are arterial values.

Figure 14

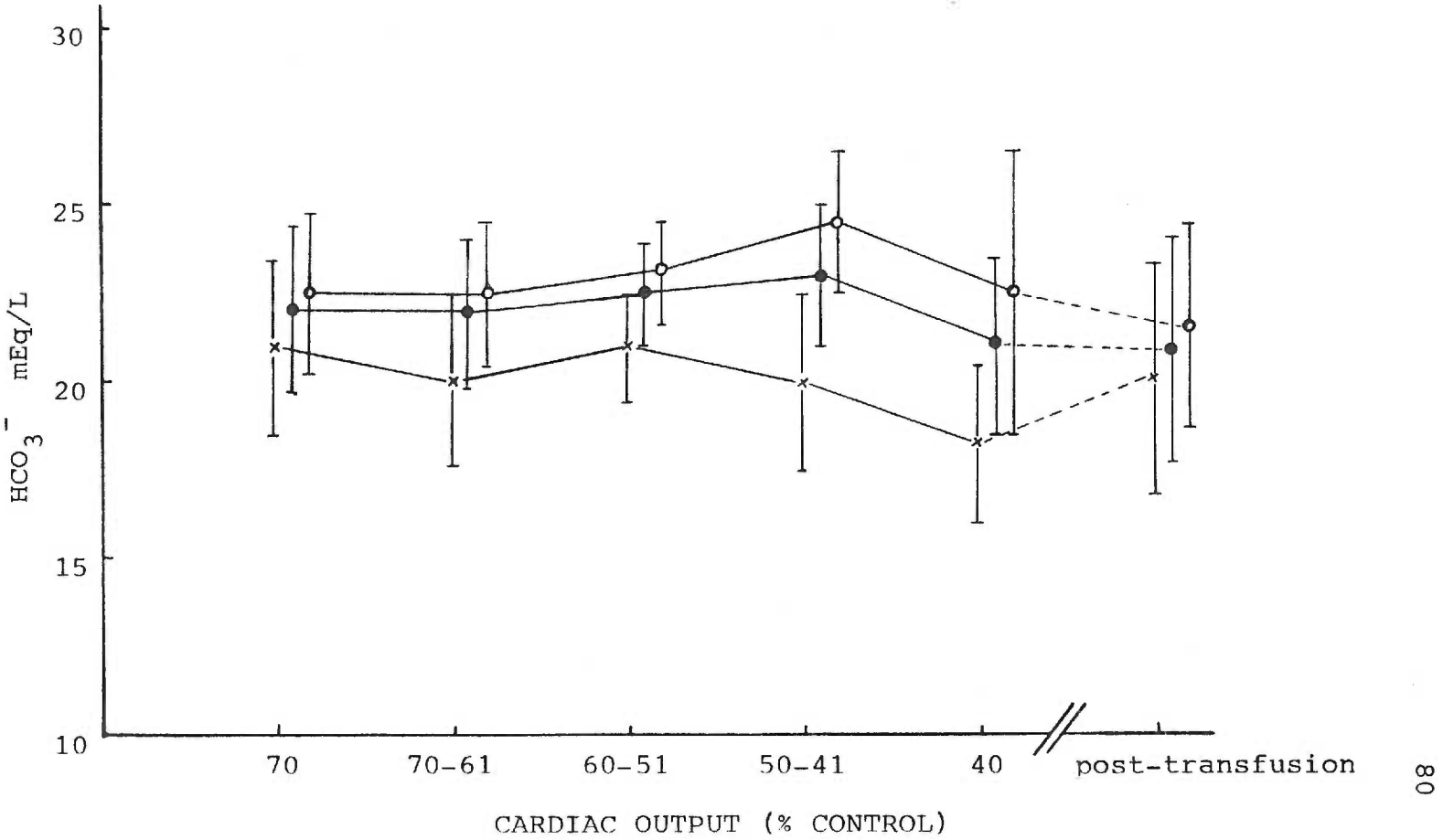

30
25
20
15
10
HCO_3^- mEq/L
70
70-61
60-51
50-41
40
post-transfusion
CARDIAC OUTPUT (% CONTROL)

Figure 15. A comparison of pO_2 values in femoral venous, mixed venous and arterial blood at varying reductions in cardiac output from control, and after transfusion. O are femoral venous values, ● are mixed venous values and x are arterial values.

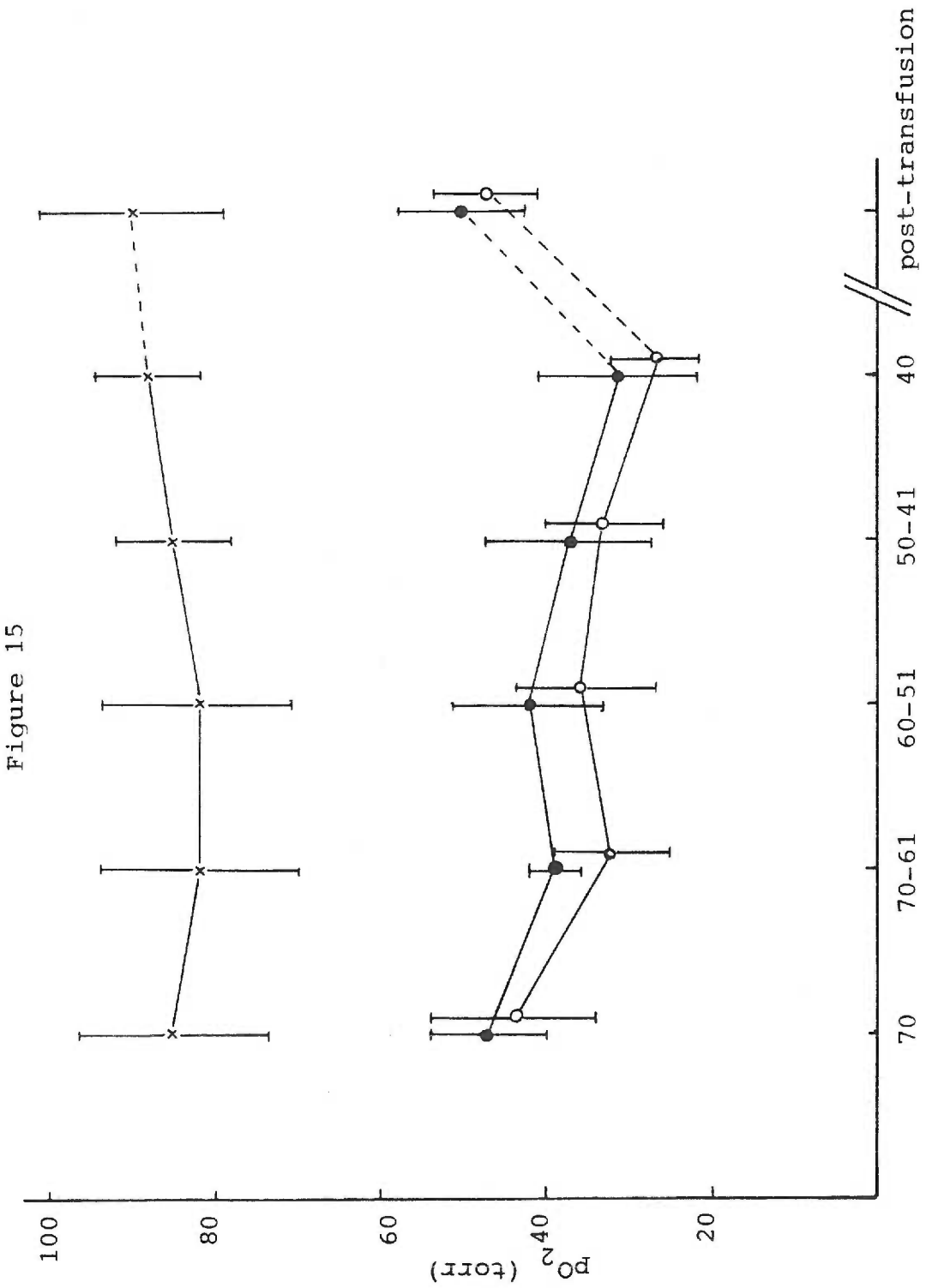

100
80
60
40
20
pO_2 (torr)
70
70-61
60-51
50-41
40
post-transfusion
CARDIAC OUTPUT (% CONTROL)

Figure 15

Figure 16. A diagram of femoral venous, mixed venous and arterial pH and [HCO_3^-] values obtained during hemorrhage periods. Line AB represents the total body buffer curve for dogs. Mean control arterial pCO_2 (39 torr) isobar and mean control femoral and mixed venous pCO_2 (43 torr) isobar are included.

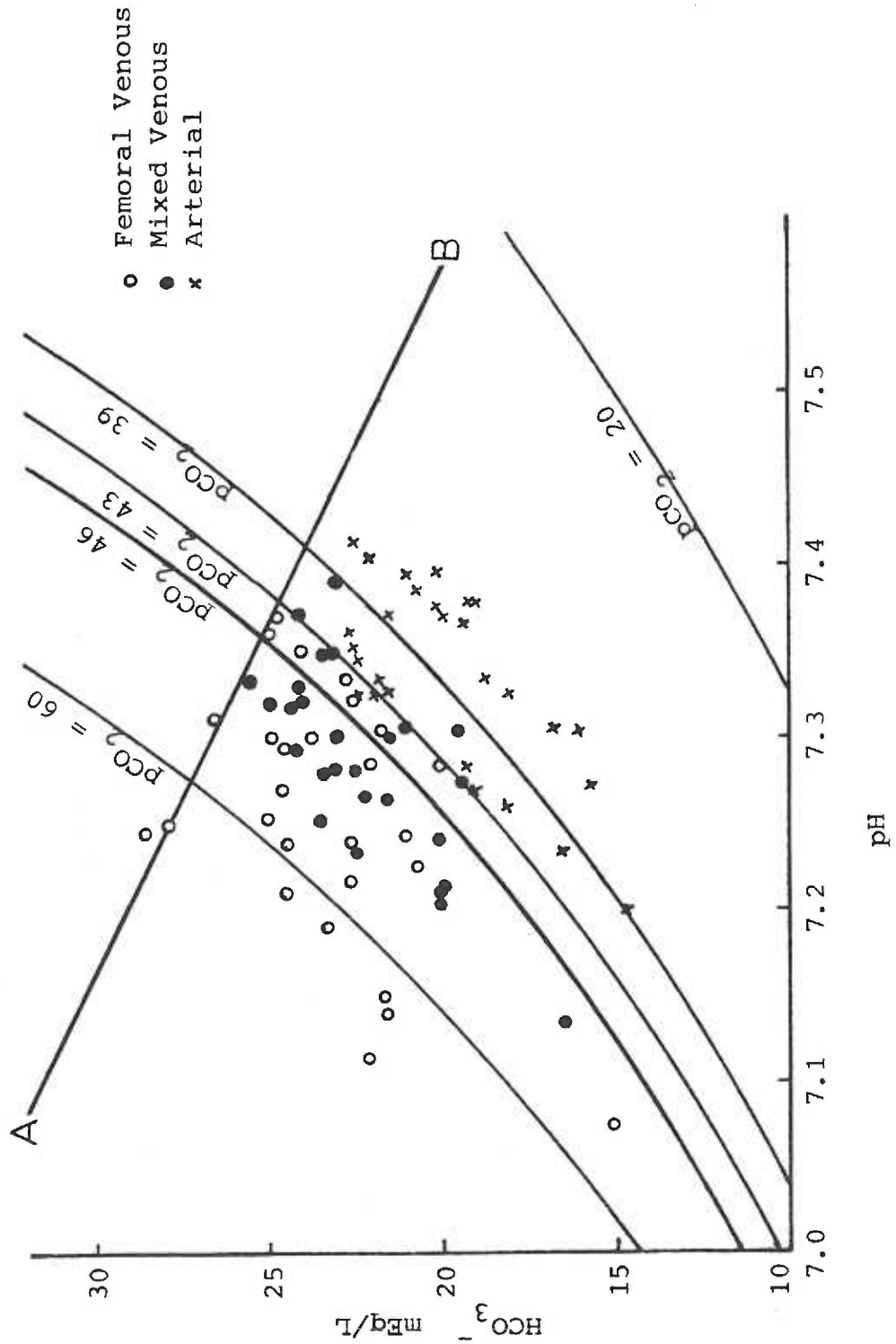

Femoral Venous
Mixed Venous
Arterial
A
B
PCO2 = 60
PCO2 = 46
PCO2 = 43
PCO2 = 39
PCO2 = 20
HCO3- mEq/L
pH
30
25
20
15
10
7.0
7.1
7.2
7.3
7.4
7.5

Figure 16

CHAPTER IV

DISCUSSION

In these experiments hemorrhagic shock was induced in dogs to study the effect of reduced cardiac output on the blood-gas composition of arterial, femoral venous and mixed venous blood. It was hypothesized that the blood-gas composition of femoral venous blood might be a reliable and safe substitute for that of mixed venous blood for assessing acid-base status of systemic tissues. To facilitate the evaluation of the results in terms of this hypothesis, the discussion is organized under the following three headings:

1. How are the physiological changes that occur in shock expected to affect the blood-gas composition of arterial and venous blood?

2. How do experimental results compare to expected results?

3. Is the blood-gas composition of femoral venous blood a reliable substitute for that of mixed venous blood during reduced cardiac output?

Each of these questions is discussed in succession, and then the clinical implications and limitations of the study are presented.

How are the physiological changes that occur in shock expected to affect the blood-gas composition of arterial and venous blood?

In Chapter I, a physiological model (Figure 1) was used to illustrate the relationships of arterial, femoral venous and fixed venous blood under normal physiological conditions. As discussed in Chapter I, arterial blood-gas composition reflects cardiopulmonary function, while venous blood-gas composition reflects tissue perfusion and metabolic activity. Based on these relationships, it is possible to predict how physiological changes occuring in shock will affect femoral venous, mixed venous and arterial gas composition.

Femoral venous blood-gas composition. With a sudden reduction in blood volume, left ventricular filling pressure and cardiac output would be decreased. As a result, arterial blood pressure would be reduced and blood flow through each of the separate circuits represented in Figure I would also be reduced. The blood-gas composition of femoral venous blood would be affected by changes in perfusion of skeletal muscle in the lower limbs. With mild to moderate blood loss, the immediate response of this tissue to hypotension is sympathetic mediated vasoconstriction of both arterioles

and venules. This enables capillary pressure to be maintained at nearly normal or only slightly reduced levels (Wallace, 1981). With hypotension, interstitial fluid enters the capillary and helps restore lost blood volume (Starling's Law of the Capillary). Cells compensate for decreased oxygen delivery by increased oxygen extraction. If blood loss becomes more severe, however, increased oxygen extraction would not meet cell needs. This level of tissue hypoxia causes a shift from aerobic to anaerobic metabolism with increased lactic acid production. Bicarbonate concentration would decrease as hydrogen ions dissociated from lactic acid were buffered. Carbon dioxide concentration would also increase in venous blood as more CO_2 was produced by cell metabolism than could be removed due to the reduced blood flow.

Vasoconstriction tends to maintain arterial pressure initially in the presence of decreased cardiac output. However, with prolonged low blood flow, the local acidosis produced by lactic acid and accumulated CO_2 impairs the autonomic vasoconstrictor effects. As peripheral resistance is diminished, arterial pressure falls and tissue perfusion and oxygenation would degenerate further. The blood-gas composition of femoral blood should reflect the extent of metabolic acidosis in

skeletal muscle tissue, i.e., decreased pH, $[HCO_3^-]$ and pO_2 with increased pCO_2. Because skeletal muscle is poorly perfused in shock, it is likely that femoral blood will reflect a more severe acidosis than may be found in other systemic tissues (Figure 1).

Mixed venous blood-gas composition. The degree to which perfusion of any given organ (or blood flow through any circuit in Figure 1) is reduced is dependent in part upon the ability of the vasculature to autoregulate flow and the influence of sympathetic induced vasoconstriction. For example, blood flow to the head is maintained in shock because cerebral blood vessels lack sympathetic innervation (Wallace, 1981). The kidneys have the capacity to autoregulate renal blood flow with moderate decreases in cardiac output but sympathetic vasoconstriciton dominates with marked reductions in cardiac output (Wallace, 1981). Blood flowing from each separate circuit, therefore, may be of somewhat different composition than other circuits, but will reflect the adequacy of blood flow relative to metabolic conditions of that tissue bed. Mixed venous blood-gas composition in the pulmonary artery is a flow weighted average of the gas composition of all tissues in the body. Blood from tissues such as the brain with relatively normal perfusion and mild acidosis in shock mixes with blood

from tissues such as skin with poorer perfusion and more severe acidosis. It is likely that mixed venous blood-gas composition would be less acidotic than that of femoral venous blood during states of reduced cardiac output.

Arterial blood-gas composition. The blood-gas composition of arterial blood reflects cardiopulmonary function. In hemorrhagic shock myocardial performance is normal initially, but ventricular function becomes depressed as shock persists, and the depression causes further reduction in cardiac output. Hypotension produces an immediate change in lung function by stimulation of peripheral baroreceptors to effect hyperventilation. Hyperventilation causes pCO_2 to decrease in arterial blood and pO_2 to rise. A decrease in pCO_2 will shift Equation 1 (p. 8) to the left decreasing $[H^+]$ and $[HCO_3^-]$ in arterial blood and moderating the fall in pH.

If cardiac output has been only mildly to moderately reduced, a reduction in pCO_2 (and, therefore, H_2CO_3) due to hyperventilation might offset the metabolic acidosis in venous blood. With severe reductions in blood volume, circulating vasoconstrictor substances (norepinephrine and serotonin) cause pulmonary vasoconstriction and, thus, increased vascular resistance

(Shoemaker, 1972). However, these changes are not uniform throughout the lung, and shunting occurs. This shunting causes perfusion of alveoli that are either underventilated (mismatching ventilation and perfusion) or nonventilated (true shunt). Thus, pCO_2 would be higher, and pO_2 would be lower than expected in mixed arterial blood as the result of hyperventilation because of the increased mismatching of ventilation with perfusion.

In mechanically ventilated subjects, respiratory compensation due to hyperventilation is very difficult unless subjects can trigger the respirator. Even if arterial pO_2 did not change, a decrease in arterial pCO_2 and $[HCO_3^-]$ would still be expected due to the Haldane effect. Basically, if the subject can increase ventilation, then arterial pCO_2 would be normal and the acidosis would be uncompensated.

Transfusion. If resuscitative measures, which would include volume expansion such as blood transfusion, were successful, a reversal of the acid-base disturbances just described would be expected. Since venous blood-gas composition is a reflection of tissue perfusion and oxygenation, it is reasonable to expect that any change in tissue status and perfusion would be reflected in venous blood. Arterial blood-gas composition would

reflect gas exchange matching of ventilation and perfusion in the lung. A more accurate picture of the effects of transfusion in the systemic tissues would be provided by the blood-gas composition of venous blood.

How do experimental results compare to expected results?

Venous Blood. In both femoral and mixed venous blood, pCO_2 increased significantly while pO_2 and pH decreased significantly in hemorrhagic shock. These results are in agreement with those based on the physiological model and data reported by Brown et al. (1967) and Tung et al. (1976). Bicarbonate concentration decreased less than was predicted. It is likely that the pCO_2 added enough bicarbonate to venous blood to offset the decrease in $[HCO_3^-]$ produced by buffering fixed acids (Equation 1). The result was only a moderate decrease in bicarbonate concentration.

Venous blood-gas composition relfected a more advanced state of metabolic acidosis and tissue hypoxia than was evident in arterial blood. At final hemorrhage when cardiac output was reduced to values less than 40% of control, the acid-base picture in venous blood was one of combined acidosis with both metabolic and respiratory components (Figure 16). It needs to be emphasized that when speaking of venous blood-gas composition, the term "respiratory component" (i.e. increased pCO_2) does not

refer to a pulmonary condition. As Tung et al. (1976) pointed out, respiration is used in its broadest sense and reflects inadequate perfusion of the cells.

Arterial blood. It was found that arterial blood-gas parameters changed very little when cardiac output was reduced less than 51% of control (Table 7). It is probable that compensatory processes such as vasoconstriction, movement of fluid from ISF to the vascular compartment and redistribution of peripheral circulation, are effective in maintaining homeostasis when cardiac output is only moderately reduced.

With further decrements in cardiac output, arterial pH, pCO_2 and $[HCO_3^-]$ decreased while pO_2 increased. These findings are in general agreement with data obtained from unventilated animals reported by Brown et al. (1967), Tung et al. (1976) and Murphy (1982), except the unventilated animals showed a greater decrement in pCO_2 after hemorrhage. In arterial blood, only pH and $[HCO_3^-]$ at final hemorrhage were significantly different from control in ventilated subjects (Table 6). One might expect a higher pCO_2 and lower pH when the ability for respiratory compensation is restricted. It is probable that minimal respiratory compensation occured in two ways. 1) Hypotension due to severe blood loss produces a strong stimulus in the medulla to increase ventilation.

When cardiac output dropped appreciably, the animals began to "fight" the respirator and they may have increased their ventilation rate. 2) Mechanical ventilation is likely to increase the ventilation perfusion ratio in dependent areas of the lung. Thus, despite shunting, those areas which are perfused would be better ventilated allowing more complete exchange of CO_2 and oxygen. The result of both processes would cause a minimal reduction in arterial pCO_2 rather than a large increase. Because the fall in pCO_2 in arterial blood was so small, the decrease in pH and $[HCO_3^-]$ can be attributed mainly to addition of lactic acid to the blood. The acid-base picture of arterial blood after final hemorrhage was one of mild metabolic acidosis with minimal respiratory compensation.

Transfusion. When shed blood was reinfused, the acid-base disturbances in both arterial and venous blood were corrected. For each blood-gas parameter, post transfusion values in both arterial and venous blood were very close to control values. In arterial blood there was no significant change in pH, pCO_2 and pO_2 between final hemorrhage and transfusion periods (Table 6). This finding is not unexpected since arterial values at final hemorrhage were not greatly different from control values. By contrast, values of venous pH, pCO_2 and pO_2

Table 8. Summary of predicted acid-base disturbance in hemorrhagic shock based on a physiological model and actual experimental results.

		Predicted	Experimental
Femoral Blood	pH	↓	↓
	pCO_2	↑	↑
	HCO_3^-	↓	↓ slight
	pO_2	↓	↓
		Combined acidosis	Combined acidosis
Mixed Venous Blood	pH	↓	↓
	pCO_2	↑	↑
	HCO_3^-	↓	↓ slight
	pO_2	↓	↓
		Combined acidosis	Combined acidosis
Arterial Blood	pH	↓	↓
	pCO_2	normal	↓ slight
	HCO_3^-	↓	↓
	pO_2	↓ slight	↑ slight
		Uncompensated metabolic acidosis	Mild metabolic acidosis with minimal respiratory compensation

after transfusion were significantly different from those at final hemorrhage. This finding has important clinical implications for evaluating the effects of therapy. Venous blood-gas composition will provide more accurate information regarding the effects of treatment in hemorrhagic shock. Venous pO_2 reflects the degree of tissue oxygenation and adequacy of circulation. Venous pH and pCO_2 indicate the degree of acidosis in the tissue. At best, arterial blood-gas composition will reveal to what extent lung function has been affected in shock and the degree of respiratory compensation. These findings support the contention by Kazarian and Del Guercio (1980) that mixed venous oxygen saturation is a more reliable parameter than arterial pO_2 for assessing both the adequacy of circulation and the effects of resuscitative efforts during shock.

Is the blood-gas composition of femoral venous blood a reliable substitute for that of mixed venous blood during reduced cardiac output?

As predicted from the physiological model (Figure 1), it was found that femoral venous blood-gas composition reflected a greater degree of hypoxia and metabolic acidosis than was found in mixed venous blood. Obviously there are other systemic tissues which are better perfused in shock than skeletal muscle in the hind

limb. For femoral venous blood to be a reliable substitute for that of mixed venous blood, it must be shown that there is a correlation between blood-gas values from these two sources or a similar pattern of change in blood-gas composition as cardiac output is decreased.

The results of this study showed a strong correlation ($r = 0.79 - 0.96$) between femoral venous and mixed venous pH, HCO_3 and pO_2 over the entire range of cardiac output (Figures 8, 10, 11). The relationship between femoral venous and mixed venous pCO_2 was also strong ($r = 0.74$), but values were not as strongly correlated when cardiac output was less than 50% of control (Figure 9). Results of paired t tests between mixed venous and femoral venous blood-gas parameters showed only final hemorrhage pH and pCO_2 values to be significantly different ($\underline{p}<0.01$) from each other (Table 5).

It is apparent from inspection of Figures 12, 13, 14, and 15 that there is a remarkable similarity in the pattern of change between femoral and mixed venous blood for every blood-gas parameter. Although femoral venous pH, $[HCO_3^-]$ and pO_2 were consistently lower and pCO_2 consistently higher than respective values for mixed venous blood, the changes in each parameter in femoral

venous blood paralleled its counterpart in mixed venous blood as cardiac output decreased. These results show that femoral venous blood-gas composition reflects the same acid-base disturbances occuring in other tissues in the body, but because skeletal muscle is one of the more poorly perfused tissue beds during shock, the degree of disturbance will be exaggerated. The fact that some individual femoral venous values were significantly different statistically from those of mixed venous blood is clinically unimportant. Since the pattern of change is the same for femoral venous blood and mixed venous blood, appraisal of serial blood samples from either source will indicate improvement or worsening of systemic acid-base conditions.

In comparing the blood-gas composition of peripheral venous blood from the paw to that of mixed venous, Felden (1982) found poor correlation when cardiac output was less than 50% of control. In contrast to our findings, Felden reported that peripheral venous pO_2 was higher than that of mixed venous blood. In addition, peripheral venous samples became very difficult to obtain in the lowest ranges of cardiac output. It would appear that as a result of severely reduced flow to superficial tissues, the blood-gas composition in these areas becomes less reflective of other systemic tissues. While

superficial veins may be a satisfactory sampling site when cardiac output is not greatly reduced, the femoral vein may be the site of choice for moderate to severe reductions in cardiac output.

Clinical Implications

This research corroborates evidence which is accumulating in support of the use of mixed venous blood for systemic acid-base assessment. In addition, femoral venous blood was found to be a reliable alternative to mixed venous sampling. In Chapter I, it was suggested that by engaging in research of this kind, nurses contribute to new knowledge which would benefit their patients in two ways:

1) The nurses' ability to make accurate acid-base assessments and initiate appropriate intervention is increased. Blood gas analysis is but one of the many tools critical care nurses use to monitor and reassess the condition of their patients. In patients with decreased cardiac output, venous blood is the site of choice in obtaining samples for blood-gas analysis. Venous blood-gas composition will provide information concerning perfusion and oxygenation of the tissues. Continued low venous pO_2 values, for example, would alert the nurse that present treatment may not be adequate in restoring circulation. If only arterial blood-gases are

CHAPTER V

SUMMARY, CONCLUSIONS and RECOMMENDATIONS

Summary and Conclusions. Recent investigations have shown that mixed venous blood-gas composition gives a more accurate picture of systemic acid-base status than does that of arterial blood (Brown, Kim & Moorhead, 1967, Tung, Bettice, Wang & Brown, 1976, Murphy, 1982). However, mixed venous sampling is expensive, painful and associated with significant risk to the patient. The purpose of this study was to evaluate the use of femoral venous blood as an alternative to mixed venous for acid-base assessment in states of reduced cardiac output.

Ten healthy mongrel dogs were anesthetized and mechanically ventilated. Cardiac output was reduced in stages by controlled bleeding to a mean low of 38 ± 9% of control. All shed blood was then reinfused. Cardiac output was measured and simultaneous femoral venous, mixed venous and arterial blood samples were drawn following each reduction in cardiac output and reinfusion. Blood samples were analyzed for pH, pCO_2 and pO_2. Bicarbonate concentration was determined from the Henderson Hasselbalch Equation.

The results of this study showed a strong correlation ($r = 0.74$ to 0.96) between femoral venous and

mixed venous blood-gas composition for cardiac output ranging from 100-25% of control. The pattern of change in venous blood-gas composition was different from that in arterial blood. Venous blood-gas values reflected a combined metabolic and respiratory acidosis while arterial blood showed mild metabolic acidosis with minimal respiratory compensation. With transfusion, there was no significant change in arterial pH, pCO_2 and pO_2 from final hemorrhage values. In contrast venous pH, pCO_2 and pO_2 were significantly different after transfusion and showed a correction of the acid-base disturbance.

It was concluded that, with ventilated subjects, femoral venous blood-gas composition is a reliable substitute for that of mixed venous blood when cardiac output is reduced. Further, femoral or mixed venous blood is a better source than arterial blood in systemic acid-base assessment and in monitoring the effects of treatment in hemorrhagic shock.

Recommendations. It is recommended that further clinical investigations be pursued in human subjects testing the reliability of femoral venous blood-gas composition as a mirror to that of mixed venous blood. Ideally these subjects would have pulmonary arterial catheters in place and require mixed venous blood

sampling for clinical reasons. Simultaneous femoral venous blood samples should be drawn for comparison. Femoral venous and mixed venous blood should also be investigated for other models of reduced cardiac output, such as cardiogenic and septic shock.

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AN ABSTRACT OF THE THESIS OF

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For the MASTER OF NURSING

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Title: THE USE OF FEMORAL VENOUS BLOOD IN ACID-BASE ASSESSMENT WHEN CARDIAC OUTPUT IS DECREASED

Approved: [redacted] Thesis Advisor

Recent investigations have shown that mixed venous blood-gas composition gives a more accurate picture of systemic acid-base status than does that of arterial blood (Brown, Kim & Moorhead, 1967, Tung, Bettice, Wang & Brown, 1976, Murphy, 1982). However, mixed venous sampling is expensive, painful and associated with significant risk to the patient. The purpose of this study was to evaluate the use of femoral venous blood as an alternative to mixed venous for acid-base assessment in states of reduced cardiac output.

Ten healthy mongrel dogs were anesthetized and mechanically ventilated. Cardiac output was reduced in stages by controlled bleeding to a mean low of 38 ± 9% of control. All shed blood was then reinfused. Cardiac

output was measured and simultaneous femoral venous, mixed venous and arterial blood samples were drawn following each reduction in cardiac output and reinfusion. Blood samples were analyzed for pH, pCO_2 and pO_2. Bicarbonate concentration was determined from the Henderson Hasselbalch Equation.

The results of this study showed a strong correlation ($r = 0.74$ to 0.96) between femoral venous and mixed venous blood-gas composition for cardiac output ranging from 100-25% of control. The pattern of change in venous blood-gas composition was different from that in arterial blood. Venous blood-gas values reflected a combined metabolic and respiratory acidosis while arterial blood showed mild metabolic acidosis with minimal respiratory compensation. With transfusion, there was no significant change in arterial pH, pCO_2 and pO_2 from final hemorrhage values. In contrast venous pH, pCO_2 and pO_2 were significantly different after transfusion and showed a correction of the acid-base disturbance.

It was concluded that, with ventilated subjects, femoral venous blood-gas composition is a reliable substitute for that of mixed venous blood when cardiac output is reduced. Further, femoral or mixed venous blood is a better source than arterial blood in systemic acid-base assessment and in monitoring the effects of treatment in hemorrhagic shock.