THE USE OF MIXED VENOUS BLOOD TO ASSESS ACID-BASE STATUS IN STATES OF DECREASED CARDIAC OUTPUT WHEN RESPIRATION IS CONTROLLED

by

Barbara J. Berner, R.N., B.S.

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APPROVED:

[redacted]

Jack L. Keyes, Ph.D., Thesis Advisor

[redacted]

Mary McFarland, R.N., M.S.N., First Reader

[redacted]

Karen Griffith, [redacted], Second Reader

[redacted]

Carol A. Lindeman, Ph.D., Dean, School of Nursing

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Introduction

The acid-base status of patients is assessed via blood-gas analysis of a sample of arterial blood. Arterial blood is used for two reasons: first, its composition is uniform throughout the arterial tree, hence, a sample may be obtained from any artery, and second, the blood-gas composition of arterial blood provides data necessary for assessment of pulmonary function.

Obtaining arterial samples requires puncture of an artery. In critically ill patients, arterial puncture may be repeated several times a day. Frequently, a cannula is placed in the artery to facilitate sampling. These procedures cause trauma to the artery and can produce permanent damage (Felden, 1982). Nurses have become more concerned about reducing the risks associated with sampling blood for acid-base assessment. Carveth (1979) and Schriver (1981) used an animal model to show that peripheral venous blood could be used in lieu of arterial blood for assessment of acid-base status. Felden (1982) has shown that in dogs peripheral venous blood can be used to assess acid-base status even when cardiac output is reduced to 50% of control values. Thus, evidence is accumulating that arterial sampling is not always required for acid-base assessment.

Arterial blood has been used for over 60 years for assessment of acid-base status. However, in the last decade it has been argued that acid-base status may be assessed more

accurately by analysis of mixed venous rather than arterial blood. The rationale for this argument is outlined in the Theoretical Framework.

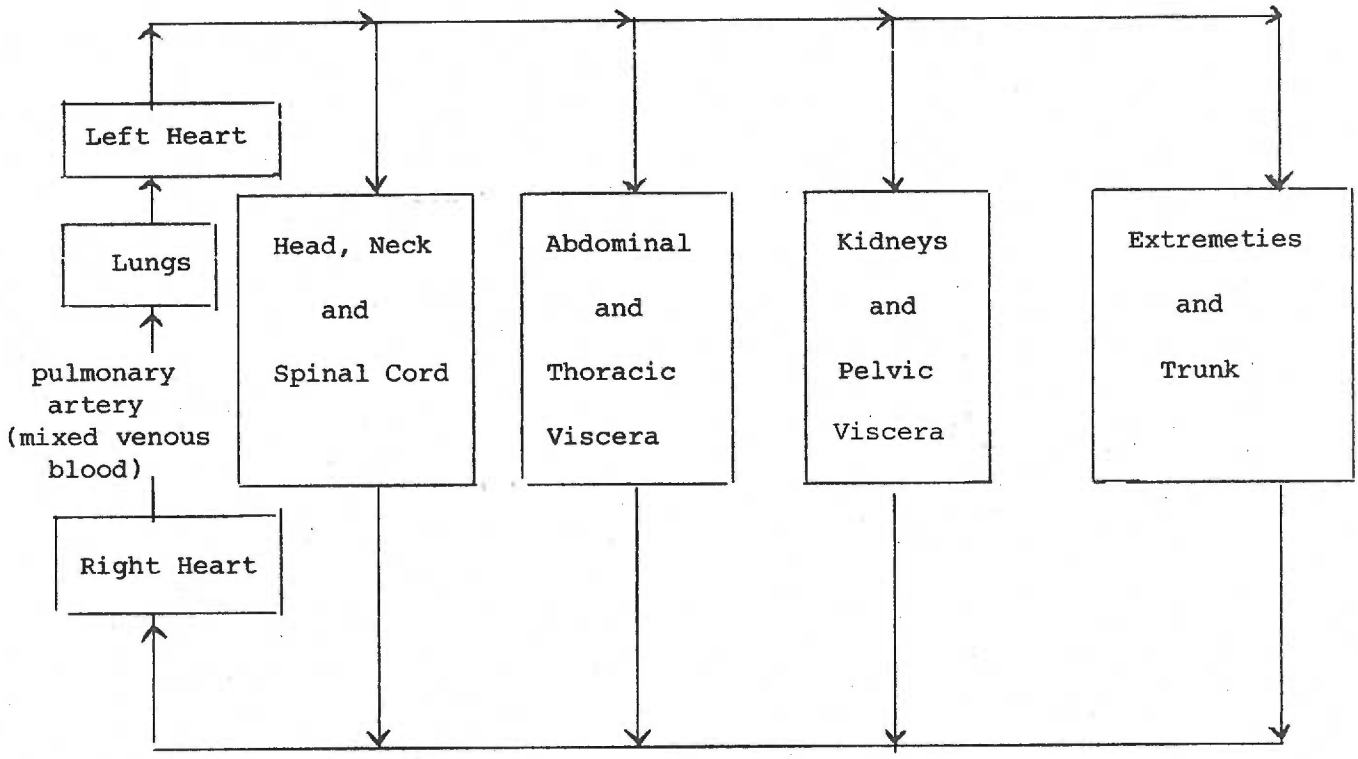
Theoretical Framework

Arterial blood represents the output of the respiratory system. Blood flows through pulmonary capillaries where gas exchange occurs with alveoli. Therefore, the blood-gas composition of pulmonary venous blood reflects the balance between blood flow, ventilation and gas exchange with alveoli. This blood is then delivered to the left ventricle where it is mixed and then pumped into the systemic arterial network. Arterial blood is, therefore, of uniform composition throughout the arterial system.

Figure 1 represents a physiological model of the circulatory system. Blood flow to different organs varies and is altered by changes in metabolic activity of tissues. It follows that the blood-gas composition of venous blood may vary depending on the site from which a venous sample is obtained. Venous blood from different organs is mixed in the right ventricle of the heart. Pulmonary arterial blood is, therefore, of uniform composition and is the flow weighted average of systemic venous blood. Mixed venous blood must then be obtained from the pulmonary artery.

The internal milieu of the body is the interstitial fluid. Arterial blood equilibrates with interstitial fluid in systemic capillaries. The blood-gas composition of blood

Figure 1



Arterial blood is the output from the lungs and represents the input to systemic tisues. Venous blood-gas composition represents the output from these systemic tissues. The difference between arterial and venous blood is what the lungs add and remove, i.e., oxygen and carbon dioxide, respectively. The four pathways depicted represent parallel blood flow through systemic circulation, the totals of which are mixed venous blood.

(Adapted from Griffith, 1980)

which has drained from these capillaries will, then, have the same gas composition of the interstitial fluid. Since the mixed venous blood represents the flow weighted average of all systemic venous blood, it would follow that mixed venous blood-gas composition also represents the true average gas composition of the interstitial fluid, i.e., systemic cell environment. When one discusses acid-base status of the body, one is actually referring to the acid-base status of the interstitial fluid. It is therefore reasonable to conclude that samples of the mixed venous blood rather than arterial blood represent the true acid-base status of the body.

In order to use mixed venous blood for assessment purposes, it must be established that mixed venous blood-gas composition varies predictably during metabolic and respiratory acid-base disturbances as well as during changes in cardiac output. In the literature review, the validity of using mixed venous blood-gas composition to predict acid-base status during both respiratory and metabolic disturbances is established. The predictability or pattern of change in mixed venous blood-gas composition during reduction of cardiac output has not been well established. Nor has the effect of controlled ventilation on mixed venous blood-gas composition been investigated during reduced cardiac output.

It is the purpose of this study to compare changes in blood-gas composition of mixed venous blood with those of

arterial blood in states of reduced cardiac output while ventilation is controlled.

Review of the Literature

The literature review is divided into three sections:

1. Theoretical considerations involving the differences between mixed venous and arterial blood-gas composition.
2. Predictability of mixed venous blood-gas composition in states of respiratory and metabolic acid-base disturbances.
3. The effects of decreased cardiac output on the blood-gas compositions of mixed venous and arterial blood.

Theoretical considerations involving the differences between mixed venous and arterial blood-gas composition.

Roos and Thomas (1967) centered their discussion on the differences between in-vivo and in-vitro titration curves of carbon dioxide [CO_2] in blood. The relationship between CO_2 concentration [CO_2], bicarbonate concentration [HCO_3] and hydrogen ion concentration [H^+] are shown in equation 1. The relationship between [CO_2] and pCO_2 and pH and [H^+] are shown in equations 2 and 3 respectively.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3 \qquad (1)$$

$$[CO_2] \quad S \cdot pCO_2 \qquad (2)$$

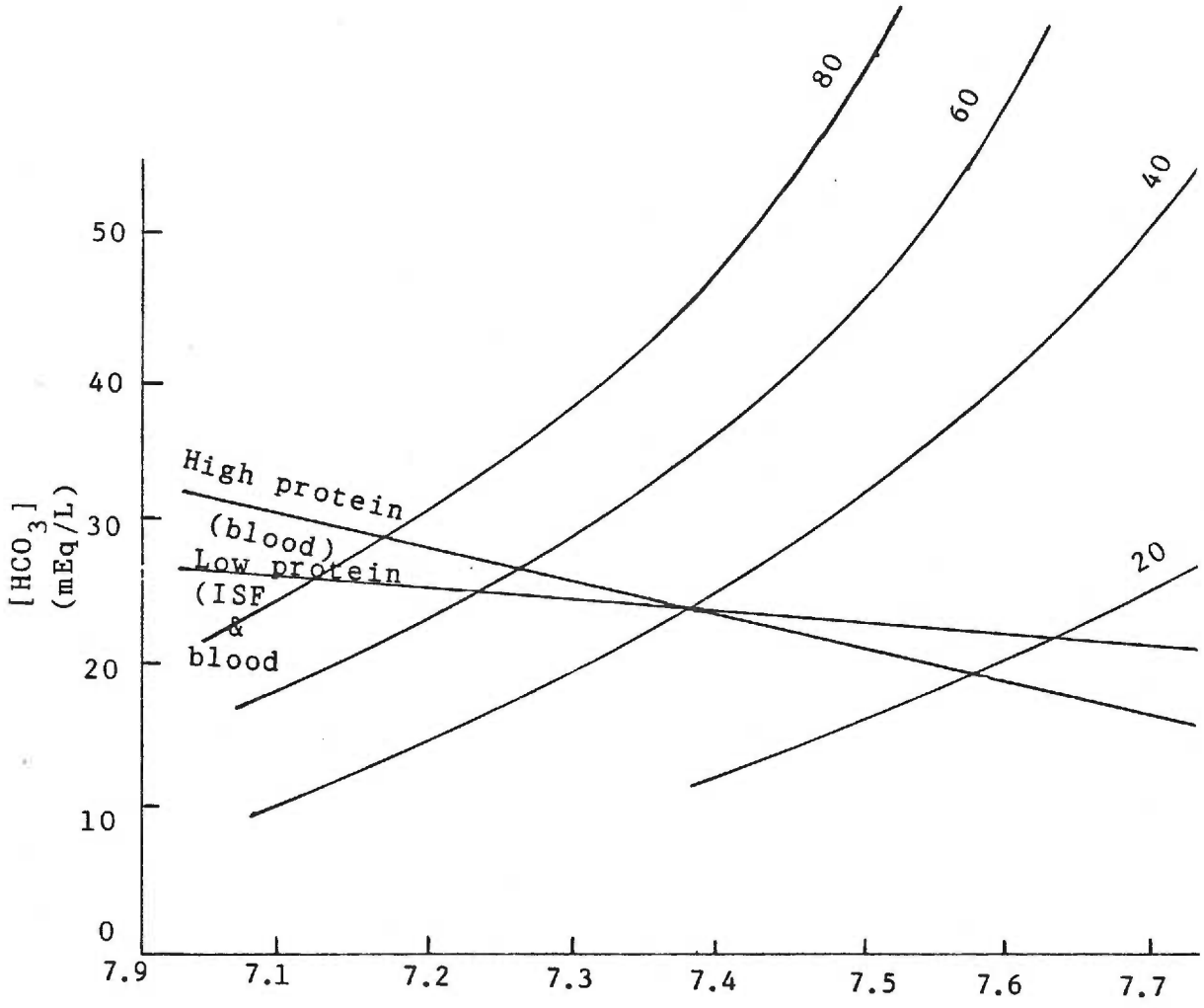
Where S is the solubility coefficient of CO_2 in plasma

$$pH = \log 1/[H^+] \qquad (3)$$

A mathematical model was used to derive values for the CO_2 titration curves when changes in hemoglobin concentration, cardiac output and interstitial fluid volume occurred. It was argued that the slope of the CO_2 titration curve for mixed venous blood represented the in-vivo CO_2 titration curve.

In vitro, the CO_2 buffering capacity of blood is mainly determined by hemoglobin and plasma protein concentrations. Any increase in pCO_2 results in increased bicarbonate concentration [HCO_3], and decreased pH. There will be a greater increase in [HCO_3] as pCO_2 increases if hemoglobin and plasma protein concentrations also increase. The pH, on the other hand, will decrease less for the same change in pCO_2 with these same changes in hemoglobin and plasma protein concentrations. In vivo, buffering is influenced by both blood buffer concentration and the volume of interstitial fluid (ISF) with which blood equilibrates. Interstitial fluid contains no hemoglobin and very little protein, hence, ISF cannot buffer carbonic acid produced from added CO_2 (equation 1). When CO_2 is buffered in blood, the HCO_3 formed diffuses not only throughout the plasma, but also into the ISF. The net effect is to dilute the change in [HCO_3], or in other words, the effect is the same as if the ISF volume were added to the blood thereby diluting blood buffers. Hence the slope of the CO_2 buffer curve in vivo is less than that for blood alone in vitro (Figure 2). It should be noted that

Figure 2



The difference in the slopes of the CO_2 titration curves for blood, and blood plus interstitial fluid during changes in CO_2 concentration.

Roos and Thomas did not include cellular buffering in their model.

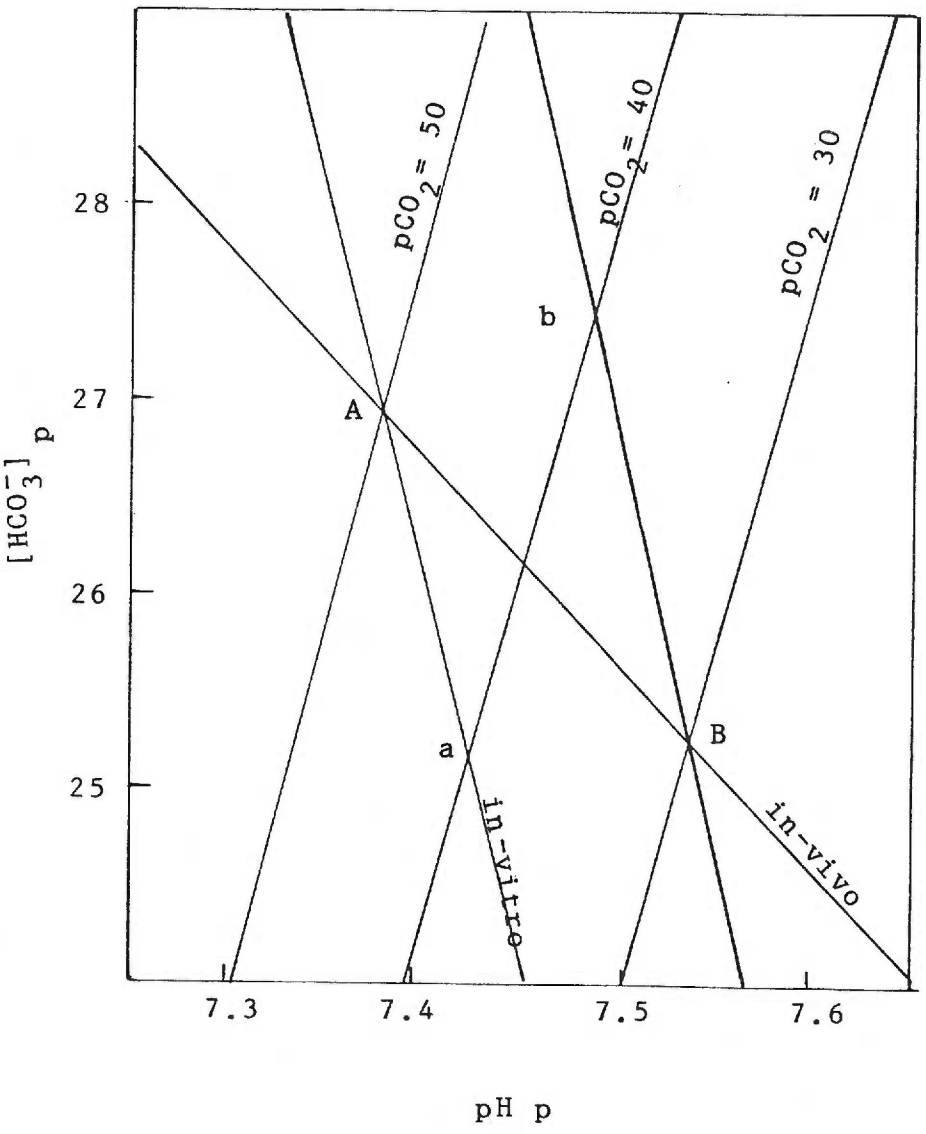
Differences between in-vivo and in-vitro buffering curves can be displayed graphically. The authors, in an attempt to eliminate the confounding problem of the Haldane effect, assumed the blood was 100% saturated with oxygen. Figure 3 shows the in-vivo and in-vitro titration curves of mixed venous blood.

Michel (1968) extended the theory proposed by Roos and Thomas (1967) by including the Haldane effect on the in-vivo buffering of volatile acid (CO_2). He described how the Haldane effect influences in-vivo buffering during hypoxemia and respiratory exchange in the lungs and systemic tissues. He also described how the arterial-venous (A-V) differences in oxygen (O_2) saturation of hemoglobin were altered by the Haldane effect in-vivo. Michel concluded that the true in-vivo CO_2 blood buffer curve was that of mixed venous blood.

The Haldane Effect

A decrease in O_2 saturation of hemoglobin leads to an increase in the blood's ability to buffer CO_2. This increase in buffering ability, called the Haldane effect, is influenced in-vivo by exchanges occurring with interstitial fluid and tissue cells. These exchanges cause a dilutional effect on blood buffers. As a result, the in-vivo scope of this buffering curve is less than the in-vitro slope and the Haldane effect in-vivo is less than that in-vitro (Figure 4).

Figure 3



"Normal in-vivo CO_2 titration curve of true oxygenated mixed venous plasma (AB), and two in-vitro curves (Aa and Bb), obtained on mixed venous blood withdrawn at pCO_2 = 50 (A) and 30 (B), respectively." Redrawn from Roos and Thomas, 1967, page 1050.

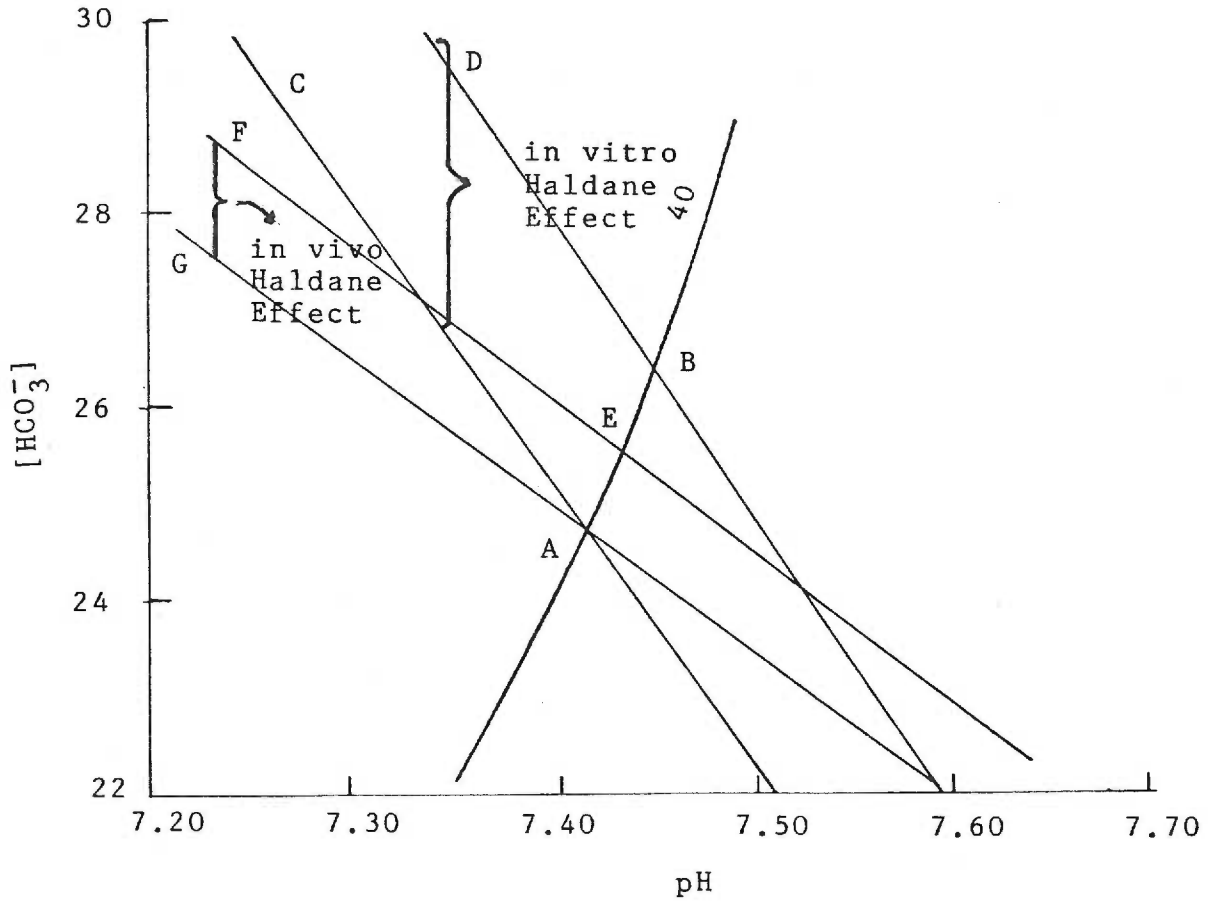
The Haldane Effect During Hypoxemia

The Haldane effect plays an important role in hypoxemia. The effects of changing O_2 saturation on pH and $[HCO_3]$ were considered by Michel. As a first approximation, Michel assumed cardiac output and O_2 consumption remained unaffected by hypoxemia. When fully oxygenated blood is deoxygenated in-vitro at a constant pCO_2 , plasma pH increases. This is accompanied by an increase in $[HCO_3]$. If one computes this change for in-vivo conditions however, the plasma pH and $[HCO_3]$ increases by only one third that calculated from blood equilibrated in-vitro. This difference is due to the dilutional effect of interstitial fluid in-vivo. Michel did not take cellular exchange into account with in-vivo buffering.

Respiratory Exchange

In respiratory exchange in the lungs, gas equilibration occurs between the blood and the alveoli. Michel argued that the resulting changes in pH and $[HCO_3]$ followed the in-vitro curve. Evidence was presented to support the argument that bicarbonate ions do not exchange with extravascular sites in the pulmonary circulation. The dilutional effects of pulmonary extravascular fluid would, therefore, be minimal. On the other hand, Michel argued that venous blood gas composition is affected by exchange of bicarbonate ions in equilibrium with ISF in systemic capillaries.

Figure 4



The Haldane effect upon the pH and [HCO_3] relationships of blood in-vitro and in-vivo. Line AC denotes oxygenated blood in-vitro. Line BD denotes deoxygenated blood in-vitro. Line AG denotes oxygenated blood in-vivo. Line EF denotes deoxygenated blood in-vivo.

Adapted from Michel (1968), page 285.

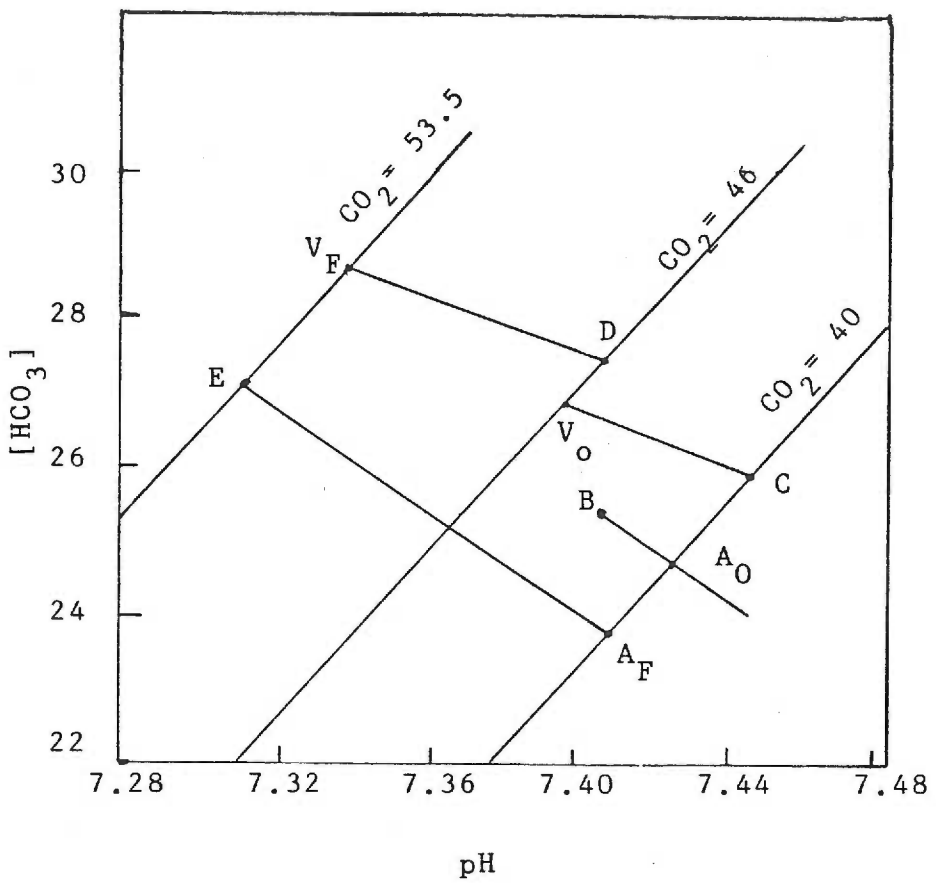
Arterial-Venous Differences

The pCO_2 and pO_2 of arterial blood were maintained in this mathematical model at a constant level by assuming a constant alveolar ventilation rate. When the A-V difference for saturation of hemoglobin was doubled, as would be found clinically with a reduced cardiac output or increase in metabolism, the result was a doubling of the desaturation of O_2 in the venous blood. Figure 5 shows changes in the composition of arterial and venous blood as the A-V difference for oxygen saturation increases.

Point A_o represents arterial blood at pCO_2 of 40 torr and an O_2 saturation of 100% as it leaves the lungs. Line A_oB is the in-vitro buffer line. As oxygen is delivered to the tissues, O_2 saturation of the blood is decreased. Point C represents this shift which is due to the Haldane effect. As CO_2 is added to the blood from tissue metabolism, the blood is titrated to point V_o along an in-vivo buffer line. The pCO_2 of the venous blood is now 46 torr. If a reduction in blood flow occurs there will be a further decrease in the saturation of O_2 in venous blood. The shift from point V_o to point D represents the Haldane effect resulting from this change. The CO_2 continues to increase due to this low blood flow and causes a shift from point D to point V_F again along an in-vivo buffer curve. The pCO_2 is now 53.5 torr.

When the blood is then reoxygenated in the lungs and its O_2 saturation returns to 100%, there is a shift from point V_F to point E (Haldane effect). As the CO_2 is removed from the

Figure 5



Doubling the A-V pO_2 saturation difference affects the pH and the $[HCO_3]$. Note lines A_oB and A_FE represent in-vitro slopes while V_oC and V_FD represent in-vivo slopes.

Adapted from Michel, 1968

blood in the pulmonary system, the blood is titrated to point A_F along an in-vitro buffer curve. The end result is a decrease in the pH and $[HCO_3]$ values in arterial blood (A_F as compared to A_o) even though arterial pCO_2 is constant. Since the arterial $[HCO_3]$ has decreased, (point A_F), it could be misinterpreted as a mild metabolic acidosis in spite of the fact that there has been no addition of extra acid other than carbonic acid (i.e., addition of CO_2) to venous blood. Conversely, if the A-V difference is decreased, it can be shown that there will be an increase in the arterial $[HCO_3]$ at constant arterial pCO_2.

The author concluded that venous blood represented the in-vivo CO_2 dissociation curve. The arterial blood is a "transformation of the mixed venous blood according to the in-vitro dissociation curves" (Michel, p. 290). It follows then, that mixed venous blood-gas composition should be used to determine acid-base status.

Predictability of mixed venous blood gas composition in states of respiratory and metabolic acid base disturbances.

Griffith (1980) compared arterial and mixed venous blood gas composition in respiratory acid-base disturbances over wide ranges of pH.

Ten healthy mongrel dogs of both sexes were anesthetized and tracheotomies were performed. Respiration was controlled by the use of mechanical ventilation. Temperature was monitored throughout the procedure. A cannula was inserted into the carotid artery for withdrawal of arterial samples. A Swan-

Ganz flow-directed catheter was passed into the pulmonary artery for withdrawal of mixed venous blood samples. Proper placement of the catheter was assured by monitoring pressure and wave form changes on a polygraph. Position of the pulmonary artery catheter was also checked during post mortem examination. All blood samples were drawn simultaneously and anaerobically.

After a period of stabilization, respiratory acidosis was induced in five dogs. The respirator was connected to a Douglas bag containing 3% CO_2 in O_2. Arterial and mixed venous samples were drawn and analyzed at periods of 20 minutes and 60 minutes after F_ICO_2 was increased. The animals were then given step increases in the percentage of CO_2 in O_2 from 0% (room air, control) to 3% to 5% and finally 10% CO_2 in O_2. Again samples were drawn at 20 and 60 minutes following each step increase in fraction of inspired CO_2 (F_ICO_2).

Decreasing percentages of CO_2 in O_2 were then measured in steps using decrements from 10% CO_2 in O_2 to 5% CO_2 in O_2 and finally to 3% CO_2 in O_2. Samples were obtained and analyzed as described above.

Respiratory alkalosis was induced in the last five dogs by increasing tidal volume of room air in increments of 150 ml from initial volumes of 200 ml to maximum volumes of 650 ml. Respiratory rate was kept constant. Reduction of tidal volume was then accomplished by reversing the order. Samples

were drawn and analyzed at 20 and 60 minutes after each change in tidal volume.

Results showed a high correlation between arterial and mixed venous blood-gas parameters in states of respiratory acid-base disturbances. There was a predictable pattern to the changes in mixed venous blood-gas composition during respiratory acidosis and alkalosis. The pH of mixed venous blood was uniformly lower than that of arterial blood. Since additional acids are added to venous blood from systemic tissues, this result would be expected. Mixed venous blood pH, then, while not being identical, followed changes in arterial blood pH, hence the pattern of change in arterial and mixed venous pH were the same.

The pCO_2 of mixed venous blood was uniformly greater than that of arterial blood. When a steady state exists:

$$\dot{Q} \cdot CO_{2\,mv} = \dot{Q} \cdot CO_{2\,a} + \dot{V}CO_2 \cdot f. \quad (4)$$

$\dot{Q}$ = cardiac output

$CO_{2\,mv}$ = concentration of physically dissolved CO_2 in mixed venous blood

$CO_{2\,a}$ = concentration of physically dissolved CO_2 in arterial blood

$\dot{V}\,CO_2$ = metabolic CO_2 production

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

From this equation, it is clear that the pCO_2 of mixed venous blood should be greater than that of arterial blood. This was observed in the experiment.

The pO_2 of mixed venous and arterial blood during the hypercapnic experiments was increased because of the large increase in F_IO_2. During hyperventilation episodes, however, arterial pO_2 increased, while mixed venous pO_2 decreased. This decrement could be explained by a decrease in cardiac output.

$$\text{if } [O_2]_a \dot{Q} = [O_2]_{mv} \dot{Q} + \dot{V}O_2 .$$

$[O_2]_a$ = O_2 concentration in arterial blood

$\dot{Q}$ = cardiac output

$[O_2]_{mv}$ = concentration of O_2 in mixed venous blood

$\dot{V}O_2$ = oxygen uptake

$$\text{thus } [O_2]_a - [O_2]_{mv} = \frac{\dot{V}O_2}{\dot{Q}} .$$

If inspired gas mixture, alveolar ventilation rate and oxygen uptake are constant, then a reduced cardiac output will cause a decrease in the pO_2 of mixed venous blood. The animals were anesthetized and curarized. The ventilation was controlled and body temperature was constant, therefore, the O_2 consumption was assumed to be constant. Reduced cardiac output could have been produced by mechanical positive pressure ventilation. The decrease in mixed venous pO_2, then, was likely due to this decreased cardiac output.

Changes of pO_2 in mixed venous blood did not necessarily mimic the same changes in arterial blood. A second factor

that contributed to the decreased pO_2 was the Bohr effect. The increased pH of the blood produced by hyperventilation increases the affinity of hemoglobin for O_2. Hence, the pO_2 of systemic tissues must decrease to obtain the same O_2 delivery. Since it is presumed that there is equilibration of O_2 across systemic capillaries, the pO_2 of venous blood must also decrease. Thus, it may be inferred from the evidence that since mixed venous blood is the output from systemic tissues, mixed venous pO_2 actually reflects systemic tissue oxygen utilization more accurately than arterial pO_2. A high correlation was shown between mixed venous and arterial blood bicarbonate concentrations. During respiratory acidosis, as CO_2 increased, bicarbonate concentration increased in the blood. During respiratory alkalosis, as CO_2 decreased, bicarbonate concentration decreased in the blood. Because of the high correlation between mixed venous and arterial blood bicarbonate concentrations, it was concluded that changes in mixed venous [HCO_3] mimic those changes in [HCO_3] in arterial blood.

Griffith concluded that when cardiac output was stable, arterial and mixed venous blood-gas compositions had close correlations over wide variations of respiratory acid-base disturbances. It should be kept in mind that cardiac output was not monitored in this study. The changes seen in mixed venous blood were shown to be predictable and could be used in acid-base assessment. Because the low pO_2 occurring in

mixed venous blood in states of hyperventilation were not closely correlated with arterial blood, it was argued that mixed venous blood might be a superior predictor of the pO_2 in ISF.

Bieber (1979) studied correlations between mixed venous and arterial blood over wide ranges of pH in metabolic acid-base disturbances. Nine healthy mongrel dogs were the subjects of this experiment. The animals were anesthetized and were allowed to breathe room air without mechanical assistance. Temperature, heart rate and respiratory rate were monitored throughout the procedure. A cannula in the right femoral artery was used to sample arterial blood. A Swan-Ganz flow-directed catheter was inserted into the pulmonary artery for withdrawal of mixed venous blood. Metabolic acidoses and alkalosis were induced using intravenous infusions of ammonium chloride (NH_4Cl) and sodium bicarbonate ($NaHCO_3$) respectively.

A strong correlation was found between arterial and mixed venous blood-gas compositions over a wide range of metabolic acid-base disturbances. Mixed venous pH was consistently lower than arterial pH, as would be expected because of equilibration of mixed venous blood with ISF where lactic and carbonic acids are added.

Variability in pCO_2 values during NH_4Cl infusions were noted which could be explained by responses to anesthesia. High excitability at induction could explain low pCO_2 values while depression of respiratory neurons at high pH values

would be reflected in high pCO_2 values. As would be expected, arterial pCO_2 was consistently lower than that of mixed venous blood.

The pO_2 of mixed venous blood changed in the same direction as that of arterial blood in acidotic and alkalotic states. The pO_2 of mixed venous blood was consistently lower than that of arterial blood. The arterial pO_2 values increased in acidotic states, which may have reflected respiratory compensation through hyperventilation. Lower arterial pCO_2 values observed during these acidotic states substantiated this assumption.

During alkalosis, decreased pO_2 in arterial and mixed venous blood were produced. Two explanations for this outcome were given. (1) Alkalosis could have caused a depression in the central respiratory neurons and peripheral chemoreceptors which would in turn cause a decreased ventilation rate, increased pCO_2 and a decreased pO_2 of arterial blood. If cellular O_2 requirements could not be met because of the decrease in arterial pO_2, then anaerobic metabolism would ensue initiating a lactic acidosis. This in turn, would cause a decrease in pH as was borne out in the study. (2) Respiratory compensatory mechanisms could have suppressed ventilation causing CO_2 retention and decreased pO_2 in the blood. These changes would reduce the increase in pH due to the initial alkalosis.

The HCO_3 concentrations of arterial and mixed venous blood were highly correlated in metabolic acidosis, with the $[HCO_3]$ of mixed venous blood being consistently higher than that of arterial blood. In metabolic alkalosis, however, the $[HCO_3]$ of mixed venous blood was sometimes higher and sometimes lower than $[HCO_3]$ of arterial blood. One possible explanation is that the $[HCO_3]$ might become sufficiently elevated in metabolic alkalosis that differences between arterial and mixed venous blood could become smaller than the method error.

Bieber concluded that mixed venous and arterial blood gas compositions are closely correlated over a wide range of pH in metabolic acid-base disturbances. It was also concluded that mixed venous blood might be a more appropriate indicator of systemic acid base status than arterial blood, but no evidence was presented to substantiate this conclusion.

Kappagoda, Stoker, Snow and Linden (1972) studied the in-vivo CO_2 titration curves of arterial and mixed venous blood in both humans and dogs. Their interests were assessing the differences between arterial and mixed venous CO_2 titration curves, and also the possibility of using mixed venous blood in determining acid-base status. Four dogs were anesthetized. Cannulae were inserted into the tracheas and the animals were artificially ventilated with 40% O_2. The stroke volume of the ventilator was manipulated to keep the

arterial pCO_2 at 40 torr throughout the experiment to eliminate any respiratory component to changes in pH.

Cannulae were inserted into a femoral artery, a femoral vein and the pulmonary artery. Acidosis was produced in the animals by infusion of 1 M HCl. Alkalosis was induced by infusion of 8.4% $NaHCO_3$.

Six patients were also studied during routine cardiac catheterization procedures. Arterial blood samples were obtained through brachial arteries or through aortic catheters. Mixed venous blood samples were obtained from the pulmonary arteries. Vital signs, i.e., the blood pressure, ECG, and temperature were monitored throughout the procedure.

After simultaneous control samples of mixed venous and arterial blood were obtained, the PaCO was increased by adding up to 10% CO_2 in the inspired air. The $PaCO_2$ was decreased in the dogs by increasing the ventilation rate in the Kappagoda experiment. The decrease in $PaCO_2$ was accomplished in patients through voluntary hyperventilation. All blood samples were drawn 5 to 10 minutes after the beginning of each change in either ventilation or inspiratory gas composition. The final control samples were obtained after returning the ventilation rate to its initial value.

Results showing differences between the CO_2 titration curves of arterial and mixed venous blood in-vivo supported the theoretical contentions of Roos and Thomas (1967) and

Michel (1968). The non-respiratory pH* of the arterial blood was less than that of mixed venous blood. This was explained as being due to the Haldane effect. The slope of the arterial CO_2 titration curve was greater than that of mixed-venous blood. Kappagoda et al. stated that the differences between these slopes was not significant: "the small differences in non-respiratory pH between the arterial and mixed venous blood observed in the present study indicate that there is no practical advantage in resorting to samples of mixed venous blood for the analysis of acute acid-base disorders in clinical practice " (p. 558). Since both human subjects and animals were not exercising and remained quiet during the procedures (except voluntary hyperventilation) changes in cardiac output must have been confined to a narrow range, hence, all subjects were more or less in a steady state. Michel points out that in a steady state, the CO_2 titration curve in-vivo must have the same slope as that in-vitro. Therefore, the difference in slopes should be minimal.

Kazarian and Del Guercio looked at the use of mixed venous blood-gas composition as a predictor of survival in patients in traumatic shock. Data were collected from ten trauma patients in profound shock, who were seen in an emergency room. All of these patients were intubated, resuscitated and given fluids and multiple transfusions.

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* Non-respiratory pH was defined by the authors as the pH which is unaffected by respiratory components. This was accomplished by keeping the pCO_2 at 40 torr.

They had immediate surgery for control of blood loss. Each patient had a rapid insertion of either a central venous pressure line or a Swan-Ganz catheter to "measure pressures and obtain samples for mixed venous blood-gas analysis" (Kazarian and Del Guercio, p. 179). Simultaneous mixed venous and arterial blood-gas determinations were made throughout the resuscitative, operative and post operative periods.

Only four of the ten patients survived. All of the patients received 100% oxygen. The pO_2 of arterial blood in all patients was greater than 100 mm Hg (saturation 90%). The mixed venous blood oxygen saturation, however, averaged 46% in survivors but only 25% in non-survivors.

The authors pointed out the relationship of mixed venous O_2 saturation to adequacy of circulation and ultimate survival. Oxygen saturation of 70% in mixed venous blood "represents perfusions of 100% of tissue needs." (Kazarian and Del Guercio, p. 181). Oxygen saturation of less than 70% is indicative of poor perfusion causing the cells to extract more oxygen from a given volume of blood. Of the six non-survivors, four had an initial mixed venous O_2 saturation of less than 30%, but only one of the four survivors had a mixed venous O_2 saturation of less than 30%. The authors then stated that "mixed venous blood-gases may more accurately indicate the progress and ultimate survival of the patient and monitor the effects of treatment " (Kazarian & Del Guercio p. 180). Criticism of this study was directed by

Lipton (1980) in the area of measurement of initial mixed venous blood samples. Kazarian and Del Guercio had stated that initial mixed venous blood samples were obtained by the use of either Swan-Ganz catheters or central venous pressure lines. It is unclear in the data presented from the samples, which were obtained from either the Swan-Ganz catheter or the central venous pressure lines. Unless the CVP lines were positioned correctly in the right heart, the adequacy of the samples as truly being mixed venous blood would have to be questioned. These initial samples were used in much of the comparison data of the study. Kazarian & Del Guercio stated in their rebuttal to this criticism that "initial venous samples were taken from whatever central lines were present, usually a central line from a subclavian venipuncture " (p. 598). Postoperatively, however, Swan-Ganz catheters were placed in all patients. If, indeed, the majority of initial catheters were central venous lines, then, the average oxygen saturation from these samples would tend to be greater than the true mixed venous average (Scheinman, Brown & Rapaport, 1969). This then would give even more credence to the conclusion of the authors, that low mixed venous pO_2 saturations were indicative of serious problems and potential demise.

The effects of decreased cardiac output on the blood-gas compositions of mixed venous and arterial blood.

Boyd, Tremblay, Spencer and Bahnson (1959) studied cardiac outputs and blood O_2 saturations in 34 post-surgical patients following intracardiac surgery with pulmonary by-pass. During thoracotomy, catheters were inserted into the pulmonary artery, left atrium and femoral artery for measurement of O_2 saturation of mixed venous and arterial blood. Cardiac output was estimated by the Fick method.

Results showed that 19 patients who had a post-surgical cardiac output of greater than 2.4 liters per minute with mixed venous oxygen saturations greater than 60%, had no serious cardiovascular difficulties during the early post-operative course. Ten of the 15 patients, however, who exhibited a decrease in cardiac output to less than 2.0 liters per minute and had mixed venous oxygen saturations of less than 50%, died. The arterial oxygen saturations of both groups of patients were greater, in all cases, than 95%.

The authors concluded that "of the various determinations, the oxygen saturation of mixed venous blood obtained from the pulmonary artery was most helpful in evaluating the patient's cardiovascular status ... In the absence of arterial unsaturation or anemia, the single determination of mixed venous saturation gave more information than any other measurement" (Boyd et al., p. 616).

Tung, Bettice, Wang and Brown (1976) studied changes in cardiac output due to hemorrhagic shock on arterial and mixed

venous blood-gas composition. (For purposes of this review, the portion of the study dealing with changes in intracellular responses is not discussed).

Twenty-two mongrel dogs were anesthetized and nephrectomized. Hemorrhagic shock was induced until a reduction of the mean carotid arterial pressure to 50 mm Hg was reached. The animals were allowed to stabilize and blood samples were obtained at 30, 60, 90 and 120 minutes after bleeding. Body temperature was monitored throughout the procedure. Results showed that differences between arterial and mixed venous blood-gas parameters increased when cardiac output was reduced. The pCO_2 of mixed venous blood increased during reduction of cardiac output. The pCO_2 of arterial blood, however, decreased. Because of this reduced cardiac output, resulting from hypovolemia, tissue perfusion was inadequte. Anaerobic metabolism ensued with production of lactic acid. In arterial blood, this caused a decrease in pH, as was noted in the study. Arterial $[HCO_3]$ was reduced via buffering of hydrogen ions from lactic acid. As pH decreased, respiratory compensation in the form of increased alveolar ventilation was apparent. This caused a decrease in the arterial pCO_2 as was shown in the study.

The venous blood however, reflected the decreased cardiac output caused a decreased flow in the tissues. Since CO_2 continued to be produced from tissue metabolism, the decreased flow of blood results in an accumulation of CO_2 in ISF which caused an increase in pCO_2 in venous blood. The

combination of increased venous pCO_2 and lactic acid would also contribute to the precipitous decrease in venous pH that was seen in the study.

The pO_2 of arterial blood increased while mixed venous pO_2 decreased. The increase in pO_2 of arterial blood may be explained by increased ventilation rate which occurred as a respiratory compensation to decreased pH. Decreased blood pressure also stimulates ventilation. This change in arterial pO_2 caused only a slight increase in the saturation of hemoglobin with oxygen.

In contrast, in mixed venous blood, the fall in pO_2 resulted in a significant decrement in oxygen saturation of hemoglobin. The A-V pO_2 saturation difference increased from 31% to 81%. It can be concluded that, in states of severe hypotension, there is a marked elevation in oxygen extraction from blood in systemic capillaries.

The authors concluded that the blood gas composition of arterial blood represented a state of partially compensated metabolic acidosis. The blood-gas composition of mixed venous blood, however, represented a metabolic acidosis with a superimposed respiratory acidosis.* The low pH and $[HCO_3]$ in mixed venous blood coupled with increased pCO_2 and decreased pO_2 are indicative of inadequate tissue perfusion.

* It should be noted that the authors use the term respiratory acidosis in its broad sense, i.e., pCO_2 greater than 40 torr, pH less than 7.4, and $[HCO_3]$ greater than 26 meq/L.

Kaznitz, Druger, Yorra, and Simmons (1976) evaluated the use of mixed venous pO , cardiac output and arterial pO in predicting the development and degree of lactic acidosis, as well as ultimate survival of critically ill patients with pulmonary and/or cardiac disease.

Twenty patients with severe respiratory and/or circulatory disease were selected for study. Diagnoses varied with half having primarily respiratory and the other half having primarily circulatory dysfunctions. All patients required placement of a Swan-Ganz catheter for diagnostic purposes.

Blood-gas determinations were made by standard methods. Cardiac outputs were measured in 15 cases by the Fick Method. One case had cardiac output measured via the indocyanine green dye dilution method. The last four cases required clinical estimates (educated guesses) of cardiac outputs because of the inability to make measurements during shock. These outputs were estimated to be 1.5 liters per minute. Precise procedures were followed to insure accurate measurement of lactate concentrations.

Results showed that both reduced cardiac output and reduced mixed venous pO correlated closely with increased lactic acid concentration. In seven of eight patients with cardiac output less than 2.5 liters per minute, lactate concentration was greater than normal (2 mEq/liter).

The pO_2 of mixed venous blood was less than 30 mm Hg in nine of ten patients who had lactic acid concentrations greater than 2 mEq/l. In contrast, there was little correlation between arterial pO_2 and lactic acid levels.

Low survival rates also correlated closely with increased blood lactate concentrations, low cardiac output and low mixed venous pO_2. Ten patients had blood lactate concentrations greater than 2 mEq/l. None of the ten survived. However, when lactate concentrations were 2 mEq/l or less, eleven of twelve survived. Therefore, changes in blood lactate concentrations predicted patient survival in 19 of 20 cases (95%).

No patient in this study survived when cardiac output was less than 2.5 l/minute. In addition, three patients whose cardiac output was greater than 2.5 l/minute did not survive. Cardiac outputs of all survivors, however, were greater than 2.5 l/minute. Therefore, cardiac output predicted survival or non-survival in 17 of 20 cases (85%)

Nine patients whose mixed venous pO_2 was 28 mm Hg or less did not survive. Only two patients whose mixed venous pO_2 was greater than 28 mm Hg died. Mixed venous pO_2 predicted survival and non-survival in 18 of 20 cases (90%).

No critical level of arterial pO_2 was identifiable with survival or non-survival.

Kasnitz et al. stated that although both cardiac output and mixed venous pO correlated well with lactate concentra-

tion, monitoring of mixed venous pO_2 was "considerably simpler and probably more accurate than measuring cardiac output in seriously ill patients" (p. 573).

Murphy (1982) studied mixed venous and arterial blood-gas composition in states of decreasing cardiac output. Patterns of change of mixed venous blood-gas composition were also studied in states of reduced cardiac output.

Ten healthy mongrel dogs were anesthetized, and intubated. They were allowed to breathe room air spontaneously throughout the procedure. Cannulae were inserted into the pulmonary artery and femoral artery for simultaneous withdrawal of samples of mixed venous and arterial blood respectively. Cardiac output was monitored during the experiment. The animals were bled periodically from the femoral artery to cause staged reduction in cardiac output. The arterial and mixed venous samples were obtained anaerobically in greased glass syringes then immediately placed in an ice bath. Samples were analyzed for pH, pCO_2 and pO_2. The $[HCO_3]$ was determined using the Henderson-Hasselbalch equation. Temperature, heart rate and respiratory rate were monitored throughout the procedure.

Results showed that the pattern of change in blood-gas composition of arterial blood was different from that of mixed venous blood when cardiac output was reduced. As cardiac output decreased arterio-venous differences

increased. The pH of both arterial and mixed venous blood decreased when cardiac output was reduced, but the decrement in the mixed venous blood was more precipitous. The decrease in mixed venous pH was explained as being due to (1) tissue hypoxia secondary to the decrease in cardiac output, (2) lactic acid build-up in the tissues as a result of this hypoxia, and (3) CO_2 accumulation from cell metabolism due to low blood flow. The decrease in arterial pH was due to metabolic acidosis resulting from anaerobic metabolism, but was moderated by respiratory compensation.

The mean pCO_2 of arterial blood decreased during reduction in cardiac output as the result of increased ventilation rate. The mean pCO_2 of mixed venous blood, however, was essentially unchanged from control to final values. This lack of change was explained as being due to (1) reduced systemic delivery to the capillary bed secondary to decreased arterial pCO_2 and (2) reduced blood flow due to decreased cardiac output. Reductions of cardiac output, blood flow and arterial pCO_2 in the experiments offset the increased venous pCO_2 and there was no net increase in mixed venous pCO_2 (Equation #2).

The mean pO_2 of the arterial blood increased resulting in slight overall increase in oxygen saturation. This increase was explained as being due to hyperventilation resulting from reduced blood pressure and increased $[H^+]$ in arterial blood. The mean mixed venous pO_2 decreased from a

control value of 50.3 (80% saturation) to 27.4 torr (50% saturation). This represented acute tissue hypoxia in spite of a slightly elevated arterial pO_2.

The $[HCO_3]$ of mixed venous blood was always greater than that of arterial blood. There was a decrease in $[HCO_3]$ in both arterial and mixed venous blood. Arterial $[HCO_3]$ decreased more precipitously as a result of the increase in ventilation rate. The $[HCO_3]$ in mixed venous blood decreased less rapidly due to two counteracting effects. The first was a buffering of lactic acid which decreased $[HCO_3]$. The second increased $[HCO_3]$ due to the accumulation of CO_2 in the tissues, and therefore, venous blood. The net effect was a decrease in $[HCO_3]$, but not as precipitously as that seen in the arterial blood.

In summary, arterial blood-gas analysis showed a pattern of compensated metabolic acidosis, while mixed venous blood-gas analysis showed a combined respiratory and metabolic acidosis.

The conclusions made substantiated the hypothesis that a predictable pattern for the change in mixed venous blood-gas composition could be seen in states of decreased cardiac output. This pattern was different from that seen in arterial blood. It was also concluded that mixed venous blood-gas composition was a better indicator of true tissue acid base status than that of arterial blood when cardiac output was decreased by hypovolemia.

Summary of Literature Review

1. The changes in blood-gas compositions in the lungs lie on an in-vitro titration curve and are represented by arterial blood. Mixed venous blood, on the other hand, represents an in-vivo titration curve because of equlibration with ISF.

2. A given decrease in pO_2 of mixed venous blood usually produces a larger decrement in O_2 content than the same pO_2 change in arterial blood.

3. Changes in cardiac output may unpredictably alter arterial blood gas composition to the extent that interpretation may generate erroneous assumptions concerning true systemic acid-base status.

4. Close correlations between arterial and mixed-venous pCO_2, $[HCO_3]$ and pH have been demonstrated over a wide range of metabolic and respiratory acid base disturbances.

5. Mixed venous and arterial blood-gas compositions respond in different ways to decreased tissue perfusion resulting from a decrease in cardiac output.

Statement of the Problem

In this study, three questions will be answered.

1. In what ways do mixed venous and arterial blood-gas compositions differ in states of reduced cardiac output when ventilation is controlled?

2. In what ways do mixed venous and arterial blood-gas compositions differ with reinfusion of blood after hemorrhage?

3. Is there a predictable pattern to the change in mixed venous blood-gas composition in states of reduced cardiac output when ventilation is controlled?

Nursing Implications

The nursing process embodies four main stages: (1) assessment, (2) planning, (3) implementation, and (4) evaluation. The nursing action (implementation) is validated

by the other three stages. In deciding upon a course of action, the nurse must make independent clinical decisions which utilize the components of assessment, planning and evaluation.

Nursing assessment of the rapidly changing status of patients in critical care settings, emergency rooms and on general medical-surgical nursing units must be accurate. Nurses caring for these patients must possess highly developed, knowledge-based abilities which will assist them in recognizing, interpreting and intervening in these disorders.

Patients in each of these settings often have acid-base disturbances. A nursing assessment of these alterations is accomplished by developing a data base involving respiratory, circulatory and metabolic status. The essential nursing components necessary to complete this data base include four areas: (1) use of communication skills to elicit subjective symptoms, (2) observation of physiologic changes (3) understanding the recordings of technological devices such as electrocardiograms, and (4) interpretations of biochemical findings.

Blood-gas analysis, in the area of biochemical findings, is considered to be the most precise method for determination of acid-base status. Symptoms (subjective data) may not always be reliable. Moreover, subjective data may be totally

unavailable if the patient is comatose, and/or unable to function without mechanical support.

Observation of physiologic changes may be helpful in determining the presence of an acid-base disorder, but will not specify the exact problem. For instance, a person who is hyperventilating may be either in an alkalotic or an acidotic state. Thus, an observed physiologic response may have more than one reasonable interpretation.

The recordings of technological devices such as electrocardiograms may be quite useful in determining underlying disorders causing acid-base disturbances. These devices, however, will not pinpoint the actual acid-base disturbance.

Precise delineation of an acid-base disorder requires the biochemical measurements of the partial pressure of oxygen, and carbon dioxide, the bicarbonate concentration and the pH of blood, i.e., blood-gas analysis. Arterial blood-gas analysis has been, and continues to be useful in assessing pulmonary function. Arterial blood-gas analysis has also been traditionally used to help determine metabolic and circulatory function. If, however, mixed-venous blood-gas analysis or its equivalent can be shown to be superior for accurate assessment of metabolic and circulatory function, then nursing practice will be impacted in the following areas:

Nursing assessment and planning:

Nursing assessment and analysis of blood-gas findings will be changed. Nurses will need to be educated concerning normal parameters of mixed venous blood-gas composition. In implementing their plan of action it is critical that nurses know in which situations mixed-venous blood should be used to most accurately assess a patients' acid-base and cardiovascular status. This analysis will also incorporate evaluation of cardiac output.

Nursing implementation:

Nursing interventions, i.e., nursing care and procedures, will be affected in terms of obtaining specimens for analysis. Swan-Ganz catheters are frequently placed for measurement of cardiac output and pulmonary artery pressure in patients who have acid-base disorders. In addition, these catheters are occasionally used to obtain mixed venous blood-gas samples. Blood-gas sampling from this site is strongly advocated since it will provide the most accurate information on circulatory and metabolic states. Dependence on arterial samples alone for accurate assessment of acid-base status may, in fact, be misleading. Without simultaneous sampling of mixed-venous blood, accurate assessment of circulatory function and metabolic status may not be possible.

Nursing evaluation:

The final nursing implication involves the evaluation of patient outcomes. Time is a critical factor in serious acid-

base disturbances. Minutes wasted may make the difference between life and death. If it can be shown that changes in metabolism and/or circulation are reflected sooner in mixed venous than in arterial blood-gas composition, use of mixed venous blood for assessment will result in earlier medical and nursing interventions. This will give a greater potential for correction of the disturbance, and hopefully, a greater chance for patient survival.

In conclusion then, the use of mixed-venous blood in assessment of acid-base disorders will necessitate changes in all four areas of the nursing process. Implementing these changes will serve to significantly improve the quality of patient care.

Chapter II

Methods

Statement of the Variables

The independent variables were (1) the decrements in cardiac output produced by hemorrhage until cardiac output was less than 50% of control values, (2) maintaining control of respiration by the use of a mechanical respirator.

The dependent variables were the pO_2, pCO_2, pH and $[HCO_3]$ of arterial and mixed venous blood.

Design

The design of the study was experimental. Each subject served as its own control. Repeated measures were obtained on each subject. An animal model was used in the experiment.

Procedure:

Ten mongrel dogs were anesthetized with intravenous injections of Sodium Pentobarbital (30 mg per kg). Anesthesia was maintained by intravenous doses of 30-45 mg as needed. Curare was given as needed to control respirations.

The anesthetized dogs were then intubated using endotracheal tubes. Respiratory rate was maintained at a constant value by the use of a mechanical ventilator at a rate of 12-15 per minute. Tidal volume was adjusted according to the size of the animal. The animals breathed room air.

A cannula was placed in the left carotid artery for withdrawal of arterial blood and monitoring blood pressure. A number 7 French Swan-Ganz flow-directed catheter was

inserted into the right external jugular vein. The catheter was connected to a pressure transducer to monitor pulmonary artery pressure. Proper placement of the catheter was assured by monitoring pressure and wave form changes on a grass polygraph recorder (Model 7C). Post-mortem examination was done to confirm the location when there was any question concerning proper placement of the catheter. The left carotid artery was cannulated for removal of blood. This cannula was also used for administering drugs as needed.

All cannulae were kept patent by periodically infusing 1 to 3 ml of heparinized saline. This heparinized saline was prepared by using 1000 units of sodium heparin combined with 100 ml of normal saline.

The animals were allowed to stabilize for 45 minutes after the completion of the surgical procedures. At the point of stabilization, control baseline vital signs were recorded, which included respiratory rate, heart rate and pulmonary artery blood temperature. The thermodilution technique was used to determine baseline cardiac output.

An Edwards Laboratories cardiac output computer (Model 9520A) was used in these experiments. Thermodilution curves were recorded on an Edwards Laboratories Strip Chart Recorder (Model 9810). Proper functioning was assured by placing the machine on a self-test cycle before its use. Three milliliter volumes of 5% glucose and water were cooled and main-

tained at 0-5° in an ice bath. These were injected when cardiac output was measured. A minimum of five successive measurements were made for each determination of cardiac output. The cardiac output was then determined by computing the mean of the three closest values.

Control samples of arterial and mixed venous blood were drawn after the animals stabilized. Irrigation fluid was removed from the cannulae before sampling by withdrawing an amount equal to twice the catheter volume. The syringes were prepared so that samples were not contaminated by air. Silicone stopcock grease was used to lubricate the plungers and barrels of the one milliliter glass syringes to prevent any air leakages. Sodium heparin in the amount of approximately 0.01 milliliter was drawn into the syringe. A seal was provided by drawing a small drop of mercury into the syringe. This mercury also facilitated mixing of the sample prior to analysis.

Mixed venous blood samples were drawn using these prepared syringes, with excess heparin removed. A one milliliter sample was drawn over a period of at least one minute. If an air bubble appeared in the syringe while the sample was being withdrawn, the sample was discarded and another drawn. Arterial blood was obtained from the carotid artery at the same time the mixed venous samples were being obtained. This sample was also collected anaerobically (see previously described mixed-venous blood sample drawing). Prior to being

analyzed, the samples were capped and cooled in an ice bath to slow any red cell metabolism and O_2 consumption. The hematocrit and plasma protein concentration samples were collected from a separate arterial sample and analyzed.

Decrements in cardiac output were produced by controlled hemorrhage from the carotid artery after baseline samples were obtained. The volume removed initially depended on the animal's weight and estimated blood volume. Vital signs were monitored closely after bleeding. The animal was allowed to stabilize for a period of at least 45 minutes after each bleeding episode. The blood samples drawn prior to the last hemorrhage were analyzed at this time.

Blood-gas composition was analyzed using a Radiometer Model BGA3, Mark 2 blood-gas analyzer. Samples were analyzed in a random order. The pO_2 and pCO_2 readings of each sample were recorded until three values are obtained which agreed within 0.1 mm Hg. The pH readings were recorded until three readings agreed within 0.005 pH units of the others. The blood gas analyzer was calibrated prior to analyzing each set of samples to insure accuracy.

Cardiac outputs were determined after each stabilization period prior to each set of samples. Hematocrit and plasma protein concentrations were made at the time of each set of samples. The animal was then bled again. This pattern was repeated until cardiac output was less than 50% of the con-

trol values. Blood was then reinfused and blood samples again were taken after reinfusion.

The animals were sacrificed at the end of each experiment and a post-mortem examination was done if there was concern over the placement of the Swan-Ganz catheter.

Anaylsis of Data

Calculations were made of mean pH, pCO_2 and pO_2 values. the $[HCO_3]$ was calculated using the Henderson-Hasselbalch equation with pk = 6.1. Partial pressure of pH, O_2, CO_2 and $[HCO_3]$ of mixed venous and arterial blood were plotted as a function of the cardiac output to see if the pattern obtained fit the proposed model. The correlation coefficient Pearson's r, of the relationships were also calculated.

CHAPTER III

Results

General Description

Ten mongrel dogs of both sexes ranging in weight from 17.7 to 27.3 kg were used for this study. A summary of values of cardiac output, hematocrit, plasma protein concentration, and core temperature are shown in Tables 1 (control) and 2 (maximum hemorrhage). Only cardiac output changed significantly during the course of the experiments ($p < 0.01$).

Dog #8 was found to be hemorrhaging from a dislodged venous catheter shortly before the first controlled hemorrhage was to take place. The catheter was replaced and blood loss was estimated to be about 200 ml. In addition, dog #8 was also found to have a very low control cardiac output. This was caused by a failure to deflate the balloon at the tip of the Swan-Ganz catheter. The inflated balloon obstructed flow from the right ventricle to the pulmonary vascular bed. The resulting acidosis made it impossible to have stable control values. Therefore, while specific data obtained from dog #8 have been included in the tables for completeness, these data are not included in any of the statistical analyses because of the lack of adequate control values.

The hematocrit values from five animals were greater after final hemorrhage than at control. The well known splenic contraction and consequent increase in circulating red blood cell mass which occurs in dogs following hemorrhage is the most likely explanation for this result (Dukes, H. H., 1970).

Table 14 contains a complete summary of all blood gas data and corresponding values for cardiac output. Since cardiac output is a function of body size, i.e., the greater the body mass, the greater the corresponding cardiac output. Changes in cardiac output are presented in terms of percent of control.

Specific Parameters

The results in this section are organized according to specific parameters. The format used in the sections on pH, pCO_2, $[HCO_3]$ and pO_2 is one of comparison. Initially, data obtained from control and maximal hemorrhage are compared. Then, data obtained after transfusion of shed blood are compared to those obtained from the period of maximum hemorrhage. Following these four sections, the results on change in O_2 content and acid-base status are presented.

pH

The mean pH values for control arterial and mixed venous blood samples were 7.368 and 7.348 respectively (Table 3). The mean pH of arterial blood decreased after hemorrhage to 7.302, but the decrement was not statistically significant (Tables 4 and 6). The mean pH of mixed venous blood however, decreased significantly from control to 7.238 when cardiac output was at its nadir (Tables 4 and 6). The mean pH of arterial blood after transfusion increased to 7.321 (Table 7). The mean pH of mixed venous blood increased to 7.306 after transfusion (Table 5). This mean increase was statistically significant, $P < 0.01$, (Table 7).

pCO_2

The mean control values for pCO_2 in arterial and mixed venous blood were 39.0 and 42.5 torr respectively (Table 3). After hemorrhage, the mean arterial value for pCO_2 decreased to 36.7 torr, but the change did not differ significantly from the mean control value (Tables 4 and 6). The mean pCO_2 of mixed venous blood, however, increased significantly to 50.6 torr after hemorrhage (Table 4 and 6). The mean pCO_2 of arterial blood after transfusion remained essentially unchanged at 39.1 torr (Tables 5 and 7). The mean pCO_2 of mixed venous blood, however, decreased significantly to 42.4 torr after transfusion (Tables 5 and 7).

$[HCO_3]$

The mean control values for $[HCO_3]$ in arterial and mixed venous blood plasma were 21.8 and 22.7 meq/L respectively (Table 3). The mean $[HCO_3]$ of arterial blood plasma decreased to 17.8 meq/L (Table 4). This decrease was statistically signficant (Table 6). The $[HCO_3]$ of mixed-venous blood plasma, however, was essentially unchanged at 21.2 meq/L after final hemorrhage (Tables 4 and 6). After transfusion, the mean $[HCO_3]$ of arterial blood plasma increased significantly to 20.0 meq/L (Tables 5 and 7). The mean $[HCO_3]$ of mixed venous blood plasma decreased slightly to 20.9 meq/L after transfusion, and this decrement was not significant (Tables 5 and 7).

PO_2

The mean control values for pO_2 in arterial and mixed-venous blood were 83.6 and 46.5 torr respectively (Table 3). During hemorrhage, the mean pO_2 of arterial blood increased to 87.3 torr, but the increment was not statistically significant (Tables 4 and 6). After transfusion the mean pO_2 of arterial blood increased to 90.2 torr (Table 5). This increase was not statistically significant. The pO_2 of mixed venous blood, however, increased significantly to 50.2 torr after transfusion (Tables 5 and 7).

Arterial-Venous Differences

Table 8 and Figures 6, 7, 8, and 9, show the mean values of blood-gas variables as a function of percent of control cardiac output. Table 9 shows mean arterial-venous differences for the same specified ranges of cardiac output. It can be seen that arterial and mixed venous differences increase progressively as cardiac output is decreased.

A paired t-test was used to determine if the mean arterial-venous differences between control and final hemorrhage for all blood-gas parameters were significantly different (Table 10). For all parameters, the mean differences for control were significantly different from the mean differences after final hemorrhages ($p < 0.01$).

A paired t-test was also used to determine if the mean arterial-venous differences between final hemorrhage and transfusion for all blood-gas parameters were significantly

different (Table 11). The mean differences for all parameters following transfusion were significantly different from the mean differences after final hemorrhage ($p < 0.01$).

Total O_2 Content

The mean values for hemorrhage and transfusion for O_2 concentration are compared in Table 12. Arterial oxygen content increased by an average of nearly one volume percent from final hemorrhage to post transfusion periods. Mixed-venous oxygen content, however, increased by an average of 6.3 volumes percent from final hemorrhage to transfusion values. The mean increase in O_2 concentration in mixed venous blood was significantly greater than that of arterial blood ($p < 0.001$)(Table 13). These values are shown graphically in Figure 10.

Acid-base Status

All points obtained in the experiments except for controls, retransfusion and Dog #8 are plotted on a pH/[HCO_3] diagram (Figure 11). The [HCO_3] was calculated from the Henderson-Hasselbalch equation. A majority of points from arterial blood (63%) fall into the region of a minimally compensated metabolic acidosis, i.e., $pH < 7.37$, $pCO_2 < 39$ torr, and [HCO_3] < 22 meq/L. The majority of the points from mixed venous blood (70%) fall into the region of combined acidosis, i.e., $pH < 7.35$, and $pCO_2 > 46$ torr. However, if the mean control pCO_2 of 42.5 torr is used as the limit

separating compensated metabolic acidosis from combined acidosis, 89 percent of the points from mixed venous blood fall into the area of combined acidosis.

Table 1

Control Values for Cardiac Output, Ventilation Rate, Hematocrit, Protein Concentration, Temperature and Estimated Blood Volume

Dog	Cardiac Output (L/min)	Frequency/ Tidal Volume	Hematocrit	Plasma Protein Concentration (gm%)	Temperature (Centigrade)	Estimated Blood Volume(ml)
1	2.33	12/--	--	--	35.0	1240
2	2.99	12/255	0.41	6.8	37.5	1270
3	3.56	12/300	0.48	7.0	39	1430
"	3.24	-/315	0.475	6.4	38	1400
5	3.77	12-15/250	0.38	5.2	38	1770
6	5.60	12.5/300	0.34	5.2	40	1400
7	2.53	12/300	0.42	5.2	39	1340
8	5.03	-/380	0.51	6.2	40	1900
9	2.01	15/350	0.65	7.2	37.5	1650
10	3.43	12/350	0.48	6	38	1680
$\bar{x}$	3.27		0.45	6.1	38	
S.D.	1.05		0.09	0.85	1.39	
Range	2.01 - 5.60		0.34 - 0.65	5.2-7.2	35 - 40	

Table 2

Cardiac Output, Hematocrit, Protein Concentration, Temperature, and Estimated Blood Volume After Maximum Hemorrhage

Dog	Cardiac Output (L/min)	Hematocrit	Plasma Protein Concentration (gm %)	Temperature (Centigrade)	Estimated Blood Volume
1	1.02	0.56	6.1	36	635
2	1.00	0.45	5.6	37.5	435
3	0.99	0.49	6.0	-	530
4	1.25	0.50	5.2	37	575
5	1.22	0.35	4.8	-	1270
6	1.38	0.30	4.8	39	900
7	1.0	0.45	5.0	-	840
8	1.9	0.45	5.4	40	1100
9	1.01	0.59	6.1	36.1	1000
10	1.64	0.53	5.9	37.5	1180
$\bar{x}$	1.17	0.47	5.5	37.2	
S.D.	0.23	0.095	0.55	1.1	
Range	0.99-1.90	0.30 - 0.59	4.8 - 6.1	36 - 40	

Table 3

Control Values for Blood-Gas Parameters (pH, pCO_2, $[HCO_3^-]$, and PO_2) for Dogs 1 - 10

	pH		pCO_2(torr)		$[HCO_3]$(meq)		pO_2(torr)	
Dog	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous
1	7.308	7.282	39.5	46.2	19.19	21.15	104.5	46.7
2	7.348	7.350	45.1	48.1	24.0	25.8	81.6	50.4
3	7.338	7.333	48.0	46.0	25.0	23.5	66.6	53.7
4	7.429	7.415	35.3	37.0	22.7	23.0	90.3	50.6
5	7.317	7.293	46.4	50.5	23.0	23.7	59.6	33.0
6	7.376	7.346	38.2	43.0	21.7	22.8	70.5	42.4
7	7.397	7.365	35.3	41.7	21.1	23.1	96.9	46.2
8	7.344	7.329	36.1	37.3	19.1	19.1	89.1	62.5
9	7.373	7.354	29.9	32.4	16.9	17.5	91.9	51.9
10	7.447	7.427	33.3	37.3	22.3	23.8	90.4	44.0
$\bar{x}$ *	7.368	7.348	39	42.5	21.8	22.7	83.6	46.5
S.D.	+0.016	+0.054	6.29	5.93	2.47	2.29	15.1	6.3
	-0.016	-0.047						

* pH values were determined by first converting pH to (H+) because pH is exponential. The mean (H+) was determined, then converted back to pH.

Table 4

Final Hemmorrhage Values for Blood-Gas Parameters (pH, pCO_2, $[HCO_3^-]$, and PO_2) for Dogs 1 - 10.

	pH		pCO_2(torr)		$[HCO_3]$(meq)		pO_2(torr)		Cardiac Output
Dog	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed-Venous	Arterial	Mixed-Venous	%Control
1	7.232	7.204	40.4	52.9	16.48	20.23	92.5	36.1	44
2	7.304	7.211	33.3	51.3	16.0	20.0	89.5	30.6	33
3	7.370	7.283	35.5	51.0	19.9	23.4	92.0	45.2	28
4	7.369	7.285	33.7	48.7	18.9	22.4	88.2	31.2	39
5	7.286	7.236	41.7	54.5	19.3	22.4	79.6	16.3	32
6	7.200	7.135	38.8	50.4	14.7	16.4	79.1	28.5	25
7	7.334	7.264	36.2	48.9	18.7	21.5	94.3	31.5	40
8	7.353	7.308	37.7	46.1	20.3	22.4	92.5	38.5	38
9	7.272	7.217	35.4	50.6	15.8	19.9	83.5	33.2	50
10	7.387	7.331	35.5	47.5	20.7	24.3	87.1	26.8	48
$\bar{x}$	7.302	7.238	36.7	50.6	17.8	21.2	87.3	31.0	37.7
S.D.	+0.072	+0.056							
	-0.061	-0.055	2.92	2.16	2.11	2.36	5.53	7.69	8.76

Table 5

Transfusion Values for Blood-Gas Parameters (pH, pCO_2, $[HCO_3^-]$, and pO_2) for Dogs 1 - 10.

Dog	pH		pCO_2(torr)		$[HCO_3^-]$(mEq)		pO_2(torr)		Cardiac Output %Control
	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous	Arterial	Mixed Venous	
1	7.289	7.273	33.1	37.0	15.4	16.6	113.3	56.6	116
2	7.307	7.291	42.4	46.2	20.6	21.6	96.6	52.6	104
3	7.378	7.354	40.4	44.0	23.1	23.8	90.1	64.4	131
4	7.399	7.385	38.5	39.6	23.1	23.0	91.2	43.7	86
5	7.337	7.321	43.4	45.9	22.6	23.0	78.6	37.8	93
6	7.186	7.181	42.3	44.8	15.5	16.3	74.7	50.3	91
7	7.335	7.313	37.5	42.6	19.4	20.9	87.3	48.6	99
8	7.393	7.369	35.5	39.1	21.0	21.9	101.3	53.0	54
9	7.305	7.295	35.7	38.8	17.2	18.3	88.4	44.8	93
10	7.398	7.385	38.2	42.9	22.8	24.9	91.8	52.6	105
$\bar{x}$	7.321	7.306	39.1	42.4	20.0	20.9	90.2	50.2	102
S.D.	+0.078 -0.065	+0.073 -0.062	3.4	3.3	3.2	3.2	11.0	7.8	14.1

Table 6

Results of Paired t-Test Between Control and Hemorrhage Values of Arterial and Mixed Venous Blood Gas Parameters

Control-Hemorrhage Arterial Δ

	d	S.D.	Paired t	df	P
pH	0.140	0.234	1.7962	8	> 0.01
pCO_2	2.2778	4.652	1.4695	8	> 0.01
$[HCO_3^-]$	3.9344	2.3637	4.9935	8	< 0.01 *
pO_2	23.5	2.0196	1.2928	8	> 0.01

Control-Hemorrhage M-V Δ

pH	0.111	0.05	6.5294	8	< 0.01 *
pCO_2	8.1778	4.650	5.2760	8	< 0.01 *
$[HCO_3^-]$	1.5356	.8127	1.8894	8	> 0.01
pO_2	15.5	1.3149	11.7879	8	< 0.01 *

* Statistically signficant

Table 7

Results of Paired t-Test Between Hemorrhage and Transfusion Values of Arterial and Mixed Venous Blood Gas Parameters

Hemorrhage-Transfusion Arterial Differences

	d	S.D.	Paired t	d.f.	P
pH	0.0724	0.0558	0.4325	8	> 0.01
pCO_2	2.333	0.9613	2.427	8	> 0.01
$[HCO_3^-]$	2.14	0.4991	4.2878	8	< 0.01 *
pO_2	2.9111	1.963	1.4830	8	> 0.01

Hemorrhage-Transfusion Mixed Venous Differences

pH	0.070	.008	11.6667	8	< 0.01 *
pCO_2	8.222	1.2224	6.726	8	< 0.01 *
$[HCO_3^-]$	0.237	0.361	0.6556	8	> 0.01
pO_2	19.111	1.5461	12.3609	8	< 0.01 *

* Statistically significant

Table 8

Mean Values of Blood Gas Variables As A Function of Percent of Control Cardiac Output

Cardiac Output Intervals % Control		pH		pCO_2		$[HCO_3]$		pO_2	
		Art	M.V.	Art	M.V.	Art	M.V.	Art	M.V.
> 70 N = 11	$\bar{x}$	7.355	7.336	39.0	43.3	21.2	22.5	85.3	46.3
	S.D.	+0.057	+0.055						
		-0.050	-0.049	5.9	6.5	2.6	2.3	7.0	5.7
61-70 N = 4	$\bar{x}$	7.360	7.324	36.5	43.1	20.2	22.0	82.4	39.1
	S.D.	+0.050	+0.042						
		-0.046	-0.047	2.4	0.3	2.3	2.2	12.0	2.4
51-60 N = 6	$\bar{x}$	7.342	7.312	40.0	46.3	21.1	22.8	79.2	41.8
	S.D.	+0.016	+0.055						
		-0.017	-0.048	4.2	4.2	1.8	1.4	10.1	10.5
41-50 N = 9	$\bar{x}$	7.337	7.286	38.2	49.4	20.0	23.0	86.7	36.4
	S.D.	+0.06	+0.053						
		-0.054	-0.048	3.0	2.4	2.5	2.1	5.6	9.8
< 40 N = 5	$\bar{x}$	7.301	7.227	36.6	51.2	18.1	21.1	85.7	30.4
	S.D.	+0.080	+0.063						
		-0.067	-0.069	3.6	2.1	2.6	3.0	5.9	10.3

Table 9

Mean A-V Differences for Each Blood Gas Parameter
Intervals of Percent of Control Cardiac Output

Cardiac Output Intervals % Control			pH	pCO_2	$[HCO_3]$	pO_2
> 70	N = 11	$\bar{x}$	0.019	4.672	1.582	38.1
		S.D.	0.009	2.793	1.094	13.3
61 - 70	N = 4	$\bar{x}$	0.036	6.625	1.80	43.28
		S.D.	0.007	2.20	0.949	10.387
51 - 60	N = 6	$\bar{x}$	0.029	6.283	1.7	37.33
		S.D.	0.012	2.777	0.990	13.912
41 - 50	N = 9	$\bar{x}$	0.051	11.256	2.989	50.278
		S.D.	0.019	2.92	1.049	11.453
< 40	N = 5	$\bar{x}$	0.076	14.58	3.0	55.32
		S.D.	0.018	2.489	0.871	6.60

Table 10

Results of Paired t-Test Between Control and Hemorrhage Values for Arterial Venous Differences

	Control $\bar{x}$	A - VΔ S.D.	Final $\bar{x}$	A - VΔ S.D.	Paired t	df	P
pH	0.019	0.01	0.065	0.02	4.8213	8	< 0.01
pCO_2	3.91	1.81	13.9	2.11	8.3828	8	< 0.01
$[HCO_3^-]$	1.273	0.626	3.34	0.737	6.4846	8	< 0.01
pO_2	37.04	13.81	56.27	5.84	4.7259	8	< 0.01

Table 11

Results of Paired t-Test Between Hemorrhage and Transfusion Values for Arterial-Venous Differences

	Hemorrhage $\bar{x}$	A-VΔ S.D.	Transfusion $\bar{x}$	A-VΔ S.D.	Paired t	df	P
pH	0.065	0.02	0.151	0.0057	7.6061	8	< 0.01
pCO_2	13.9	2.11	3.3667	1.2257	12.1889	8	< 0.01
$[HCO_3^-]$	3.34	0.737	0.9889	0.5925	8.2068	8	< 0.01
pO_2	66.27	5.84	40.0556	10.0834	5.4444	8	< 0.01

Table 12

Comparison of Hemorrhage and Post Transfusion Total Oxygen Content of Arterial and Mixed Venous Blood

Dog	Total Volumes % O_2 Arterial Hemorrhage	Total Volumes % O_2 Arterial Post Transfusion	Total Volumes % O_2 Mixed Venous Hemorrhage	Total Volumes % O_2 Mixed Venous Post Transfusion
1	23.8	23.2	13.6	19.1
2	17.9	20.2	9.0	15.3
3	21.0	21.4	16.4	19.3
4	21.2	21.2	11.8	17.1
5	14.7	14.9	2.5	10.0
6	12.5	15.2	5.3	12.5
7	19.4	19.0	11.0	15.3
9	24.8	26.8	13.2	20.7
10	22.8	22.7	9.6	20.0
$\bar{x}$	19.8	20.5	10.3	16.6
S.D.	4.1	3.8	4.3	3.6

Table 13

Results of Paired t-Test Between Hemorrhage and Post Transfusion Differences for Total Concentration of Oxygen

Arterial Hemorrhage-Transfusion $\bar{x}$	Arterial Hemorrhage-Transfusion S.D.	Mixed Venous Hemorrhage-Transfusion $\bar{x}$	Mixed Venous Hemorrhage-Transfusion S.D.	Paired t	df	P
0.967	1.1	6.3	2.2	7.7669	8	<0.001

Table 14

Summary of Data for Dogs 1 - 10

	Cardiac Output		pH		pCO_2 mmHg		$[HCO_3^-]$ mEq/L		pO_2 mmHg	
	l	%control	A	MV	A	MV	A	MV	A	MV
Dog 1	2.33	100	7.308	7.282	39.5	46.2	19.2	21.2	104.5	46.7
	1.73	74	7.271	7.257	42.9	54.4	19.1	23.5	97.0	44.5
	1.32	57	7.261	7.243	41.2	48.1	18.0	20.1	98.3	43.2
	1.02	44	7.232	7.204	40.4	52.9	16.5	20.2	92.5	36.1
	2.71	116	T7.289	7.273	33.1	37.0	15.4	16.6	113.3	56.6
Dog 2	2.99	100	7.348	7.350	45.1	48.1	24.0	25.8	81.6	50.4
	1.70	57	7.346	7.321	47.0	48.7	22.3	24.3	83.5	47.7
	1.48	49	7.355	7.333	41.8	50.1	22.6	25.8	85.4	43.5
	1.32	44	7.378	7.296	35.4	51.1	20.2	24.2	95.6	35.3
	1.00	33	7.304	7.211	33.3	51.3	16.0	20.0	89.5	30.6
	3.10	104	T7.307	7.291	42.4	46.2	20.6	21.6	96.6	52.6
Dog 3	3.56	100	7.338	7.333	48.0	46.0	25.0	23.5	66.6	53.7
	2.07	58	7.323	7.303	44.8	47.8	22.5	23.0	66.7	56.5
	1.61	45	7.362	7.320	41.3	48.5	22.7	24.2	79.1	53.3
	1.53	43	7.373	7.323	38.3	49.4	21.6	24.9	89.4	46.1
	0.99	28	7.370	7.283	35.5	51.0	19.9	23.4	92.0	45.2
	4.68	131	T7.378	7.354	40.4	44.0	23.1	23.8	90.1	64.4
Dog 4	3.24	100	7.429	7.415	35.3	37.0	22.7	23.0	90.3	50.6
	1.65	51	7.413	7.390	36.3	39.3	22.5	23.1	83.4	40.8
	1.65	51	7.398	7.350	33.6	43.4	20.1	23.2	80.0	35.3
	1.55	48	7.368	7.302	34.5	44.6	19.3	21.4	93.9	37.4
	1.25	39	7.369	7.285	33.7	48.7	18.9	22.4	88.2	31.2
	1.89	58	T7.371	7.330	36.9	45.8	20.7	23.4	93.9	38.8
	2.80	86	T7.399	7.385	38.5	39.6	23.1	23.0	91.2	43.7
Dog 5	3.77	100	7.317	7.293	46.4	50.5	23.0	23.7	59.6	33.0
	2.27	60	7.325	7.284	42.3	50.6	21.4	23.3	68.2	25.9
	1.85	49	7.327	7.268	41.1	50.3	20.9	22.3	79.3	22.1
	1.22	32	7.286	7.236	41.7	54.5	19.3	22.4	79.6	16.3
	2.00	53	T7.327	7.293	40.4	47.3	20.5	22.2	83.2	30.7
	3.50	93	T7.337	7.321	43.4	45.9	22.6	23.0	78.6	37.8
Dog 6	5.60	100	7.376	7.346	38.2	43.0	21.7	22.8	70.5	42.4
	3.39	61	7.337	7.309	39.9	43.4	20.7	21.1	66.3	35.7
	1.38	25	7.200	7.135	38.8	50.4	14.7	16.4	79.1	28.5
	5.12	91	T7.186	7.181	42.3	44.8	15.5	16.3	74.7	50.3
Dog 7	2.53	100	7.397	7.365	35.3	41.7	21.1	23.1	96.9	46.2
	1.55	61	7.395	7.350	35.4	43.3	21.0	23.2	93.3	39.9
	1.0	40	7.334	7.264	36.2	48.9	18.7	21.5	94.3	31.5
	2.50	99	T7.335	7.313	37.5	42.6	19.4	20.9	87.3	48.6
Dog 8	5.03	100	7.344	7.329	36.1	37.3	19.1	19.1	89.1	62.5
	2.57	51	7.358	7.307	35.8	42.5	19.5	20.6	93.1	44.7
	1.90	38	7.353	7.308	37.7	46.1	20.3	22.4	92.5	38.5
	2.72	54	T7.393	7.369	35.5	39.1	21.0	21.9	101.3	53.0
Dog 9	2.01	100	7.373	7.354	29.9	32.4	16.9	17.5	91.9	51.9
	1.78	89	7.327	7.306	35.3	40.0	17.9	19.4	79.4	46.3
	1.32	66	7.308	7.274	34.5	42.9	16.8	19.3	80.5	41.3
	1.01	50	7.272	7.217	35.4	50.6	15.8	19.9	83.5	33.2
	1.87	93	T7.305	7.295	35.7	38.8	17.2	18.3	88.4	44.8
Dog 10	3.43	100	7.447	7.427	33.3	37.3	22.3	23.8	90.4	44.0
	2.16	63	7.408	7.373	36.1	42.8	22.1	24.2	89.5	39.6
	1.64	48	7.387	7.331	35.5	47.5	20.7	24.3	87.1	26.8
	3.60	105	T7.398	7.385	38.2	42.9	22.8	24.9	91.8	52.6

Key: A = Arterial Blood
MV = Mixed Venous Blood

Figure 6

The pH in arterial and mixed venous blood as a function of percent of control cardiac output.

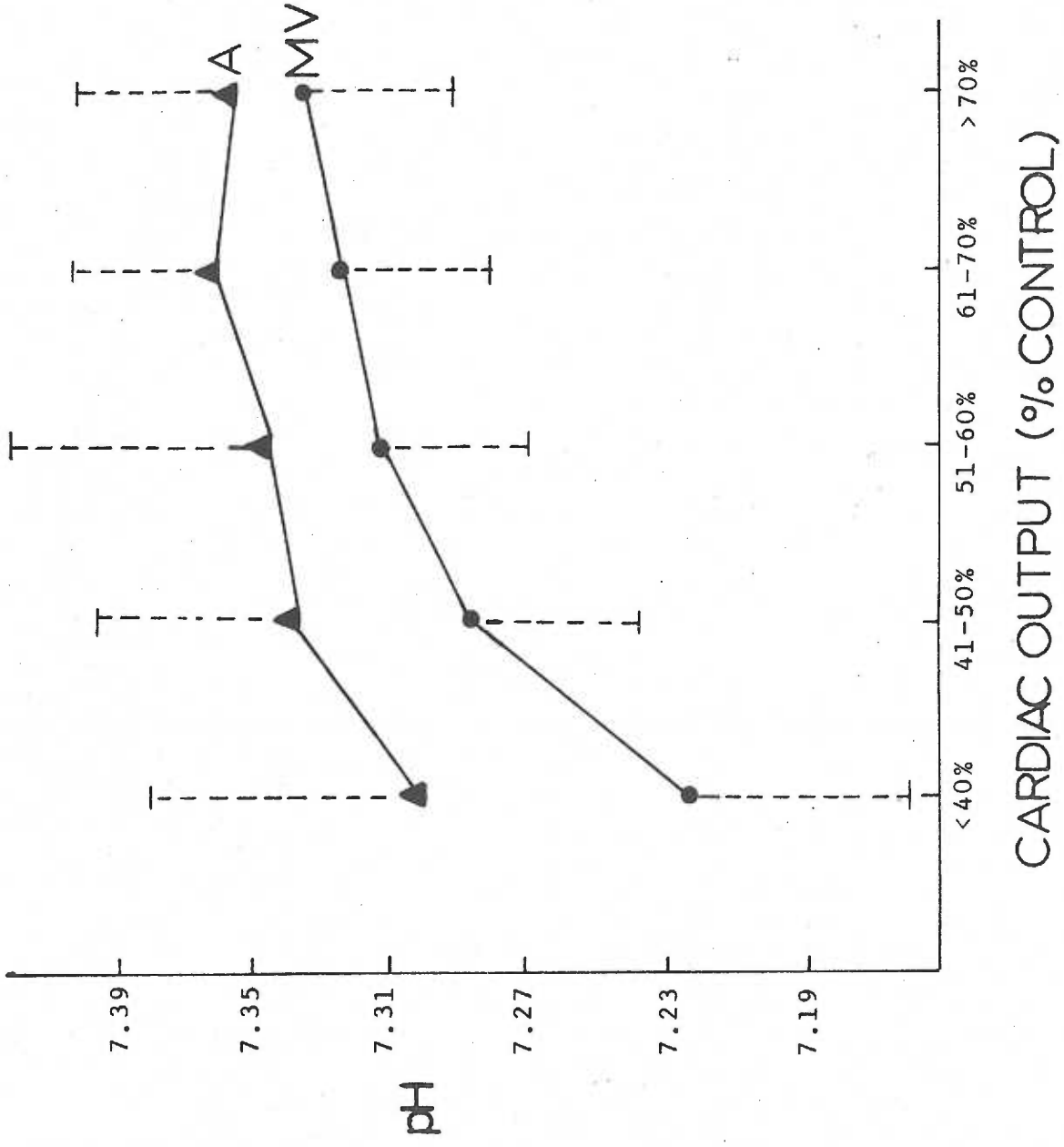

A
MV
7.39
7.35
7.31
7.27
7.23
7.19
pH
< 40%
41-50%
51-60%
61-70%
> 70%
CARDIAC OUTPUT (% CONTROL)

Figure 7

pCO_2 in arterial and mixed venous blood as a function of percent of control cardiac output.

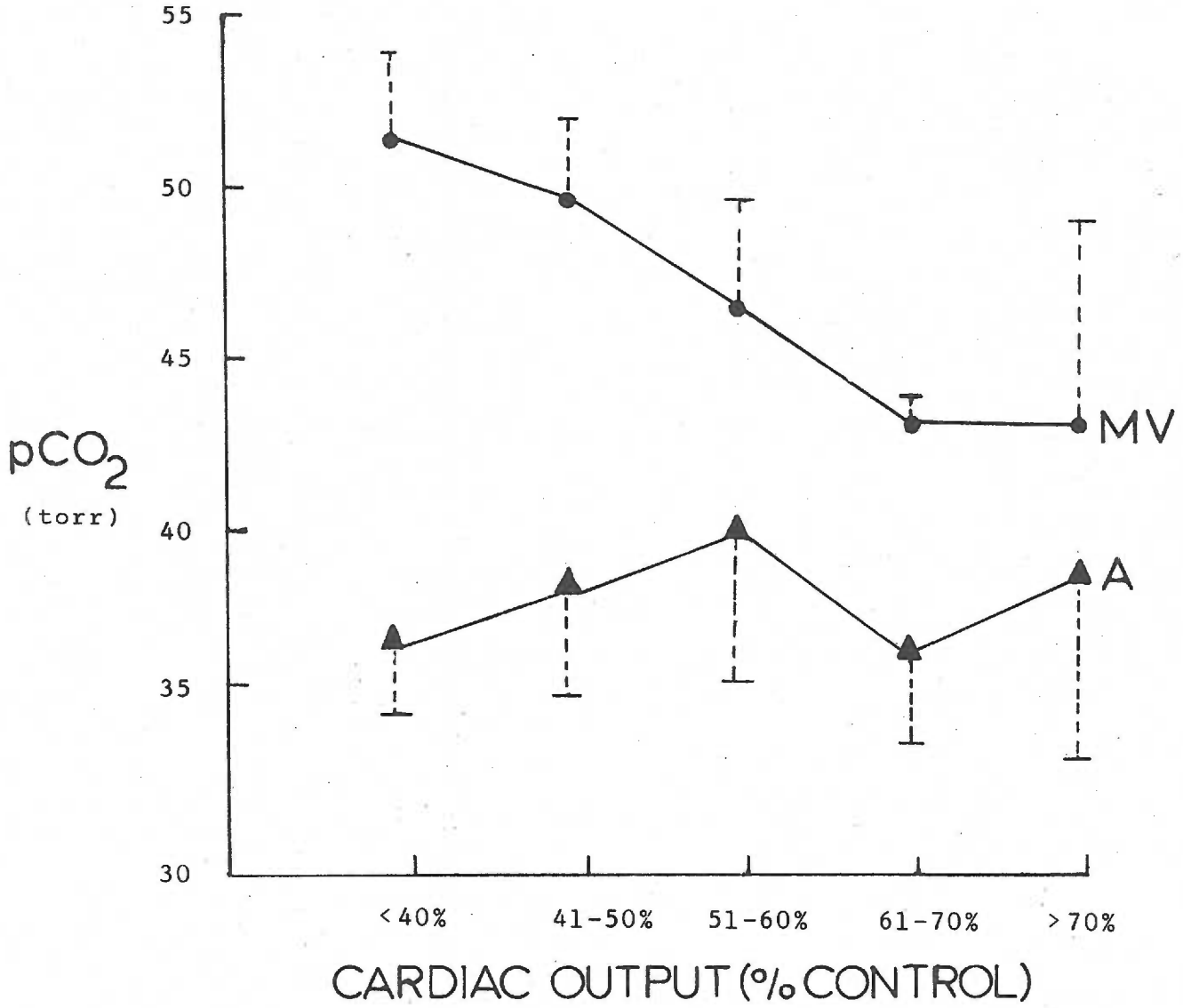

55
50
45
40
35
30
pCO_2
(torr)
MV
A
< 40%
41-50%
51-60%
61-70%
> 70%
CARDIAC OUTPUT (% CONTROL)

Figure 8

The bicarbonate concentration in arterial and mixed venous blood as a function of percent of control cardiac output.

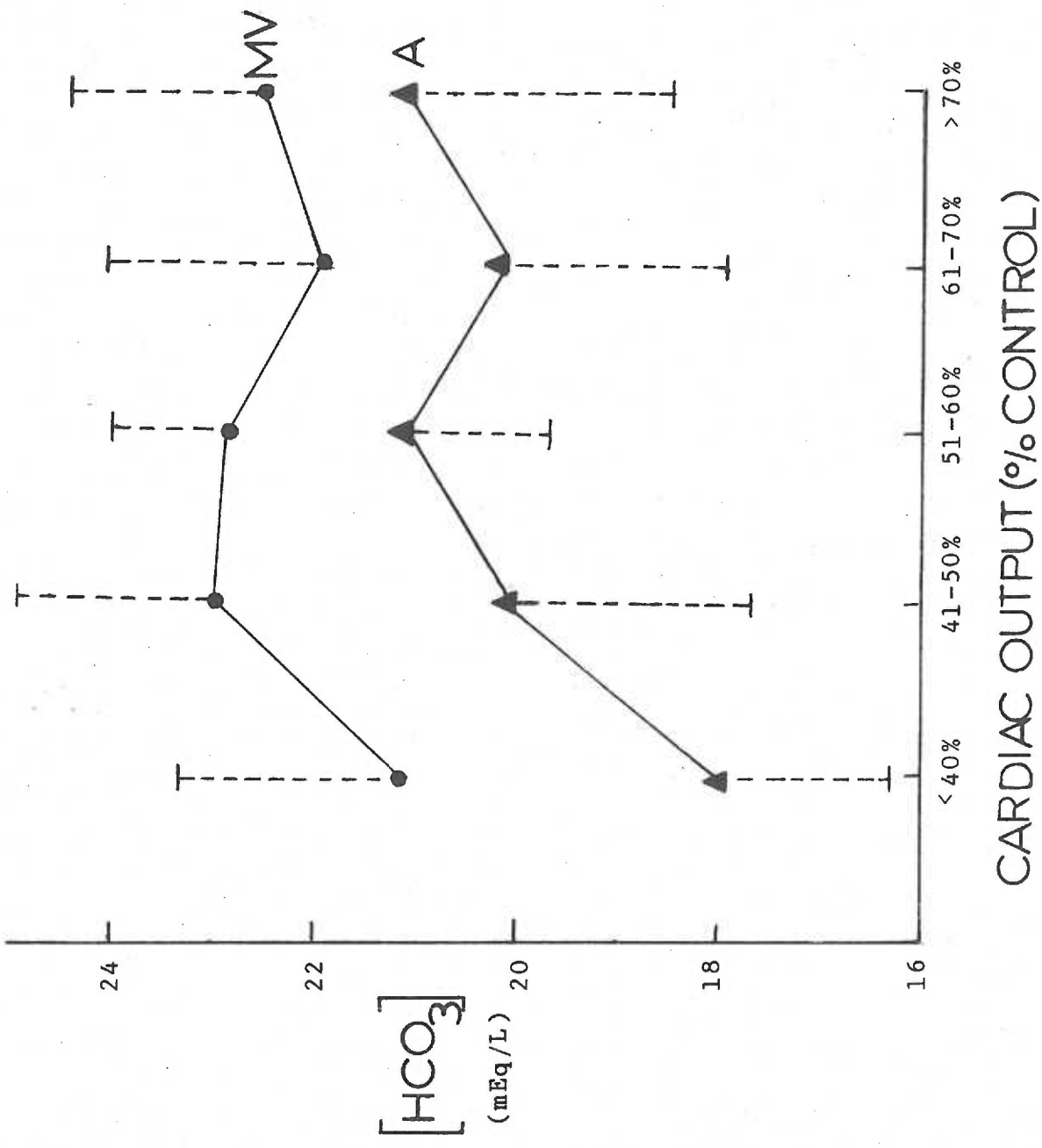

MV
A
24
22
20
18
16
[HCO3]
(mEq/L)
< 40%
41-50%
51-60%
61-70%
> 70%
CARDIAC OUTPUT (% CONTROL)

Figure 9

PO_2 of arterial and mixed venous blood as a function of percent of control cardiac output.

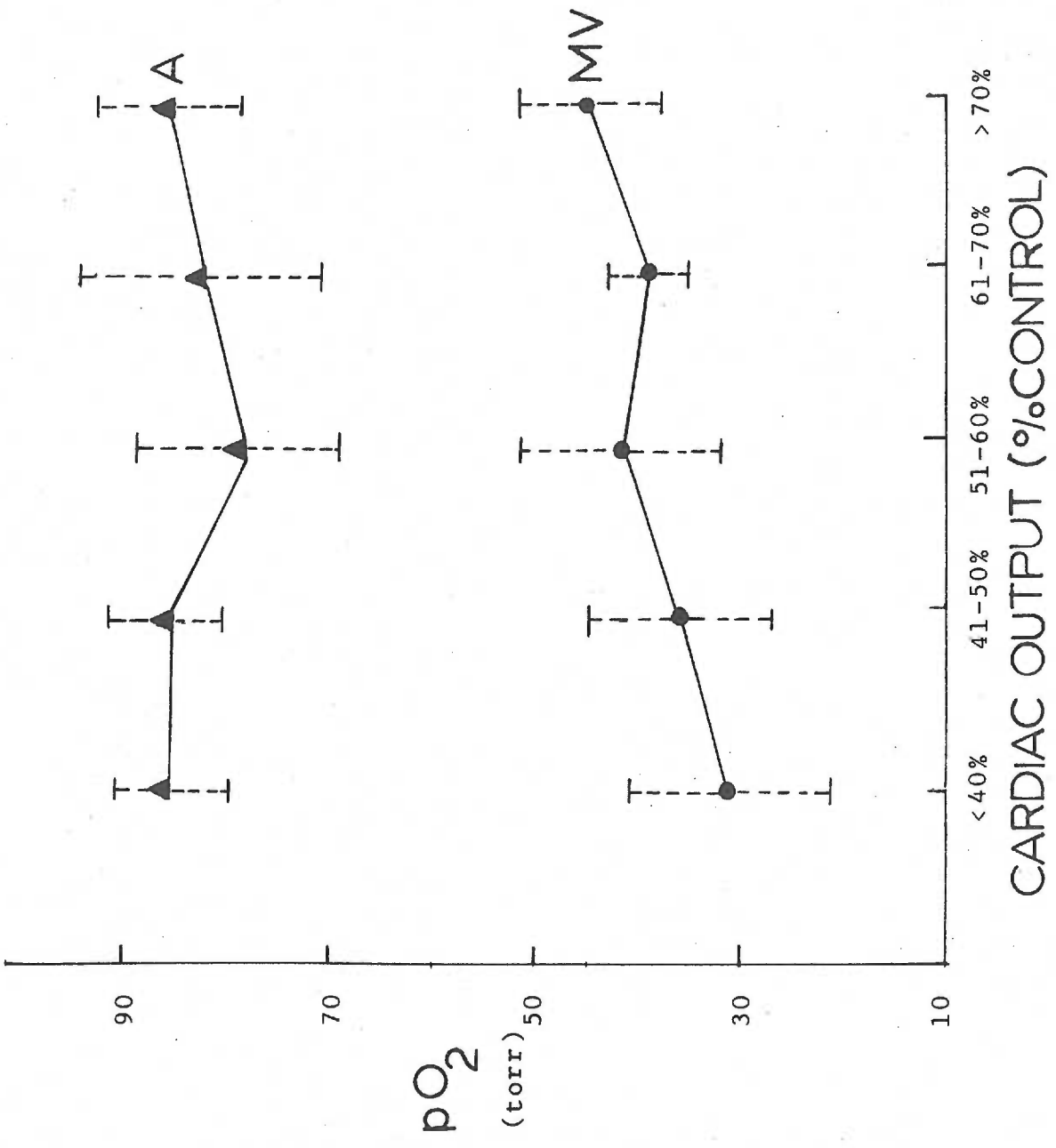

A
MV
90
70
50
30
10
pO_2 (torr)
< 40%
41-50%
51-60%
61-70%
> 70%
CARDIAC OUTPUT (%CONTROL)

Figure 10

Final and post transfusion concentrations of oxygen in arterial and mixed venous blood.

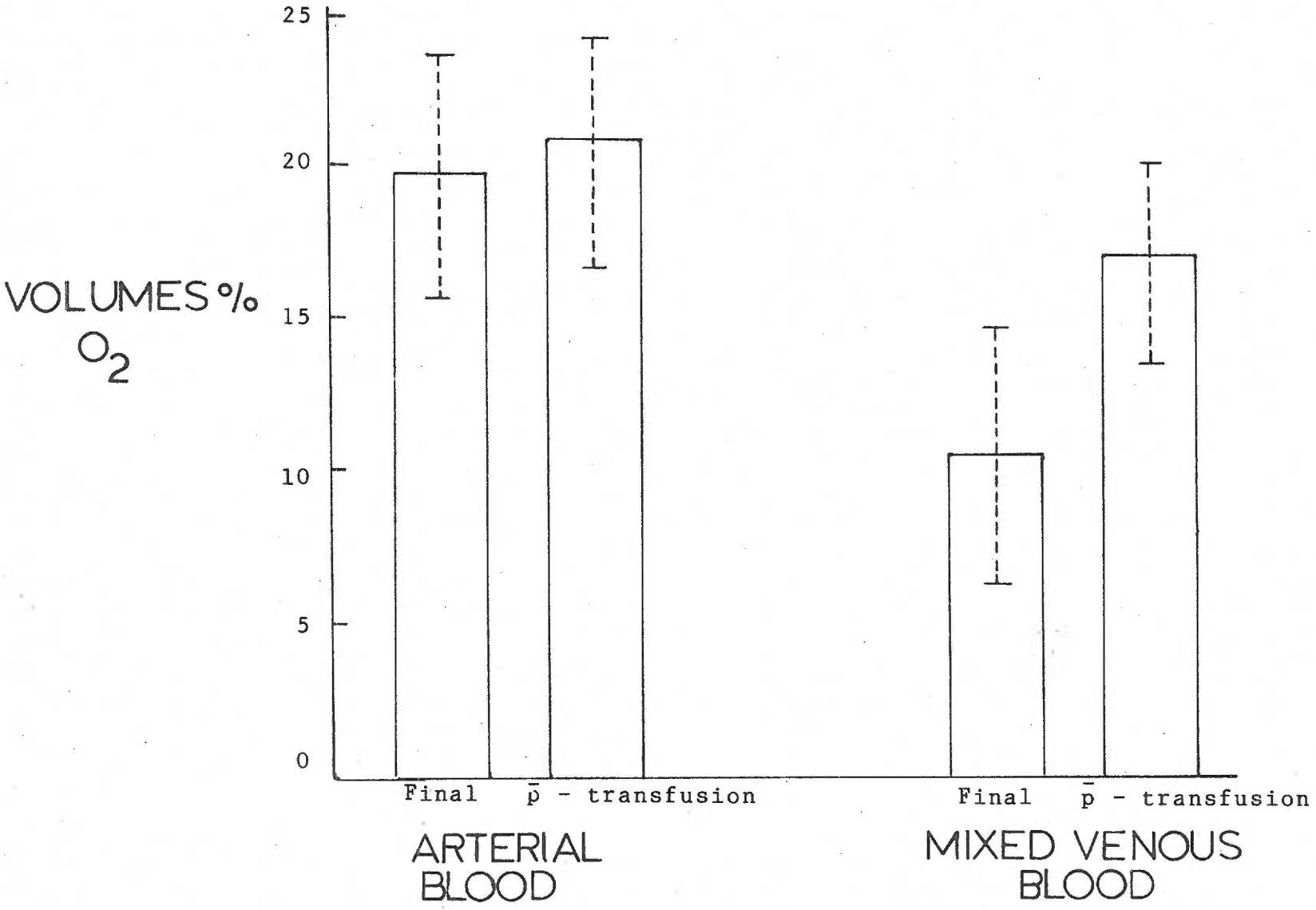
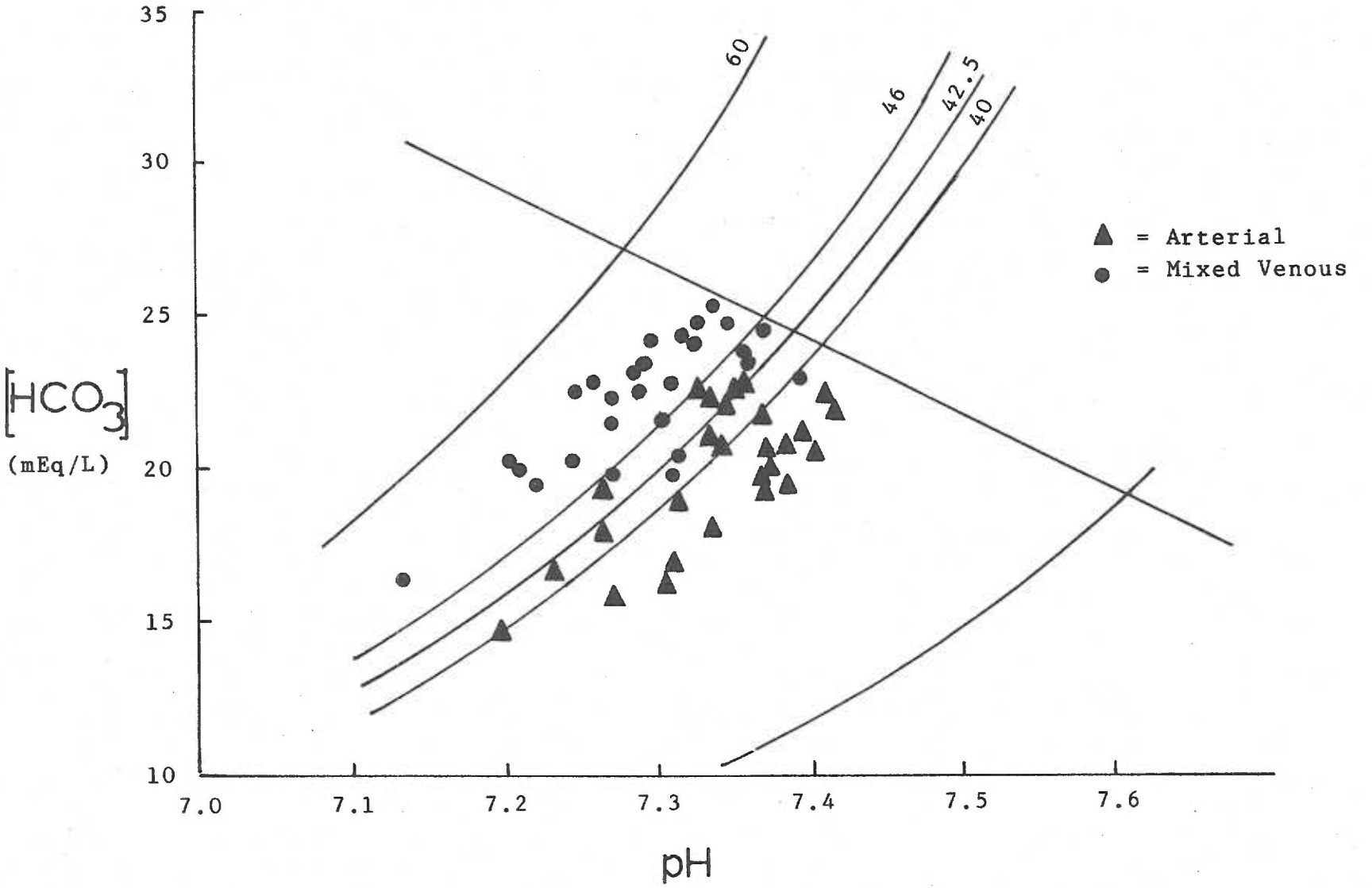

VOLUMES %
O_2
25
20
15
10
5
0
Final
$\bar{p}$ - transfusion
Final
$\bar{p}$ - transfusion
ARTERIAL BLOOD
MIXED VENOUS BLOOD

Figure 11

Arterial and mixed venous blood-gas parameters during reduced cardiac output in nine dogs.


35
30
25
20
15
10
[HCO3]
(mEq/L)
60
46
42.5
40
▲ = Arterial
● = Mixed Venous
7.0
7.1
7.2
7.3
7.4
7.5
7.6
pH

CHAPTER IV

Discussion

The discussion is organized under the following major headings:

1) In what ways do mixed venous and arterial blood-gas compositions differ during reduced cardiac output when ventilation is controlled?
2) In what ways do mixed venous and arterial blood-gas compositions differ with reinfusion of blood after hemorrhage?
3) Is there a predictable pattern to the change in mixed venous blood-gas composition in states of reduced cardiac output when ventilation is controlled?
4) A discussion of clinical implications of mixed venous blood-gas sampling.
5) A discussion of the validity of the animal model.

The blood-gas parameters are discussed separately in the first two sections to emphasize the differences between mixed venous and arterial blood.

In what ways do mixed venous and arterial blood-gas composition differ during reduced cardiac output when ventilation is controlled?

pH

The pH of mixed venous blood was consistently less than that of arterial blood. This arterio-venous difference

reflects the presence of carbonic acid in the venous system. Carbon dioxide, produced from metabolism in tissue cells, diffuses into blood in systemic capillaries and is hydrated to form carbonic acid. This causes an increased $[H^+]$ and, thus, a decreased pH in venous blood. When venous blood reaches the pulmonary capillaries, the CO_2 diffuses out reducing CO_2 concentration, hydrogen ion concentration and thereby increases pH in the arterial blood.

The pH of both arterial and mixed venous blood decreased during hemorrhage, but the decrement in mixed venous blood was more pronounced. The increased arterio-venous difference was due to increased accumulation of carbonic acid in the venous blood. Decreased cardiac output causes an increase in the concentration of CO_2 in capillary blood over that encountered with normal blood flow. Hence $[H^+]$ increases in systemic capillary and venous blood. This increased accumulation of CO_2 in venous blood is then eliminated when blood flows through the lungs. The increase in carbonic acid concentration was therefore, not reflected in arterial blood.

Decreased cardiac output also resulted in decreased tissue perfusion with tissue hypoxia. The consequence of this hypoxia was probably increasing anaerobic metabolism with a subsequent increase in lactic acid production which was reflected in decreased pH of blood in both arterial and venous systems. It may be assumed then, that although the pH of

both mixed venous and arterial blood decreased as a result of the increased production of lactic acid, only the venous blood reflected the increased accumulation of carbonic acid.

pCO_2

The mean pCO_2 of arterial blood decreased only slightly as a result of hemorrhage. Because ventilation was controlled, the usual CNS response to hypovolemia and acidosis, i.e., hyperventilation, was somewhat inhibited. Therefore, the hyperventilation response and subsequent decrease in arterial pCO_2 which were seen in the findings of Murphy (1982) were not as apparent in this study (Figure 7).

The mean pCO_2 of mixed venous blood increased significantly as a result of hemorrhage. This finding is in agreement with the results reported by Tung et al. (1976), but in disagreement with those of Murphy (1982). The apparent discrepancy may be explained by reviewing the processes by which mixed venous pCO_2 is determined. From Equation 4, it can be seen that mixed venous pCO_2 is a function of cardiac output, metabolic CO_2 production, concentration of physically dissolved CO_2 in arterial blood and the fraction of CO_2 produced that is transported as physically dissolved CO_2. In contrast to the results in the present study, the mixed venous pCO_2 in Murphy's study did not change with reduction in cardiac output. In Murphy's study, arterial pCO_2 decreased significantly because of hyperventilation, but this decrease was not reflected in mixed venous pCO_2 for two

reasons. First, cardiac output was decreased and second, there was increased production of CO_2 from increased metabolic rate in respiratory muscles due to hyperventilation. The net change in mixed venous pCO_2 was, therefore, negligible.

In the present study, however, because ventilation was controlled, CO_2 production ($\dot{V}CO_2$) was apparently not increased, nor was mean arterial pCO_2 decreased. Therefore, the reduced cardiac output with its consequent low rate of tissue perfusion was responsible for the significantly increased mixed venous pCO_2.

$[HCO_3]$

The $[HCO_3]$ of arterial blood decreased significantly during hemorrhage, while that of mixed venous blood decreased only slightly. These findings were predicted and are consistent with the findings of Tung et al. (1976) and Murphy (1982). The significant decrease in $[HCO_3]$ of arterial blood may be explained by (1) bicarbonate buffering of fixed acids (lactic acid) produced by tissue hypoxia, resulting from decreased cardiac output, (2) the slight increase in ventilation that occurred even though the respiration of the animals was controlled with mechanical ventilation and (3) the ability of the lungs to equilibrate increased CO_2 pressures to normal during gas exchange. The slight decrease of the $[HCO_3]$ in mixed venous blood reflects several opposing effects: (1) buffering of fixed acids produced by hypoxic

tissues which results in a decrease in mixed venous [HCO_3], (2) a dilutional effect by ISF of HCO_3 produced from hydration of CO_2 in systemic capillary blood, and (3) an increase in the mixed venous [HCO_3] resulting from both accumulation of CO_2 produced by tissue metabolism, low cardiac output, and the Haldane effect. The net effect of these opposing processes was a slight decrease in [HCO_3] with hemorrhage (Table 4), but not of the same magnitude as that seen in arterial blood.

pO_2

The mean pO_2 of arterial blood did not change significantly (physiologically or statistically) from control to minimum values of cardiac output. The slight increase observed may be explained by an increase in the ventilation-perfusion ratio resulting from the slowing of blood flow through the lungs. There was essentially no change in O_2 saturation.

The mean pO_2 of mixed venous blood decreased markedly from control values to those obtained after maximum blood removal. The decrement in the O_2 saturation of hemoglobin (from approximately 78% to less than 50%) was even more profound. This decrease in saturation reflects the increased slope of the oxyhemoglobin saturation curve at low values of pO_2. This finding is in agreement with those of Boyd (1959), Tung et al. (1976), Kasnitz et al. (1976), Kazarian and Del Guercio (1980) and Murphy (1982). The effect of this low

value of mixed venous oxygen saturation was a state of acute tissue hypoxia. This hypoxia was not reflected in the arterial pO_2 which remained in the normal range. Thus arterial pO_2 provided no information on the tissue hypoxia produced by hemorrhage.

In what ways do mixed venous and arterial blood-gas compositions differ with reinfusion of blood after hemorrhage?

pH

The pH of both arterial and mixed venous blood increased after transfusion. There are two reasons for this increase: (1) the transfused blood contained a large buffering capacity in the forms of bicarbonate, hemoglobin and plasma proteins, all of which served to buffer the acids present, and (2) the increased cardiac output which resulted in increased tissue perfusion with a concomitant decrease in lactic acid production.

It is important to note however, that the increase in the pH of mixed venous blood was greater than that of arterial blood. This marked increase was due to a decrease in the amount of carbonic acid in the venous blood. Increased cardiac output resulted in a decrease in the concentration of CO_2 in systemic capillary blood. Hence $[H^+]$ decreased in capillary and venous blood.

It may be concluded then, that although pH of both mixed venous and arterial blood increased as the result of increased blood volume and decreased lactic acid production, only the change in pH of mixed venous blood reflected the decreased accumulation of carbonic acid in systemic tissues.

pCO_2

The mean pCO_2 of arterial blood increased slightly after transfusion. Because ventilation was controlled, the decrease in arterial pCO_2 during hemorrhage was minimized and arterial pCO_2 values were within the normal range. Transfusion, resulting in a return to normal cardiac output, would be expected to produce no net change in arterial pCO_2, as was demonstrated in this study.

The mean pCO_2 of mixed venous blood decreased significantly after transfusion. Two factors serve to explain this decrement: (1) the increase in blood volume with relatively low $[CO_2]$ had an initial dilutional effect on the concentration of CO_2 in the venous blood, and, more importantly, (2) the increase in cardiac output increased capillary blood flow and reduced the CO_2 accumulation and hence the pCO_2 of mixed venous blood.

$[HCO_3]$

The mean $[HCO_3]$ of arterial blood increased significantly after transfusion. This increase was caused by three processes: (1) the increase in blood volume resulting in more total buffers available, (2) a decrease in the

production of lactic acid and, (3) the aerobic metabolism of lactic acid.

The mean [HCO_3] of mixed venous blood remained essentially unchanged after transfusion. This finding reflects several opposing effects. The [HCO_3] in mixed venous blood was increased by the same factors which caused an increase in the [HCO_3] of arterial blood. However, a decrease in [HCO_3] of mixed venous blood resulted from: (1) increased cardiac output causing a decrease in the accumulation of CO_2 from tissue metabolism and, (2) the Haldane effect (Figure 4).

pO_2

The mean pO_2 of arterial blood increased slightly after transfusion. This increase effected no measurable change in O_2 saturation when compared to that during maximum blood loss. This lack of change in O_2 saturation reflects the markedly decreased slope of the oxyhemoglobin saturation curve at high levels of pO_2. There was a slight, but insignificant increase in total O_2 content of arterial blood reflecting the slight increase in pO_2 and slight increase in hemoglobin concentration from retransfusion.

After transfusion, the mean pO_2 of mixed venous blood increased significantly (Table 5). The O_2 saturation increased from less than 50% at maximum blood loss to approximately 82% after transfusion. This marked change in O_2

saturation reflects the steep slope of the oxyhemoglobin saturation curve at these mixed venous pO_2 values.

The total concentration of O_2 in mixed venous blood increased significantly after transfusion. The increase in O_2 saturation, the increase in pH and decreased pCO_2 (the Bohr effect), and the slight increase in hemoglobin concentration all contributed to this rise.

It is apparent, by the increase of both oxygen saturation and oxygen content in mixed venous blood, that tissue oxygenation was adequate. This finding is in agreement with the results of Boyd et al. (1959). Again, the change in arterial pO_2, saturation, and total O_2 content did not provide information on changing hemodynamic conditions which occurred as the result of transfusion.

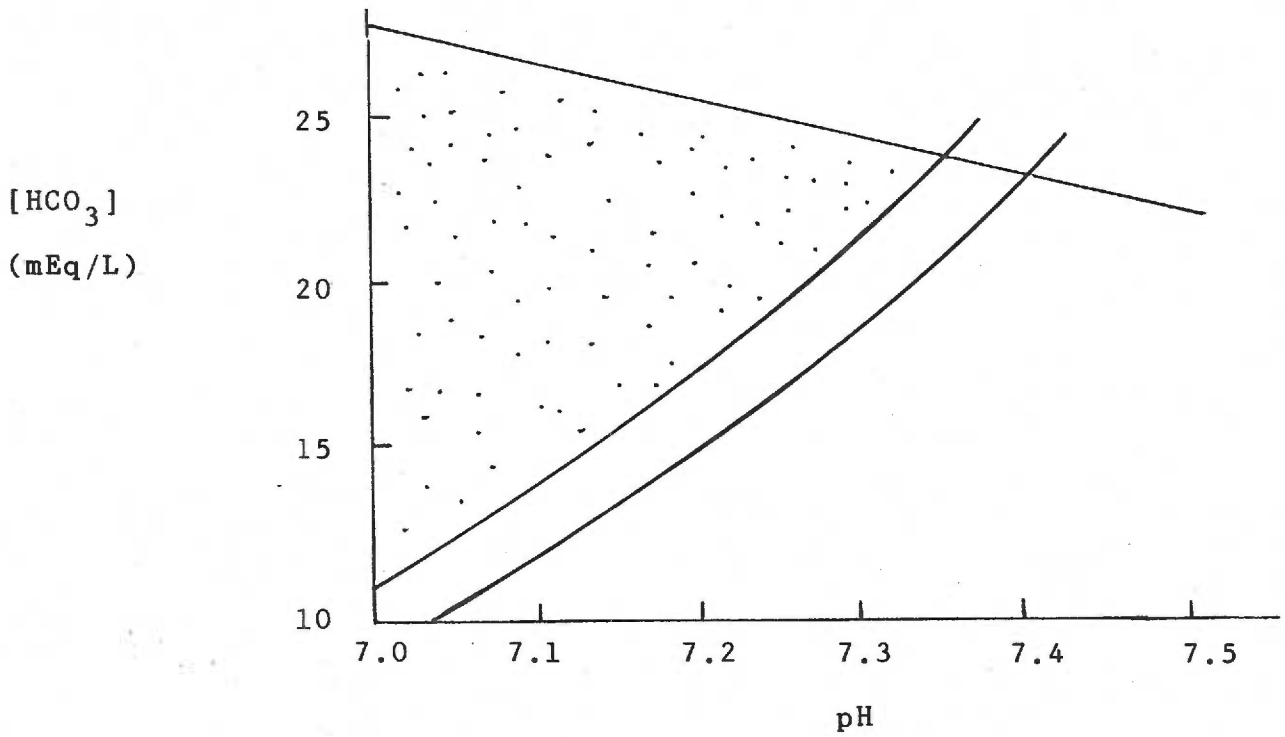
Is there a predictable pattern to the change in mixed venous blood-gas composition in states of reduced cardiac output when ventilation is controlled?

Reduction of cardiac output has been shown in this study, to increase the arterio-venous (A-V) differences for all blood-gas parameters even with control of ventilation (Figures 6, 7, 8 and 9). The results of this study are in agreement with those of Murphy (1982) and show that a regular pattern of changes in blood-gas composition exists during reduction of cardiac output.

Specific patterns are predicted based on the following considerations. When cardiac output is reduced, the body's physiologic responses to this reduction will be reflected in both arterial and venous blood, but in different ways. For example, a reduction in cardiac output leads to increased anaerobic metabolism in systemic tissues. Lactic acid, the end product of this metabolism, diffuses into capillary blood causing an increase in $[H^+]$ of blood and reducing pH and $[HCO_3]$. Stimulation of the chemoreceptors by this increasing $[H^+]$ results in increased ventilation rate. Increased alveolar ventilation, in turn, reduces arterial pCO_2 and increases arterial pO_2 (Murphy, 1982), unless ventilation is either controlled by a mechanical ventilator or is depressed by some other mechanism. When mechanical ventilation is used, there will be no significant change in arterial pCO_2 or pO_2 from control values. Any changes in the acid-base status of arterial blood may be graphically represented on the pH/$[HCO_3]$ diagram (Figure 12) as falling on the pCO_2 40 torr isobar (control pCO_2 isobar) below the CO_2 buffer line.

The blood-gas values of mixed venous blood differ from those of arterial blood even in states of normal cardiac output (Tung, et al., 1976 and Griffith, 1980). The pCO_2 of mixed venous blood is usually about 46 torr (6 torr above that of arterial blood). This higher pCO_2 will result in a lower pH and a slightly higher $[HCO_3]$ in mixed venous blood than will be found in a corresponding sample of arterial

Figure 12



pH/[HCO_3] diagram depicting areas of metabolic acidosis (below the pCO_2 = 40 isobar) and combined metabolic and respiratory acidosis (shaded area).

blood. The pO_2 of mixed venous blood is normally approximately 40 torr at rest, i.e., more than 50 torr less than arterial pO_2.

When cardiac output is reduced, a marked decrease in mixed venous pO_2 follows because of decreased tissue perfusion, resulting in increased extraction of O_2. The increased production of lactic acid from anaerobic metabolism causes a decrease in the pH of mixed venous blood. Accumulation of CO_2 resulting from decreased blood flow increases mixed venous pCO_2. The $[HCO_3]$ of mixed venous blood would decrease slightly from normal, but will remain higher than that seen in arterial blood. These changes in mixed venous blood may be graphically represented on the $pH/[HCO_3]$ diagram (Figure 12) as falling within the shaded area A.

Assessment of acid-base status using arterial blood will result in different interpretations than if mixed venous blood is used. Analysis of arterial blood will result in the conclusion that an uncompensated metabolic acidosis is present. Analysis of mixed venbus blood, however, will result in the conclusion that a combined acidosis exists which contains both respiratory and metabolic components.

These predictions are borne out in the present study as shown in Figure 11. The mean control pCO_2 of arterial blood in this study was 39.1 torr. If a pCO_2 isobar of 39 were

drawn on Figure 11, arterial pCO_2 values during reduction in cardiac output would cluster close to this isobar. It is evident, then, that little respiratory compensation was possible because of controlled ventilation. From these arterial values during reduced cardiac output, one would be led to conclude that an uncompensated or minimally compensated metabolic acidosis was present.

The mean control value of pCO_2 in mixed venous blood was 42.5 torr. Most mixed venous pCO_2 points during reduction in cardiac output cluster above this value and below the CO_2 buffer line in Figure 11. This indicates that in mixed venous blood, a state of combined acidosis involving both metabolic and respiratory components, was present. Because mixed venous blood represents the flow weighted average of systemic blood flow and thus, the status of ISF, one must conclude that a state of combined acidosis existed in the ISF of these animals. Arterial blood did not reflect this combined acidosis.

If only arterial blood-gases were analyzed, the conclusion that only an uncompensated metabolic acidosis were present would indeed be erroneous and could give rise, in a human application, to inappropriate interventions. For example, treatment for this uncompensated metabolic acidosis in a human patient who is receiving mechanical ventilation might include increasing the ventilation rate and depth to effect a respiratory compensation by reducing $[CO_2]$. When

ventilation is increased, however, there will be a further reduction in cardiac output because of (1) decreased venous return (Harken, Brenna, Smith & Barsamian, 1974) and (2) a direct depression of cardiac contractility (Liebman, Patten, Manny, Shepro, & Hecktman, 1978). This reduction in cardiac output would further compromise tissue perfusion and only exacerbate the acid-base imbalance.

Animal studies have demonstrated that mixed venous blood should be used to determine true ISF acid-base status, particularly in states of reduced cardiac output (Tung et al. 1976, Griffith, 1980, and Murphy, 1982.) Several human studies (Boyd et al., 1959, Kasnitz et al., 1978, and Kazarian and Del Guercio, 1980) have also demonstrated this finding. It is important now to continue this research in humans. Areas of future study should include determination of systemic differences which occur in different types of shock. For instance, does traumatic shock differ from congestive heart failure in its effect on systemic circulation as demonstrated by changes in mixed venous blood-gas parameters? It would also be extremely helpful to develop specific criteria concerning irreversible shock. For example, is there a certain point in reduction of cardiac output and changes in mixed venous blood-gas values in humans at which irreversible shock takes place? Is there a time factor which would correlate with these low values? Answers to these

questions would have a large impact on patient assessment and intervention for both the nurse and the physician.

Clinical implications of mixed venous blood-gas sampling

Clinical decision making involves many processes beginning with accurate data. When the clinician must assess the acid-base status of the patient, use of mixed venous blood-gas data will give the most accurate information for this assessment. Arterial blood gives information about adequacy of pulmonary exchange processes and input to the tissues, but clearly does not give accurate information regarding tissue conditions. This is exemplified by the greater change in pH and different directions of change in pCO_2 and pO_2 which occur during reduction of cardiac output when comparing arterial and mixed venous blood. One might conclude then that mixed venous blood should always be used to assess acid-base status. Pulmonary artery catheterization is not, however, without possible complications. Repeated sampling from the pulmonary artery catheter to obtain blood-gases may increase the risks of complications associated with this catheter.

In a study conducted by Sise, Hollingsworth, Brim, Peters, Virgilio and Shackford (1981), complication rates of insertion and maintenance of pulmonary artery catheters were compiled. Major complications included pneumothoraces, arrhythmias and thrombosis which occurred in 3% of the total

catheterizations in the study. However, in a 1979 review of the literature concerning pulmonary artery catheter complications, however, Baigree and Morgan (1979) concluded that most complications were preventable. Both technical errors and patient related complications were found less often when "a high level of expertise is frequently exercised" (Baigree & Morgan, p. 890). The authors recommended specific protocols with rigid quality control by experienced staff, which, the authors concluded, would effectively minimize these complications. It is clear, then, that although mixed venous blood-gas determination is the method of choice in monitoring acid-base status, it is not necessarily an innocuous procedure. Nurses in the clinical setting must be familiar with both the technical problems and patient-related complications arising from placing and maintaining pulmonary artery catheters. Nurses must then, be educated in the methods of reducing these complications particularly if increased sampling from the pulmonary catheter is necessary.

A site with fewer risks and complications may be available. Several investigators have proposed using peripheral venous blood in lieu of mixed venous blood (Carveth, 1979, Schriver, 1981, and Feldon, 1982). Peripheral venous blood has historically been considerd unreliable because of the diversity of findings from

different sites. Results from the animal studies done by Carveth, Schriver and Feldon suggest that free-flowing peripheral venous blood-gases correlate well with mixed venous blood-gases. Further research in this area is strongly recommended, with particular emphasis on human studies.

Validity of the animal model

The use of the animal model is appropriate in studies by nurse researchers. The animal model has been used by nurses to study such areas as regulation of appetite, oxygenation, intramuscular injections, wound healing, cardiac contractility and neuroanatomy. The number of animal studies conducted in nursing research has been small, however, perhaps due to the opinion that animal findings are not applicable to humans (Cunningham & Mitchell, 1982).

There are several reasons for using animals in research: (1) more control may be exercised in eliminating intervening variables if animals rather than humans are the subjects of experiments, (2) the number of experiments, the time and the place can be planned according to the experimenter's needs, (3) there is more freedom to use invasive techniques in measuring physiological phenomena with the end result being the collection of more accurate data, (4) new procedures may be tested on animals which could not be initially tried on humans and (5) these new ideas may be tested to determine the

possibility of unknown side effects the result of which might preclude experimentation with human subjects.

Importance must be placed, however, on whether the results obtained from the animal model are transferable to humans. Data from these experiments must be used with caution. The animal's response must correlate closely to that of humans in the area of interest for the study to be applicable to clinical situations.

Animal research obviously cannot replace research on humans, but should precede many human studies in order to reduce the risk of human research. It should also be remembered that much of nursing science is applied from other sciences which are based on animal research.

Chapter V

Summary and Conclusions

Arterial blood has been traditionally used to assess pulmonary function and acid-base status. It has recently been challenged, however, that mixed venous blood is more representative of systemic acid-base status. This research was conducted to study the use of mixed venous blood in assessing acid-base status during reduced cardiac output with control of ventilation.

Ten mongrel dogs were used in the study. With ventilation controlled at normal rates and volumes, cardiac output was reduced in a stepwise fashion by periodic bleeding from the carotid artery until a cardiac output of less than 50% was attained. Cardiac output was then increased by transfusion of shed blood. Simultaneous blood-gas samples from arterial and mixed venous sites and cardiac output determinations were obtained for analysis after each reduction in cardiac output and again after transfusion.

The results of the study show that arterial and mixed venous blood-gas data provide different information about the acid-base status in states of decreased cardiac output and after transfusion when ventilation is controlled. As a result of decreased blood volume, the A-V differences for all parameters (pH, pCO_2, $[HCO_3]$ and pO_2) were increased. Analysis of arterial blood-gases showed a minimally

compensated metabolic acidosis, while mixed venous blood-gas analysis showed a combined respiratory and metabolic acidosis. The direction of change differed between arterial and mixed venous blood-gas parameters following transfusion.

It may be concluded that during reduction of cardiac output, and after transfusion, mixed venous and arterial blood-gas compositions change in different patterns even when ventilation is controlled. Because mixed venous blood is the flow weighted average of the output of the tissues, it must be concluded that mixed venous blood samples should be used to assess acid-base status of those tissues.

References

Baigre, R.S. and Morgan, C.D.: Hermodynamic monitoring: catheter insertion techniques, complications and troubleshooting, CMA Journal, October 1979, 121, p. 885.

Bieber, M. The use of mixed venous blood in determining acid of systemic tissues when metabolic input is manipulated. Unpublished Master's Thesis, University of Oregon Health Sciences Center, 1979.

Boyd, A.D., Tremblay, R.E., Spencer, F.C., and Bahnson, H.T. Estimation of cardiac output soon after intracardiac surgery with cardiopulmonary bypass. Annals of Surgery, 150, October, 1959, p. 613.

Carveth, L.J. The use of free flowing peripheral venous blood in assessing acid-base status. Unpublished Master's Thesis, University of Oregon Health Sciences Center, 1979.

Cunningham, S.G. and Mitchell, P.H. The use of animals in nursing research, Advances in Nursing Science, July, 1982, p. 72.

Dukes, H.H., in Dukes' Physiology of Domestic Animals, 8th Ed. Swenson, M.J., Editor, Cornell University Press, Ithaca, 1970, pg. 1433.

Felden, P.M. The use of peripheral venous blood to assess acid-base status when cardiac output is reduced. Unpublished Master's Thesis, University of Oregon Health Sciences Center, 1982.

Griffith, K.K. The use of mixed venous blood in assessment of acute respiratory acid-base disturbances. Unpublished Master's Thesis, University of Oregon Health Sciences Center, 1980.

Harken, A.H., Brenna, M.F., Smith, B. and Barsamian, E.M. The hemodynamic response to positive and expiratory ventilation in hypovolemic patients. Surgery 1974, 76:786.

Kappagoda, C.T., Stoker, J.B., Snow, H.M. and Linden, R.J. The CO titration curve of mixed venous blood. Clinical Science, 1972, 43:553-559.

Kasnitz, P., Druger, G., Yorra, F. and Simmons, D. Mixed venous oxygen tension and hyperlactatemia. Journal of the American Medical Association, 1976, 236:6, p. 570-574.

Kazarian, K., Del Guercio, L.R.M. The use of mixed venous blood gas determinations in traumatic shock. Annals of Emergency Medicine, 1980, 9:4, p. 179-182.

Kazarian, K., Del Guercio, L.R.M. Author's reply, Annals of Emergency Medicine, 1980, 9:11, p. 598-599.

Liebman, P. R., Patten, M.T., Manny, J., Shepro, D. and Hechtman, H.B. The mechanism of depressed cardiac output on positive and expiratory pressure (PEEP). Surgery 1978, 83; 594.

Michel, C.C. The buffering behavior of blood during hypoxaemia and respiratory exchange: Theory. Respiration Physiology. 1968, 4:283-291.

Murphy, J. The use of mixed venous blood for assessment of acid-base status in states of decreased cardiac output. Unpublished Master's Thesis, University of Oregon Health Sciences Center, 1982.

Pantadosi, S., Bradley, E.L., Jr. Letter to the editor. Annals of Emergency Medicine, 1980, 9:11, p. 597.

Roos, A., and Thomas, C.J. The in-vitro and in-vivo carbon dioxide association curves of true plasma. Anesthesiology 1967, 28(6):1048-1063.

Scheinman, M., Brown, M.A., and Rapaport, E. Critical assessment of use of central venous oxygen saturation as a mirror of mixed venous oxygen in seventy ill cardiac patients. Circulation. 1969, August, Vol. XL, p. 165-172.

Schriver, A.O. The use of free-flowing peripheral venous blood in the assessment of respiratory acid-base disturbances. Unpublished Master's Thesis, University of Oregon Health Sciences Center, 1981.

Sise, M.J., Hollingsworth, P., Brimm, J.E., Peters, R.M., Virgilio, R.W. and Shackford, S.R. Complications of the flow-directed pulmonary-artery catheter: a prospective analysis in 219 patients, Critical Care Medicine, 1981, 9, 4, p. 315.

Tung, S.H., Bettice, J., Wang, B.C. and Brow, E.B., Jr. Intracellular and extracellular acid-base changes in hemorrhagic shock. Respiration Physiology, 1976, 26:229-237.

AN ABSTRACT OF THE THESIS OF

BARBARA BERNER

For the MASTER OF NURSING

Title: THE USE OF MIXED VENOUS BLOOD IN ASSESSMENT OF ACID-BASE STATUS IN STATES OF REDUCED CARDIAC OUTPUT WHEN VENTILATION IS CONTROLLED.

Approved: [redacted] D., Thesis Advisor

Traditionally, arterial blood has been used to assess pulmonary function and acid base status. Recently, however, the challenge has been made and substantiated from both theory of acid-base physiology and several clinical studies, that the blood-gas composition of mixed venous blood is more representative of systemic acid-base status than is that of arterial blood. The purposes of this study were threefold: (1) to assess the ways mixed venous and arterial blood-gas compositions differ in states of reduced cardiac output when ventilation was controlled, (2) to assess the ways mixed venous and arterial blood-gas compositions differ with reinfusion of blood after hemorrhage, and (3) to determine the pattern of change in mixed venous blood-gas composition in states of reduced cardiac output when ventilation was controlled.

Ten mongrel dogs were used in the study. While ventilation was controlled at normal rates and volumes, the cardiac output was decreased by periodic bleeding from the

carotid artery. The cardiac output was then increased by transfusion of shed blood. Cardiac output was measured after each change in blood volume using a thermodilution technique with a flow directed pulmonary artery catheter. Arterial and mixed venous samples were obtained using anaerobic technique. The pH, pCO_2 and pO_2 were measured on a blood gas analyzer (Radiometer BGA 3 MKII). The $[HCO_3]$ was determined from the Henderson-Hasselbalch equation.

Results showed that arterial and mixed venous blood gas compositions have different patterns in states of reduced cardiac output and after transfusion when ventilation is controlled. Decreased cardiac output resulted in increased arterio-venous differences for all blood-gas parameters. Analysis of arterial blood-gases showed a minimally compensated metabolic acidosis, while mixed venous blood-gas analysis showed a combined respiratory and metabolic acidosis. Following transfusion, the arterial and mixed venous blood-gas parameters showed marked differences in the direction of change.

It was concluded that mixed venous blood-gases do follow a predictable pattern in states of decreased cardiac output and with transfusion even with control of ventilation. It was also concluded that Mixed venous blood-gas composition reflected the acid-base status of systemic tissues more accurately than that of arterial blood.