

THE USE OF MIXED VENOUS BLOOD IN
ASSESSING MESENTERIC TISSUE STATUS
DURING CHANGES IN CARDIAC OUTPUT

by

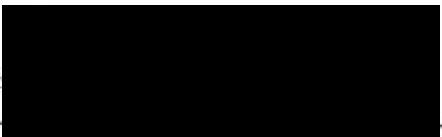
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A Thesis

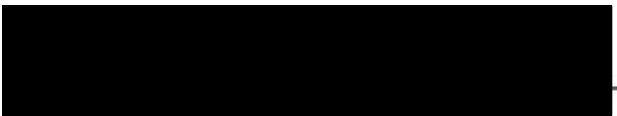
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TABLE OF CONTENTS

Chapter	Page
I. INTRODUCTION AND THEORETICAL FRAMEWORK	1
Review of the Literature	17
The Intestinal Factor in Shock	17
Theoretical Arguments for using Mixed Venous Blood in Assessing Systemic Tissue Perfusion	24
The Predictability of Mixed Venous Blood-Gas Composition Over a Wide Range of Altered Acid-Base States.	40
The Effects of Reduced Cardiac Output on Arterial and Mixed Venous Blood-Gas Compositions	42
Conclusion of the Review of the Literature. .	45
Statement of the Problem	46
Statement of the Variables	46
Hypothesis	46
Implications for Nursing	47
II. METHODS	51
Procedure	51
III. RESULTS	55
General Description	55
Comparison of Mesenteric Venous Blood- Gas Composition with Arterial and Mixed Venous Blood-Gas Composition	57
Physiological Comparison of pH, pCO ₂ , and [HCO ₃ ⁻] of Arterial, Mixed Venous and Mesenteric Venous Blood Using the pH/[HCO ₃ ⁻] Diagram to Assess Acid-Base Status	59

	Page
The Predictability of Mesenteric Venous Blood-Gas Values Based on Mixed Venous Blood-Gas Values	60
Predictability of Mesenteric Venous pH and pCO ₂ Based upon Femoral Venous and Arterial Values	61
IV. DISCUSSION	
How Does Mesenteric Venous Blood-Gas Composition Compare to Mixed Venous and Arterial Blood-Gas Composition When Cardiac Output is Decreased?	79
Is the Blood-Gas Composition of Mesenteric Venous Blood Predictable from Femoral Venous and Arterial Blood-Gas Values?	87
Clinical Implications	88
V. SUMMARY, CONCLUSIONS AND RECOMMENDATIONS	91
Summary and Conclusions	91
Recommendations	92
REFERENCES	94

LIST OF TABLES

TABLE		Page
I	Control Values for Heart Rate, Respiratory Rate, Hematocrit, Protein, Cardiac Output and Temperatures for Dogs 1-10	63
II	Final Values for Heart Rate Respiratory Rate, Hematocrit, Protein Concentration, Cardiac Output, Temperature and Blood Volume Removed for Dogs 1-10 . . .	64
III	Summary of Data for Dogs 1-10 . .	65
IV	Mean Values and Standard Devia- tions for Blood-Gas Parameters of Dogs 1-7, 9, 10	67
V	Regression Analysis MV-SV Differences	69
VI	Actual and Predicted Values for Individual Dogs 1-10 for pH and pCO ₂	70
VII	Regression Analysis Values for Actual and Predicted SV pH and pCO ₂	72

LIST OF FIGURES

FIGURE		Page
1	The Distribution of Small Blood Vessels in the Intestinal Wall	4
2	Countercurrent Exchange System in the Intestinal Villus	6
3	Two-Component Metabolic Model of Autoregulation	10
4	Model: Arterial versus Venous Blood	14
5	Normal In Vivo CO ₂ titration Curve of True Oxygenated Mixed Venous Blood and Two In Vitro Curves Obtained in Mixed Venous Blood	26
6	A Model of Fluid Compartments in Pulmonary and Systemic Tissue	31
7	Buffer Curves of Blood in Vivo and in Vitro	33
8	The Haldane Effect	35
9	The Effect of Doubling the A-V Difference for Oxygen Saturation Between Arterial and Mixed Venous Blood with Constant Arterial Blood-Gas Tensions	37
10	Mean Arterial, Mixed Venous, Mesenteric Venous and Femoral Venous pH as a Function of Percent of Control Cardiac Output	73
11	Mean Arterial, Mixed Venous, Mesenteric Venous and Femoral Venous pCO ₂ as a Function of Percent of Control Cardiac Output	74
12	Mean Arterial, Mixed Venous, Mesenteric Venous and Femoral Venous [HCO ₃ ⁻] as a Function of Percent of Control Cardiac Output	75

LIST OF FIGURES (Continued)

FIGURE		Page
13	Mean Arterial, Mixed Venous, Mesenteric Venous and Femoral Venous pO_2 as a Function of Percent of Control Cardiac Output	76
14	Arterial, Mixed Venous and Mesenteric Venous Blood-Gas Parameters for Cardiac Outputs $<89\%$ of Control Cardiac Output, Dogs 1-7, 9, 10	77
15	Identity Plots for Actual and Predicted Values for Mesenteric Venous Blood for Dogs 1-7, 9, 10 for pH and pCO_2	78
16	The Oxyhemoglobin Dissociation Curve	83

Chapter I

INTRODUCTION

Circulatory shock, a clinical complication involving many disease entities, is the failure of the circulation with hypoperfusion and inadequate oxygenation to the vital organs of the body (Smith and Kampine, 1980). While the etiology of shock may differ, the signs and symptoms are similar. A low cardiac output accompanied with hypotension and hypoxemia characterize the patient in circulatory failure and shock. Regardless of the etiology, shock will become irreversible and fatal if not promptly diagnosed and properly treated.

The irreversibility of prolonged shock has been extensively researched resulting in numerous theories. Evidence has accumulated indicating that the mesenteric vascular bed is an important primary source of factors that lead to irreversibility and a major cause of circulatory collapse during prolonged shock (Haglund, Myrvold, and Lundgren, 1978).

The presence of an intestinal factor in irreversible shock was proposed by Richard Lillehei (1957). He demonstrated in an animal model that by preserving blood flow to the intestines, the hemodynamic disorders and intestinal necrosis following shock were

prevented. Haglund et al., (1978), added support to this early observation and proposed that the cardiac decompensation following shock was caused by cardiotoxic material released from hypoxic gut tissue.

Reduced blood flow in the mesenteric circulation presents a great threat to the integrity of the intestinal tissues and therefore the prognosis of the patient. A high risk group needs to be promptly identified, diagnosed and treated. Low cardiac output may be recorded and documented by clinical assessment and/or measurement via the thermodilution technique. However, it is difficult to know for certain when a low cardiac output is compromising intestinal oxygenation. The mesenteric vascular bed is not immediately or easily accessible for sampling blood for routine analysis. Therefore, a source of blood that reflects the adequacy of perfusion of mesenteric tissues is needed to provide data for accurate assessment.

Theoretical Framework

The theoretical framework is organized under the following headings:

- 1) The intestinal factor in shock
- 2) Feedback regulation of blood flow and oxygen extraction in the small intestine

3) Assessment of mesenteric perfusion and oxygenation

The intestinal factor in shock

The splanchnic vasculature is a collection of circulatory beds and includes blood supply to the alimentary canal or gastrointestinal (GI) tract, pancreas, liver, and spleen. The celiac, superior mesenteric and inferior mesenteric arteries supply arterial blood to the GI tract. Small mesenteric arteries continue to branch to form arterioles and the microcirculation penetrating the tip of the intestinal villus (Figure 1). The arrangement of central arterioles carrying blood to the villus tip and the capillaries returning blood to the villus base have opposite directions of blood flow. This anatomical arrangement provides a counter-current exchange system for absorption from the intestinal lumen and O₂ extraction.

The small intestine is particularly vulnerable to mucosal lesions in low flow states because of this countercurrent exchange mechanism (Hallback, Godal and Lundgren, 1979). During gut absorption, highly permeable substances move down their concentration gradients between arterioles and capillaries. Oxygen is shunted from the arterioles to the capillaries at the base of the villi (Figure 2). Therefore, oxygenation at the tip of

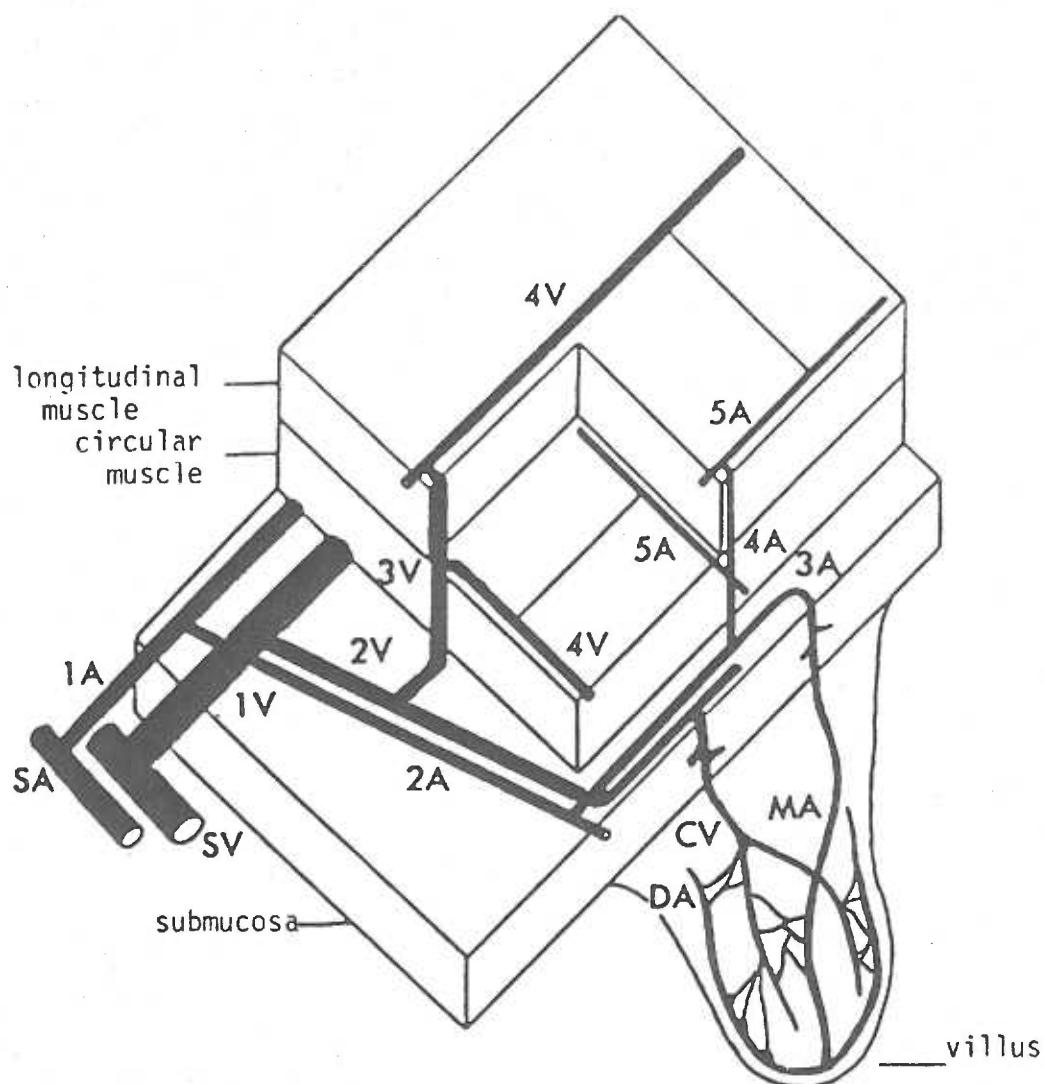


Figure 1

The distribution of small blood vessels in the intestinal wall.

SA = small artery
 SV = small vein
 1A ... 5A = first order arteriole, etc.
 1V ... 4V = first order venules, etc.
 MA = main arteriole
 CV = collecting venule
 DA = distributing arteriole

Modified from Berne, 1981, p. 245.

the villus is less than at the base. As blood flow is reduced, the countercurrent exchange mechanism is more prominent, thus the hypoxic effect of reduced blood flow is potentiated by an increase in the shunting of O_2 .

Intestinal mucosal lesions in low cardiac output states are directly related to flow (Chiu, McArdle, Brown, Scott and Gurd, 1970). Under conditions of low flow, the epithelial layer of the intestinal mucosa is lifted away from the underlying capillary network. These cells remain morphologically and biochemically normal. Though less active, intestinal absorption continues during low flow states. The fluid absorbed is less readily carried into the circulation due to capillary stasis. Fluid accumulates in the epitheal-capillary interface, resulting in a mechanical disruption, called an intestinal lesion.

Intestinal lesions and necrosis are directly attributable to hypoxia in the villus tips during states of low flow. In a variety of pathologies resulting in intestinal infarction, low flow appears to be a common denominator (Aldrete, Han, Laws, and Kirklin, 1977). Aldrete, et al., identified factors useful in the prevention of the fatal outcome of intestinal ischemia due to low cardiac output. They proposed that with early identification of high risk patients and maintenance of

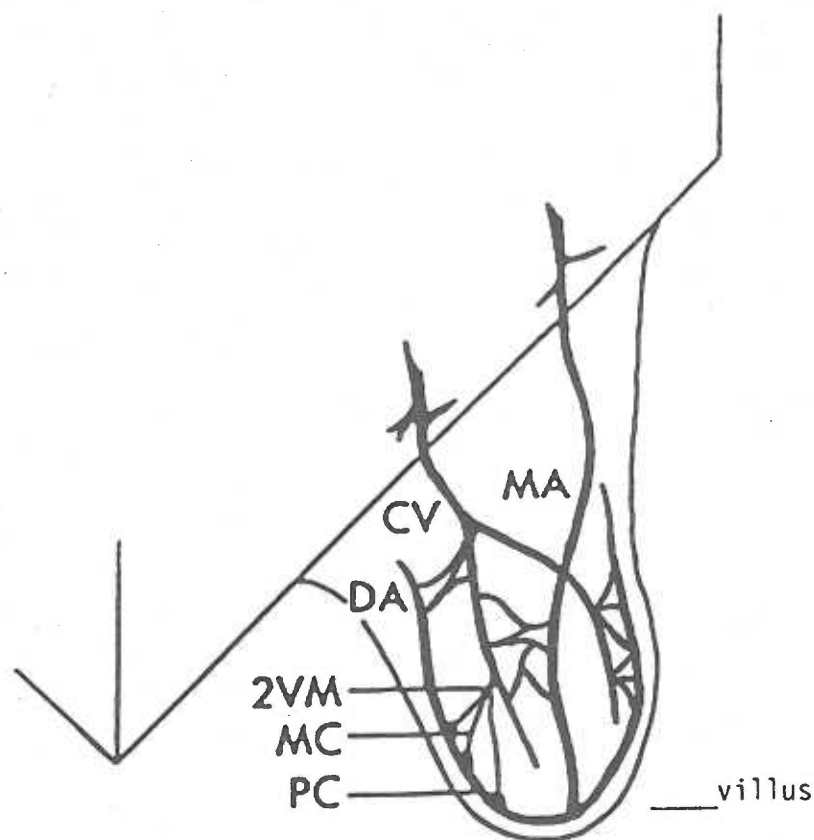


Figure 2

Countercurrent exchange system allows a substantial fraction of O_2 to be shunted from arterioles to venules near the base of the intestinal villus. The supply of O_2 to the mucosal cells at the tip of the villus is less than at the base. Shunting of O_2 during low flow states is exaggerated leading to necrosis of the intestinal villi.

MA = main arteriole
 CV = collecting venule
 DA = distributing arteriole
 2VM = second order mucosal venule
 PC = precapillary sphincter
 MC = mucosal capillary

Modified from Berne, 1981, 245.

flow, the intestinal factor in irreversible hemorrhagic shock could be prevented.

Ischemic injury to the mesenteric circulation occurring during hemorrhagic shock has been recognized since the 1950's. Lillehei (1957) emphasized the importance of intestinal circulation in hemorrhagic shock. He found evidence that the cause of irreversibility following prolonged low flow states was directly related to intestinal ischemia and necrosis. By preserving intestinal blood flow in an animal model during hemorrhagic shock, intestinal necrosis and circulatory failure were prevented.

The major cause of circulatory collapse following intestinal ischemia and necrosis associated with prolonged hemorrhagic shock is currently debated. Toxic factors released from ischemic villi have been identified and implicated as cause for cardiac demise. Evidence has been presented that substances exhibiting a negative inotropic effect on the heart are released from the tips of hypoxic villi in the intestine (Haglund, et al., 1978).

Feedback regulation of blood flow and oxygen extraction in the small intestine.

The anatomical and physiological arrangements of the blood vessels within the mesenteric vascular bed

influence flow in conjunction with the general hemodynamic condition of the cardiovascular system. Maintenance of an adequate flow and tissue oxygenation preserve the intestinal integrity via neural, hormonal and autoregulatory mechanisms.

Neural regulation through stimulation of the sympathetic nervous system, causes vasoconstriction of arterioles and venules in the mesenteric circulation. During prolonged shock this vasoconstriction shifts blood to other circulatory beds enhancing hypoxia at the villus tips.

After food is ingested, blood flow to the intestines is increased. This functional hyperemia is due to the secretion of gastrointestinal hormones, such as gastrin.

Autoregulation allows the intestine to control blood flow and oxygen consumption independently of neural or hormonal changes. Both myogenic and metabolic mechanisms are intrinsic factors responsible in local circulatory control. Granger and Norris (1980) observed that myogenic sensitivity of the intestinal vasculature was reduced in low flow states and during arterial hypoxemia, regardless of the functional (fed or fasted) state. Shepherd (1982) added evidence to these findings and proposed that autoregulation in low flow states was

due to a metabolic model with interstitial hypoxia as a feedback signal. Interstitial hypoxia is a very important feedback mechanism in the metabolic regulation of oxygen extraction and blood flow in the mesenteric vascular bed, especially in low flow states.

Figure 3, a model of autoregulation adapted from Shepherd (1982), illustrates the feedback signal of hypoxia in the control of blood flow in the intestines. Oxygen flux is regulated by metabolic feedback which dilates resistance vessels and opens precapillary sphincters. The increase in blood flow increases or at least maintains capillary pO_2 . As the oxygen availability to demand ratio decreases, as occurs in low flow states, neurogenic regulation causes vasoconstriction via sympathetic stimulation. The result is a decrease in the flux of O_2 to the cells with further interstitial hypoxia. In response to the decreased oxygen delivery, the metabolic system produces greater feedback to oppose the neurogenic vasoconstriction, via an autoregulatory escape mechanism.

Assessment of mesenteric perfusion and oxygenation.

Acid-base status and hypoxia are often assessed in the critically ill patient by arterial blood-gas analysis. Arterial blood is used because it is more uniform in composition than capillary or venous blood.

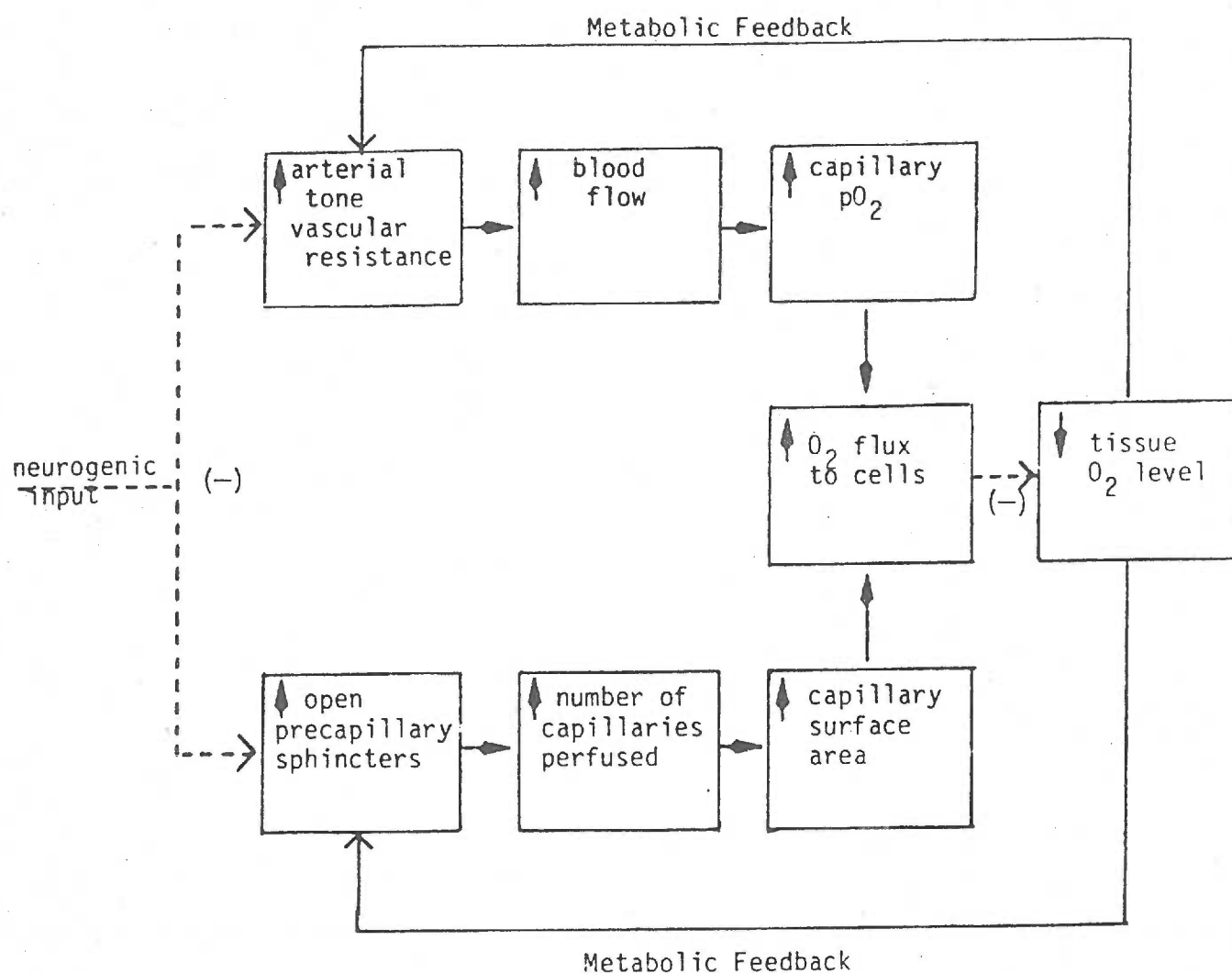


Figure 3

Metabolic feedback to resistance vessels and precapillary sphincters is regulated by the O₂ flux to the cells. The feedback signal is interstitial hypoxia. Dashed lines represent negative effects while solid lines represent a positive stimulus or effect. The negative sign indicates that an increase in input produces a change in the variable in each box opposite of that indicated. With prolonged shock, hypoxia is enhanced via neurogenic vasoconstriction. The further reduction in oxygen delivery produces greater feedback to oppose neurogenic vasoconstriction.

Modified from Shepherd, 1982, p. 2085.

The blood-gas composition of arterial blood also provides data useful in assessment of pulmonary function (Slonim and Hamilton, 1976).

Investigators are beginning to evaluate the use of mixed venous blood for assessment of systemic tissue perfusion and acid-base disturbances. From analysis of a mathematical model, Roos and Thomas (1967) questioned the use of arterial blood for acid-base assessment. They argued that mixed venous blood had a different whole body CO_2 titration curve than arterial blood. In their model they showed that an accurate in vivo CO_2 titration curve could be found only through mixed venous sampling.

Mixed venous blood-gas composition has been compared to that of arterial blood during metabolic acid-base disturbances. Bieber (1979) found that changes in mixed venous blood-gas composition paralleled those of arterial blood in dogs with experimentally induced metabolic acid-base disorders. Griffith (1980) found that changes in the blood-gas composition of mixed venous blood paralleled that of arterial during respiratory acid-base disturbances. Both Griffith and Bieber presented evidence that mixed venous pO_2 may better reflect systemic tissue oxygenation than arterial pO_2 .

Murphy (1982) studied the changes in blood-gas composition of mixed venous blood as compared to arterial

blood when cardiac output decreased. During low flow states mixed venous blood was a better and more accurate indicator of systemic tissue oxygenation than arterial blood.

During states of decreased cardiac output, the supply of oxygen is usually low. With decreased flow, O_2 extraction increases (Berne and Levy, 1981). The effects of cardiac output (Q_t) on mixed venous blood oxygen content can be predicted by the Fick equation (Cheney & Colley, 1980);

$$Q = \frac{VO_2}{C_aO_2 - C_vO_2} \quad (1)$$

where

VO_2 = oxygen consumption (ml O_2 /min)

C_aO_2 = arterial blood oxygen content (ml O_2 /ml blood)

C_vO_2 = mixed venous blood oxygen content (ml O_2 /ml blood)

Thus it is clear that:

$$C_vO_2 = C_aO_2 - \frac{VO_2}{Q} \quad (2)$$

Therefore for a given C_aO_2 , if the cardiac output decreases and/or O_2 consumption increases, it is clear that mixed venous oxygen content will decrease.

A physiological model for the use of mixed venous

blood in assessment of systemic tissue perfusion is illustrated in Figure 4. In agreement with Roos and Thomas's theory (1967) the model shows why acid-base disturbances in systemic tissue might be better assessed with mixed venous blood than arterial blood.

Arterial blood-gas composition reflects the balance between ventilation and perfusion of the pulmonary capillaries. Therefore, analysis of the blood-gas composition of arterial blood assesses pulmonary function. Mixed venous blood, however, represents output from the systemic tissues. Returning venous blood is mixed in the right ventricle and pumped to the pulmonary artery. Analysis of mixed venous blood obtained from the pulmonary artery assesses systemic acid-base status and tissue perfusion. The question remains, however, if mixed venous blood can be used to assess the acid-base status and oxygenation of the mesenteric circulation during low flow states.

In the past, it has been the theory that blood is shunted from the mesenteric vascular bed to protect the more important organs such as the brain, lungs, kidneys, etc. (Smith and Kampire, 1980). Current evidence now shows that the intestine plays a very important role in prolonged shock.

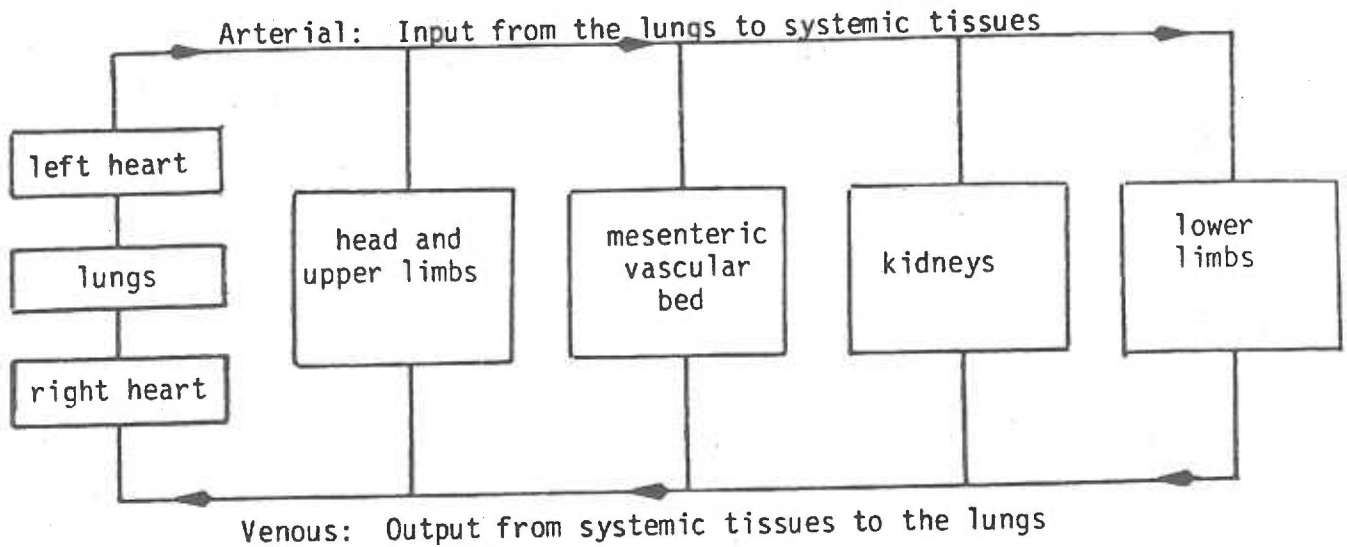


Figure 4

Model: Arterial Versus Venous Blood

Arterial and venous blood flow in opposite directions. Venous blood represents outflow from the organs and systemic tissues to the lungs. Arterial blood represents input from the lungs to the various organs and tissues of the body. Each of the subdivisions represent parallel circuits within the systemic circulation.

Modified from Beiber, 1979.

Hallback, et al. (1979) state that there is a countercurrent exchange of O_2 from arterioles to venules in the mesenteric submucosal circulation. With decreased cardiac output a large portion of O_2 is shunted from arterioles to venules which decreased the O_2 supply to the mucosal cells at the tip of the villus. Shunting of oxygen increases during reductions of intestinal blood flow which could lead to extensive necrosis of the intestinal villi. In addition, Granger and Norris (1980) demonstrated a decrease in mesenteric arterial pO_2 (less than 30 torr) during states of low flow in the mesenteric circulation which can increase the severity of hypoxia in the villus.

Pathologies such as coagulopathies, hemorrhage, and myocardial infarction along with the infusion of many of the drugs used in the critically ill patient can reduce mesenteric blood flow. It is known that hypoxia and acid-base disturbances alter enzyme function at the cellular level. It can be hypothesized that during decreased cardiac output the pH, pO_2 , and $[HCO_3^-]$ of mesenteric venous blood will decrease and the pCO_2 will increase. It can also be concluded that a reduction in cardiac output will produce acid-base disturbances in the abdominal visceral circulation which could compromise gastrointestinal function. It would be useful to know

the acid-base status of blood leaving the mesenteric region to determine if mixed venous blood accurately predicts the acid-base status of the interstitial fluid (ISF) in the abdominal viscera. It is not feasible to measure blood gas composition directly from the mesenteric circulation in the human subject. It seems appropriate therefore, to compare mesenteric venous blood with mixed venous blood-gas values during changes in cardiac output in the animal model.

Review of the Literature

The review of the literature will be organized under the following headings:

- 1) The intestinal factor in shock
- 2) Theoretical arguments using mixed venous blood in assessing systemic tissue perfusion
- 3) The predictability of mixed venous blood-gas composition over a wide range of altered acid-base states
- 4) The effects of reduced cardiac output on arterial and mixed venous blood-gas compositions

The intestinal factor in shock

The presence of an intestinal factor responsible for the development of an irreversible condition after prolonged shock was first proposed by Lillehei (1957). Lillehei noticed that the lesions of the intestines at autopsy were mucosal congestion and necrosis of the small and large bowel. He questioned the fact that the ischemic injury to other organs during prolonged shock was the basic cause of fatality. Lillehei hypothesized that the bowel lesions were of primary importance in the genesis of irreversibility of hemorrhagic shock.

The effects of maintaining arterial blood flow to various organs or circulations during shock in an animal

model was studied. Animals were sedated and separated into sets. Each set contained a donor animal and an animal to be hemorrhaged.

In the dog to be bled, the superior and inferior venae cavae were cannulated via the external jugular and femoral veins. The femoral artery was cannulated for hemorrhage and retransfusion. The donor dog was similarly prepared and another catheter placed in the femoral artery for measurement of blood pressure.

After a period of stabilization, the experimental dog was bled to a mean arterial pressure of 35 mm Hg. The shed blood was saved for reinfusion.

Each set of animals was divided into eight groups. In Group 1 the superior mesenteric artery of the experimental dog was isolated and cannulated. Bowel perfusion was maintained during shock via transfusion of arterial blood from the donor dog into the superior mesenteric arterial cannula of the experimental animal. An equal amount of blood from the venae cavae was returned from the shocked dog to the donor to maintain the state of shock. Perfusion was stopped five hours after the start of hemorrhage and the experimental dog was transfused with the initial shed blood. Cannulas were removed and the wounds were closed.

Dogs with 1-2 month old end to side Eck fistulas

(portal caval shunts) were placed in Group 2. Hemorrhage and superior mesenteric arterial perfusion was performed as in Group 1. The Eck fistula blocked flow to the liver via the portal vein while flow was increased to the mesenteric circulation.

The control group was Group 3. These animals were hemorrhaged as in Group 1, but mesenteric perfusion was not maintained.

Arterial blood flow was maintained during hemorrhagic shock to various organs in the animals in Groups 4 through 8. Perfusion was maintained via catheters to the inferior venae cavae, lower abdominal aorta, liver via the celiac axis and portal vein and the brain.

Only bowel perfused dogs in Groups 1 and 2 survived in significant numbers. In all other groups, dogs died of irreversible shock. Dogs were not considered survivors unless they were alive for at least 72 hours following hemorrhage.

Animals which expired manifested the same signs and symptoms of irreversibility. Blood pressure initially recovered upon retransfusion followed by a gradual decline with an onset of bloody diarrhea. Autopsy revealed severe mucosal congestion with necrosis of the small and large bowel, along with liver congestion. Dogs

in Group 1 were sacrificed and autopsy revealed normal bowels, but congested livers. The dogs in Group 2 also had normal bowels and the livers were not congested.

While maintaining the perfusion of the brain during shock produced a definite increase in the duration of survival, there was no significant increase in the number of permanent survivors. Irreversibility was also not prevented by maintaining perfusion to the liver, systemic arterial systems or venous systems of animals who were placed in hypovolemic shock.

Lillehei concluded that the irreversibility of hemorrhagic shock could be prevented. When the mesenteric circulation of shocked animals was perfused with arterial blood, intestinal necrosis and lesions were not observed.

The pathogenesis of intestinal mucosal lesions in low flow states was studied by Chui, et al., (1970). Hypoperfusion of the intestine was experimentally induced and morphological, hemodynamic and metabolic alterations occurring in low flow states were observed.

Anesthetized animal models were intubated and blood from the femoral artery was pumped into the superior mesenteric artery (SMA) via a calibrated roller pump. The pump flow maintained superior mesenteric arterial blood flow at near normal rates (15 ml/kg/min). In a

second group of animals, the flow to the SMA was decreased to 5 ml/kg/min. The SMA's were simply clamped in Group 3. Serial intestinal biopsies were taken at regular intervals prior to and during the hypoperfusion period.

The progression of intestinal lesions was consistent and reproducible. The process of mucosal damage was similar in all preparations, and the magnitude of the damage was a function of blood flow to the intestine. The epithelial layer of intestinal mucosa was lifted away from the underlying capillary network while the cells remained morphologically and biochemically normal. Intestinal absorption continued during low flow states but was less active. Chui et al. hypothesized that intracellular enzymes released from degenerated cells diffuse into the capillaries and lymphatics of denuded villi and enter the systemic circulation. Endotoxins and other intraluminal toxic substances might also be absorbed into the circulation by this same mechanism.

Aldrete et al. (1977), reviewed and analyzed the records of eight patients with demonstrated intestinal ischemia and necrosis due to low cardiac output. Mean age was 56 years. Cause for low cardiac output included acute myocardial infarction, severe sepsis, hemorrhage

after surgery, cardiopulmonary bypass and aortoiliac bypass. Symptoms included abdominal pain, distention, fever, diarrhea and bloody stools. Leukocytosis and high white blood count were exhibited. Seven patients had documented coronary artery disease. Cardiac output was not measured but estimated by clinical impression. Roentgenologic findings were abnormal except in two patients. Extent of intestinal infarction was documented by direct examination with laparotomy or autopsy. Occlusive thrombosis or embolism was not demonstrated in mesenteric arteries or veins and therefore not the cause for intestinal infarction. All eight patients expired, and autopsies were performed. Aldrete et al. states that the primary cause for low cardiac output was correctable in five of the eight patients and that necrosis of the intestine was thought to be the cause of death.

Three steps were proposed to decrease the mortality of patients having intestinal ischemia associated with low cardiac outputs. Patients should be immediately labeled if there is a high level of suspicion of intestinal ischemia. Included in this index are those patients involved in extensive surgery, trauma, sepsis, myocardial infarction or any disease entity in which the integrity of the circulatory system is jeopardized. Any complications such as dehydration, arrhythmias, acid-base

disturbances or hypotension increase the index of suspicion. Patients with abdominal pain, distention and fever should be promptly diagnosed. Laboratory changes associated with intestinal infarction include leukocytosis and increased serum creatinine concentration.

Second, prompt and aggressive diagnosis is essential once the suspicion of intestinal ischemia is suspected. Aldrete et al. suggested this could be accomplished via selective catheterization of the superior mesenteric artery which would confirm mesenteric vasoconstriction and spasm with impaired filling. And finally, once the diagnosis is established, a program for patient management should be followed. Sustained perfusion of papavarine into the mesenteric artery to reverse mesenteric vasoconstriction was suggested. The clinical course of the patient would then be evaluated by repeat arteriograms and subsequent laparotomies.

The infusion of papavarine into the mesenteric artery, although invasive, is logical. Repeat arteriograms and surgery however could further compromise the patient with intestinal ischemia or infarction. The use of mixed venous blood in assessing mesenteric perfusion and oxygenation in a patient with a low cardiac output is much more feasible in the program for patient management.

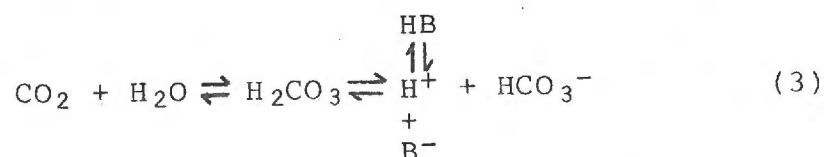
Theoretical arguments for using mixed venous blood in assessing systemic tissue perfusion.

Acid-base status of systemic tissues may not be accurately assessed if arterial blood alone is analyzed. Roos and Thomas (1967) developed a mathematical model to analyze the nature and magnitude of changes in blood-gas composition of blood exposed in vivo and in vitro to alterations in CO₂ tension. Dissociation curves were derived for true plasma, both in vitro and in vivo. They stressed that there was a major difference between the in vitro curve and in vivo curve and also between mixed venous and arterial plasma compositions during in vivo CO₂ titration. They hypothesized that only mixed venous sampling could be expected to yield an accurate in vivo titration curve.

Buffer substances in vitro are contained completely within the blood itself. When CO₂ equilibration is accomplished in vivo, both the blood and interstitial fluid is titrated with CO₂. Concentrations of buffers such as hemoglobin and protein are absent from the ISF. Roos and Thomas correctly stated that a change in pCO₂ results in a smaller change in [HCO₃⁻] and a larger change in pH in vivo than would be found in vitro.

In this model the in vitro titration slope ($\Delta[\text{HCO}_3^-] \Delta p / \text{pH}_p$) of true plasma of normal blood was

-26.9. The in vivo slope of true plasma of the same blood was only -10.1, less than half the in vitro value. The difference in slopes of the two titration curves was due to the higher concentrations of oxyhemoglobin and non-hemoglobin proteins in the blood in vitro while in vivo blood buffers were essentially diluted because of equilibrium with ISF. In other words; when CO_2 changes, the $[\text{HCO}_3^-]$ will change due to buffering. (Equation 3):



where:

HB and B^- represents the conjugate acid-base pair of a blood buffer such as hemoglobin or protein.

If CO_2 content increases, $[\text{HCO}_3^-]$ will increase by mass action. In vitro all HCO_3^- formed remains in blood. In vivo HCO_3^- diffuses into the ISF from systemic capillaries thereby reducing the magnitude of change in $[\text{HCO}_3^-]$ as compared to that found in vitro. Furthermore, as $[\text{H}^+]$ increases, pH decreases as a result of the "shift" of Equation 3 to the right when HCO_3^- diffuses into the ISF. Therefore, the in vitro curve is steeper than the in vivo curve. (See Figure 5.)

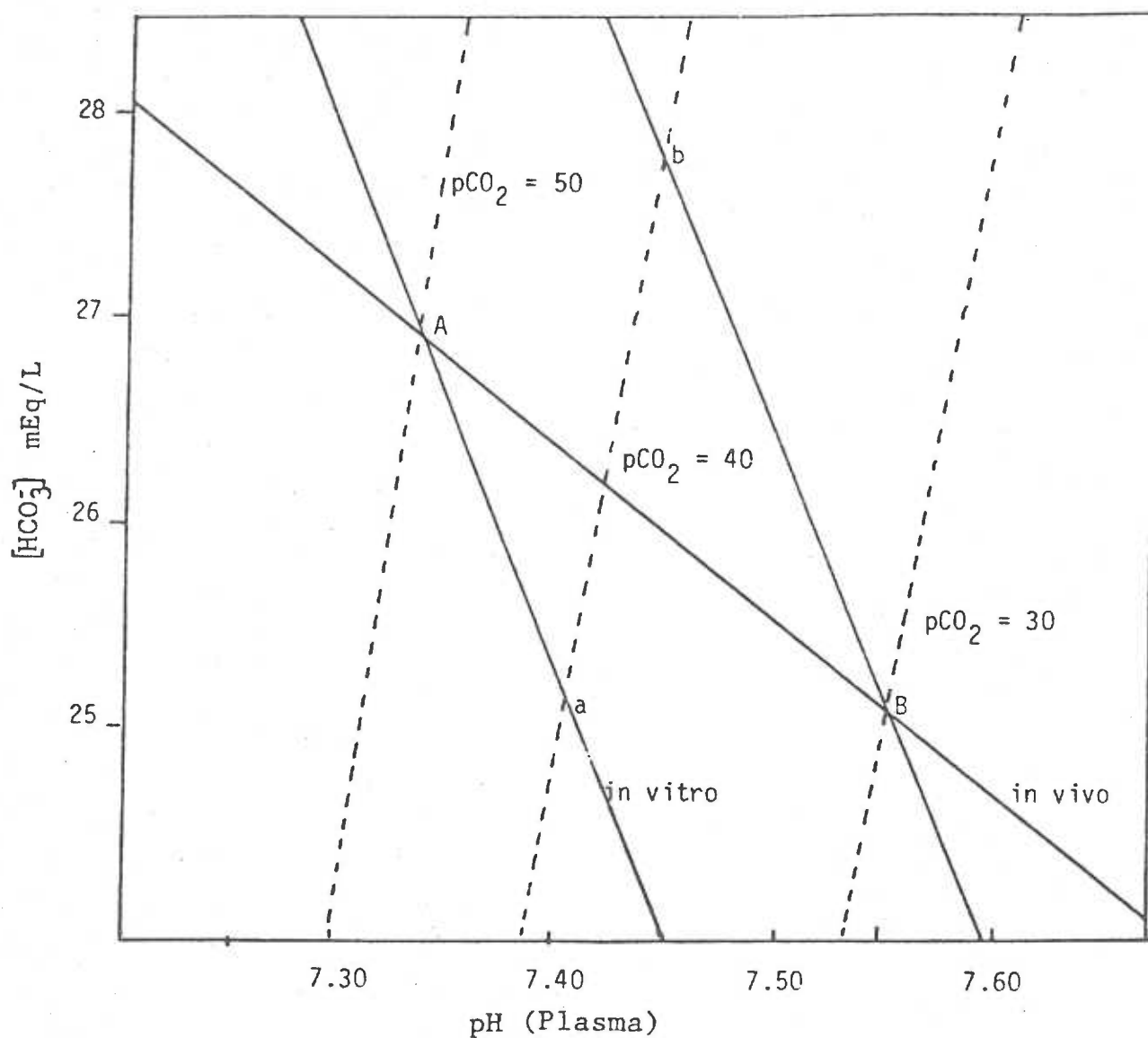


Figure 5

"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 $\text{pCO}_2 = 50$ (A), and 30, (B), respectively."

Redrawn from Roos and Thomas, 1967, p. 1050.

In a steady state of respiration, circulation and metabolism changes in composition of blood flowing through the pulmonary capillaries, are identical to those which that blood would undergo if it were exposed in vitro to changes in CO_2 . Arterial blood-gas composition is altered with changes in cardiac output. Roos and Thomas argue that arterial samples obtained after changes in pCO_2 were of limited usefulness in constructing in vivo CO_2 titration curves. They also state that peripheral venous samples will generally not give an accurate measure of the in vitro titration slope even in a steady state. They state that only when the values differ by a constant amount from corresponding mixed venous values, will peripheral venous pH and $[\text{HCO}_3^-]$ values yield a correct in vivo slope.

The in vivo CO_2 titration curve is affected by volume and composition of blood as well as interstitial fluid. Reducing plasma protein concentrations to one-half the normal value would change the in vivo slope only from -10.1 to -9.2 and the in vitro slope from -26.9 to -23.3. A decrease in interstitial protein concentration reduced the in vivo slope to 9.3 while the in vitro slope remained the same. Although these variables affected the slope of the curve, the changes in shape were small.

In their model, changes in volumes of interstitial fluid and blood had larger effects on the slopes of the curves than did changes in protein concentrations. If the interstitial space were doubled to -17.8 liters while maintaining its protein concentration constant, the in vivo slope decreased to -6.9. A reduction in the space to half the volume increased the in vivo slope to -14.6. If blood volume were reduced by 25% (1.4 liters), the slope decreased from -10.1 to -8.6.

Roos and Thomas assumed that exposures to changes in CO_2 were of short duration, though long enough to reach a steady state. This time depends to a great extent on the blood flow through the tissues. Any factor which causes a reduction in tissue flow could be expected to prolong the time required to reach a steady state.

A third variable which changes the slope of the in vivo CO_2 titration curve is exchange of ions between intracellular and extracellular fluids. Except for CO_2 and O_2 , calculations were predicted on a closed extracellular pool. Roos and Thomas stated that in exposure to abnormal CO_2 tensions for not longer than 1 1/2 hours, there would probably be no significant contributions of renal adjustments to extracellular electrolyte composition. The possibility that ion exchanges between ICF and ECF might affect the

extracellular electrolyte composition and slope of the in vivo titration curve is examined after the next review.

Michel (1968) developed a mathematical model for buffering of blood during hypoxemia and respiratory exchange. In order to facilitate understanding of the complex concepts in this model, the review of Michel's paper is organized under the following three headings:

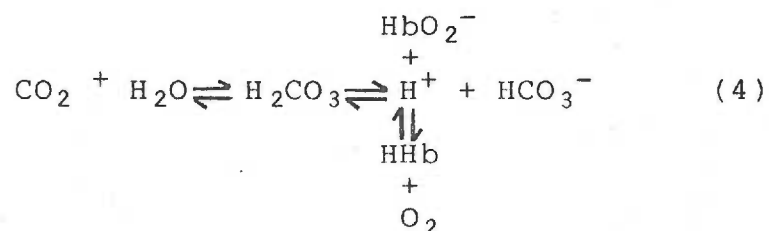
- 1) The true in vivo CO_2 titration curve
- 2) The Haldane effect in relation to arterial and mixed venous blood
- 3) Explanations of observed differences in the mixed venous blood

The true in vivo CO_2 titration curve

Michel's discussion supports the idea that mixed venous blood is represented by an in vivo CO_2 titration curve while arterial blood is represented by an in vitro CO_2 titration curve. This idea is based on the following argument.

Gas exchange occurs in two different environments within the body. These are 1) the pulmonary tissues and 2) the systemic tissues. The actual exchange processes occur in opposite directions in these two capillary beds. Also, the blood in each capillary bed is in equilibrium with different volumes of ISF. The volume of ISF in the lungs is quite small while in systemic tissues

the volume of ISF is approximately four times the plasma volume (Figure 6). This difference in ISF volume can have a marked effect on changes in blood-gas and electrolyte composition of plasma that occur when $p\text{CO}_2$ is increased. These differences would be present whether $p\text{CO}_2$ is changed via reduced cardiac output, increased metabolic rate, reduced V_A , or increased fractional concentration of CO_2 in the inspired gas (F_{ICO_2}). For example, suppose the F_{ICO_2} of inspired gas was increased. The CO_2 that diffuses into the blood in pulmonary capillaries would cause the $[\text{H}^+]$ and $p\text{CO}_2$ of blood to increase due to the reaction shown in Equation 4:



where:

HHb is deoxyhemoglobin and HbO_2^- is oxyhemoglobin.

The majority of the buffering of the H^+ produced from this reaction occurs inside the red blood cell, therefore hemoglobin is the primary buffer. As a result of the buffering of the carbonic acid produced from the change in $p\text{CO}_2$, more HCO_3^- is formed. The HCO_3^- diffuses out of the red blood cell into the plasma. The

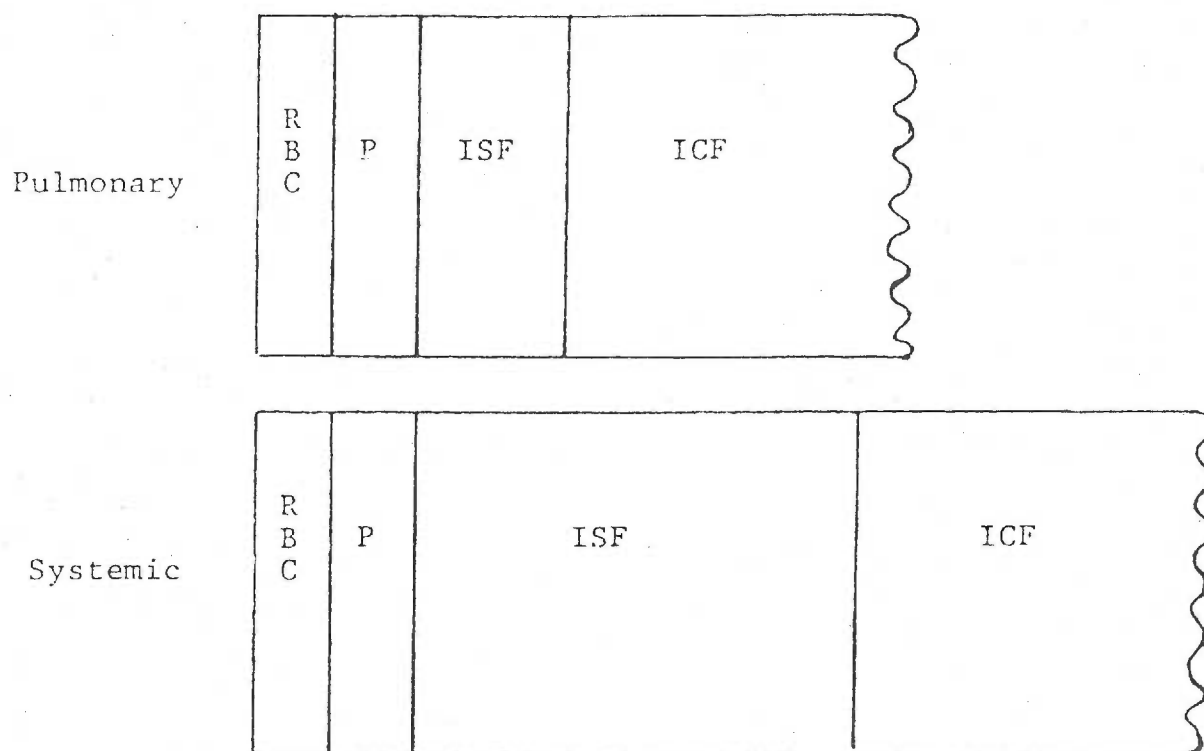


Figure 6

A model of fluid compartments in pulmonary and systemic tissues.

P = plasma
RBC = red blood cell
ISF = interstitial fluid
ICF = intracellular fluid

bicarbonate ion is not restricted to the plasma, but diffuses easily across capillary membranes into the surrounding ISF. In pulmonary tissues the volume of ISF in equilibrium with plasma is small, and therefore little HCO_3^- diffuses from the plasma into the ISF. The net effect is that at equilibrium, most of the HCO_3^- formed remains in the plasma, producing a marked increase in plasma $[\text{HCO}_3^-]$.

Suppose CO_2 was added to blood in systemic capillaries. In systemic capillary blood, the reaction shown in Equation 4 still applies. Bicarbonate formed in the red blood cell diffuses not only into the plasma but also equilibrates with a much larger volume of systemic ISF (Figure 6). The net result is that for the same change in pCO_2 , the $[\text{HCO}_3^-]$ would not increase as much in systemic capillary blood as it would in pulmonary capillary blood, because in systemic tissues, a significant portion of the new HCO_3^- formed diffuses into a relatively larger ISF volume.

In effect, the titration of carbonic acid (Equation 4) in pulmonary capillaries is essentially confined to the blood and mimics what would occur if blood were titrated in vitro. In fact, both Michel (1968) and Roos and Thomas (1967) refer to the titration of carbonic acid in the pulmonary circulation as an "in vitro" titration.

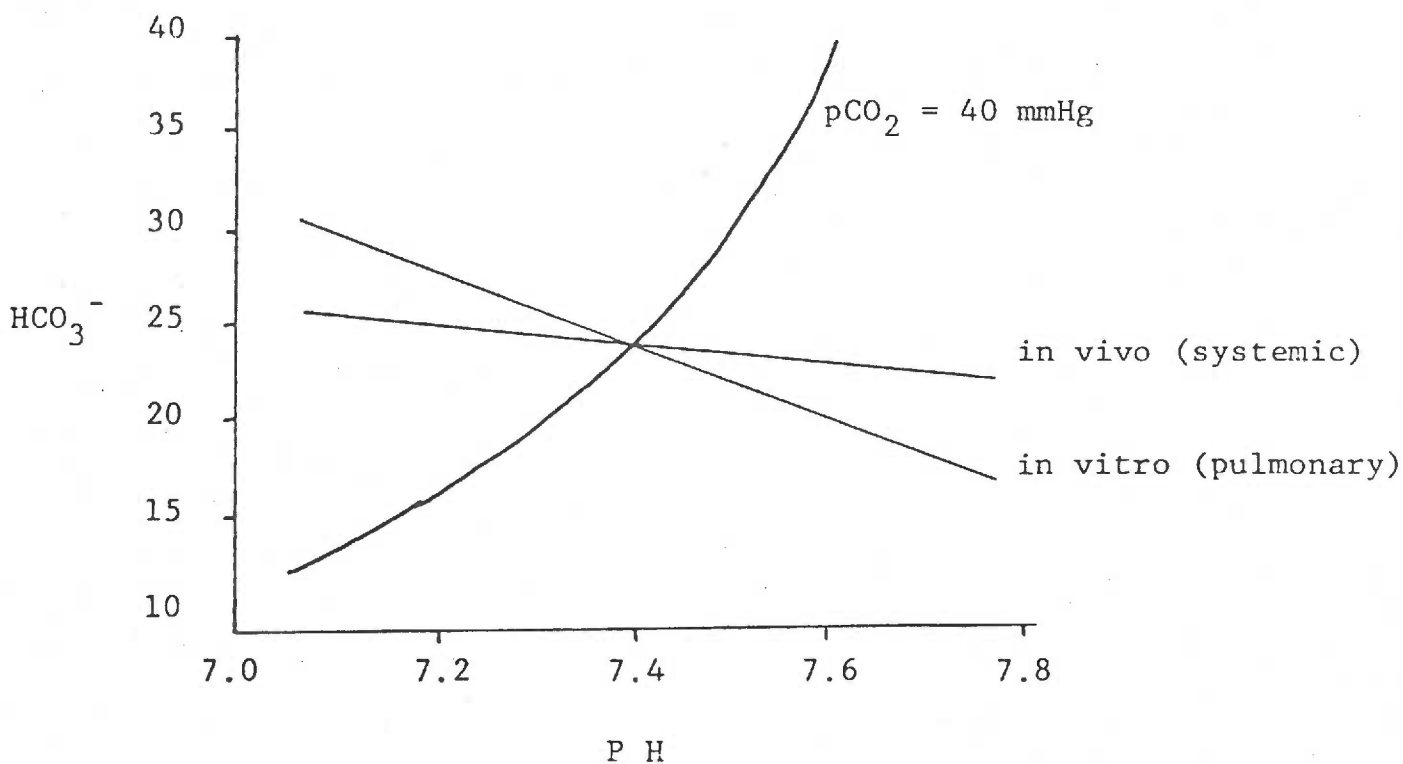


Figure 7

Electrolytes in the plasma are in equilibrium with those in the ISF. Since the ISF contains no hemoglobin and less protein than plasma, the concentrations of those buffer substances in the total volume of extracellular fluid (i.e. *in vivo*) are considerably lower than in *vitro*. Therefore, CO_2 is less effectively buffered *in vivo* than *in vitro*. In *vivo* there is a smaller change in $[\text{HCO}_3^-]$ and a greater change in pH. The *in vitro* titration line is steeper than the *in vivo* line.

Modified from Davenport, 1974, p. 52.

Since titration in systemic capillaries is accompanied by equilibration of HCO_3^- with systemic ISF, the titration is said to be "in vivo" (Figure 7).

The Haldane effect in relation to arterial and mixed venous blood.

Michel considered the magnitude of the extra buffering of CO_2 which occurs because of the Haldane effect. When oxygenated blood is deoxygenated in vitro, at a constant $p\text{CO}_2$, the pH increased due to the Haldane effect. This is accompanied by an increase in $[\text{HCO}_3^-]$ (Figure 8 and Equation 4). The mechanism of the change in $[\text{HCO}_3^-]$ is as follows. Reduced hemoglobin is a stronger base than oxygenated hemoglobin. Therefore, reduced hemoglobin combines with H^+ and the $[\text{H}^+]$ of the plasma decreases (vertical reaction, Equation 4). As a result, more CO_2 is converted to HCO_3^- (horizontal reaction, Equation 4), and the $[\text{HCO}_3^-]$ increases. In vivo, when deoxygenation occurs, the increase in $[\text{HCO}_3^-]$ is not as great as in vitro because the HCO_3^- ions diffuse from plasma into the ISF. It should be noted that the increase in CO_2 content of blood includes both an increase in $[\text{HCO}_3^-]$ and an increase in the amount of CO_2 bound to hemoglobin (carbaminohemoglobin). The latter is not illustrated in either Equation 4 or Figure 8.

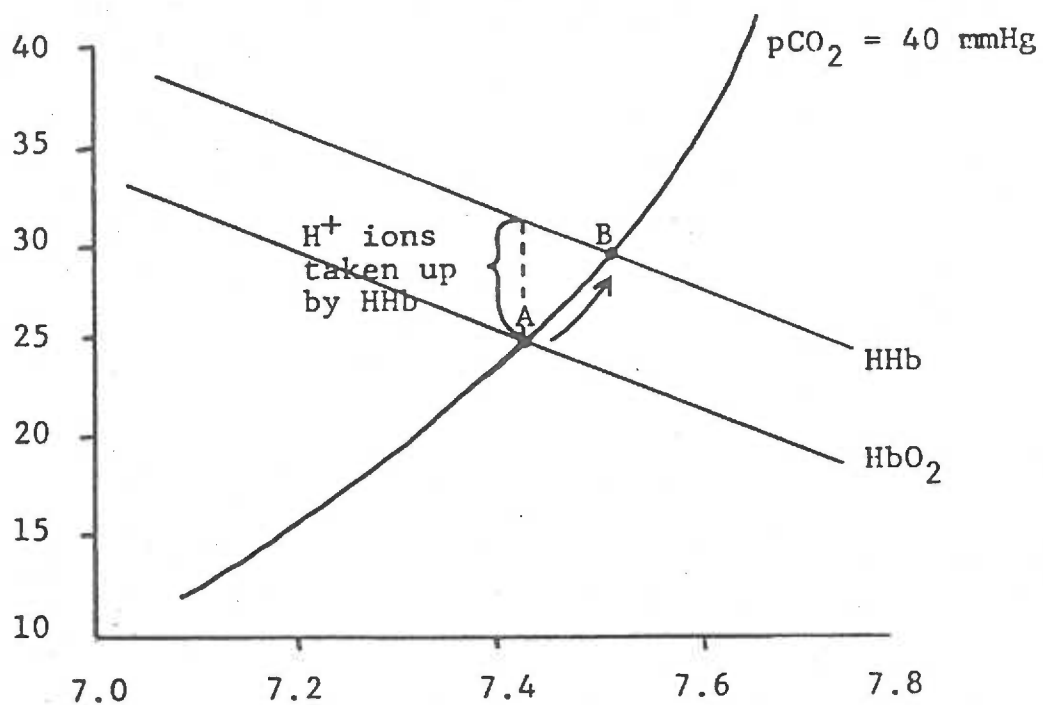


Figure 8

Haldane Effect

Deoxygenation of HHb allows it to take up more H^+ . Point A represents the normal point of oxygenated blood. Point B represents the point after deoxygenation at a constant $p\text{CO}_2$. Hence HHb is a weaker acid than HbO₂.

Explanations of observed differences in the blood-gas composition of arterial and mixed venous blood.

In his discussion of the respiratory exchange cycle, Michel assumed that the venous $p\text{CO}_2$ and $p\text{O}_2$ would change in response to changes in blood flow and metabolism. He assumed that alveolar ventilation was constant and therefore the arterial $p\text{O}_2$ and $p\text{CO}_2$ remained constant. Changes in mixed venous blood and hence the arterial-venous difference (A-V difference) would be due only to alterations in blood flow or metabolism.

Under those assumptions, doubling the A-V difference of oxygen saturation will double the desaturation of hemoglobin in venous blood. The change in oxygen saturation (ΔSO_2) determines the magnitude of the Haldane effect. Figure 9 shows the changes that occur in arterial and mixed venous blood when the A-V SO_2 difference increases. Gas exchange is illustrated in two steps in Figure 9; 1) ΔSO_2 , then 2) $p\text{CO}_2$ changes.

Point A_0 represents the initial arterial blood value. Blood composition shifts from A_0 to point A_I as the blood flows through the systemic capillaries and O_2 diffuses into the tissues. This shift is due to the Haldane effect. Carbon dioxide is added to the blood from the tissues and the blood is titrated to the mixed venous point, V_0 . This shift is along the in vitro

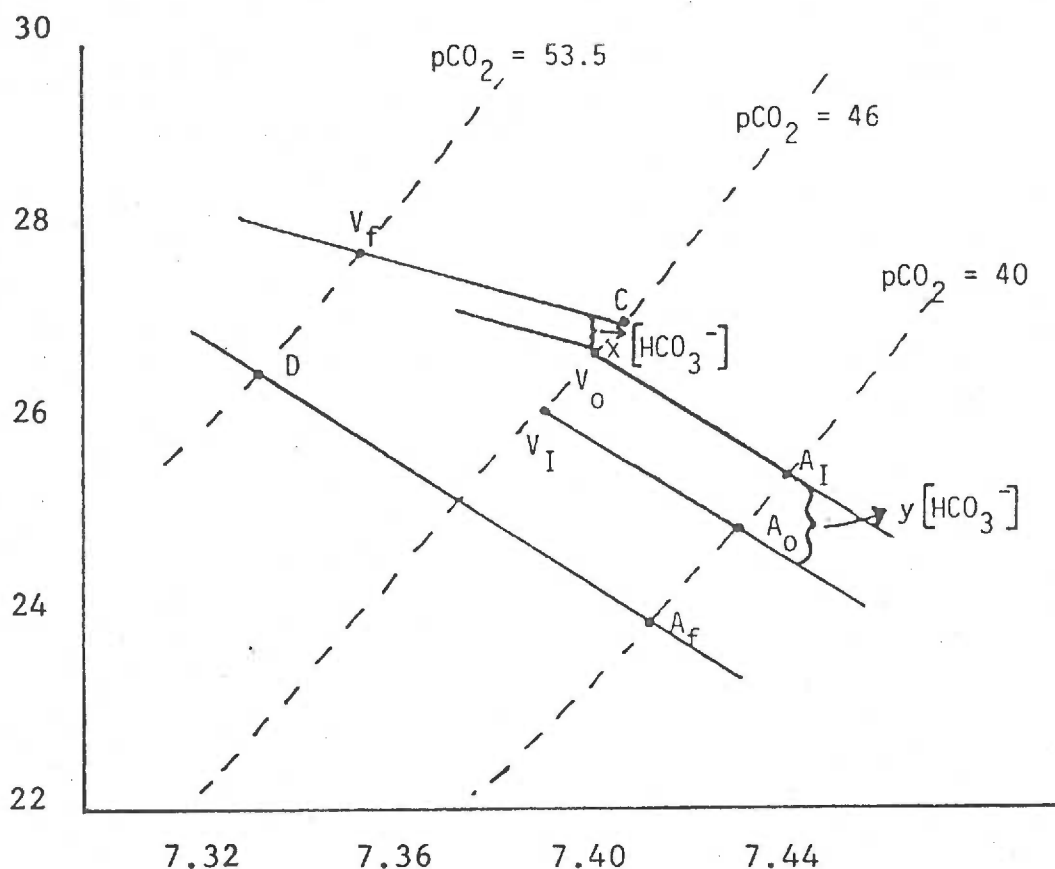


Figure 9

The effect of doubling the A-V difference for oxygen saturation between arterial and mixed venous blood with constant arterial blood-gas tensions. A_0 and V_0 represent initial arterial and mixed venous blood values. A_f and V_f represent final values. Flatter lines are in vivo while steeper lines are for in vitro (pulmonary) curves. Note that the magnitude of the Haldane effect is less in tissues than in the lungs for a SO_2 of 30%. Also note the $[HCO_3^-]$ at A_f is less than A_0 even though the pCO_2 is the same. $x[HCO_3^-]$ represents the Haldane effect in tissues in terms of $\Delta[HCO_3^-]$. $y[HCO_3^-]$ represents the Haldane effect in the lungs in terms of $\Delta[HCO_3^-]$.

titration curve from a $p\text{CO}_2$ of 40 torr to 46 torr.

When blood returns to the pulmonary capillaries and is oxygenated, the oxyhemoglobin gives up H^+ (Equation 2) and $[\text{HCO}_3^+]$ decreases to point V_I . This shift is again due to the Haldane effect. Removal of CO_2 causes titration of blood from V_I to A_O . Actually, both O_2 and CO_2 change together, hence titration is from point A_O to V_O and back.

When blood flow is reduced, for example with a low cardiac output, oxygen saturation in mixed venous blood is decreased. The decrement in saturation occurs because the tissues extract a greater amount of the O_2 delivered by the blood. Blood composition would shift from point V_O to point C due to the Haldane effect. More CO_2 would be added to the blood at the reduced flow than would accumulate at a normal flow. Therefore, the new venous point would shift from C to V_f along an in vivo titration curve, because gas exchange is occurring between the ISF of systemic tissues and capillary blood.

Oxygen saturation returns to 100% when blood returns to the lungs. Initially this oxygenation shifts point V_f to D (Haldane effect). Removal of CO_2 from the blood titrates the blood from point D back to A_f along the in vitro titration curve because gas exchange is now occurring in the pulmonary capillary beds.

Point A_f illustrates that the pH and $[HCO_3^-]$ are lower at a constant pCO_2 than the original arterial point, A_o . Michel concluded that if arterial blood alone is analyzed, one might incorrectly assume that a metabolic acidosis was present. Michel states that "it might seem that high oxygen has led to an effect of opposite sign to the Haldane effect" (p. 290).

In summary, Michel concluded that the true in vivo curve is the CO_2 titration curve for mixed venous blood. The composition of arterial and mixed venous blood are related to one another through the in vitro dissociation curve. Arterial blood is a transformation of mixed venous blood. He also concluded that the changes in arterial pH and pCO_2 cannot be predicted from dissociation curves without reference to mixed venous blood. Changes in arterial blood which seem to contradict the Haldane effect can be understood with the analysis of mixed venous blood.

Neither Roos and Thomas (1967) nor Michel considered the effect of cellular buffering. However, Giebisch, Berger and Pitts (1955) showed that a large amount of H^+ from carbonic acid was buffered because of the exchange of cellular potassium ($K^+ \rightleftharpoons H^+$, 14%) and cellular sodium ($Na^+ \rightleftharpoons H^+$, 37%) for extracellular hydrogen ions. Therefore, Michel's model applies only to

short-term acute changes in $p\text{CO}_2$ and cardiac output. If these changes last longer than 20 minutes or so, then intracellular buffering must be included in the analysis. Intracellular buffering would cause the slope of the in vivo titration curve to increase and approach that of the in vitro curve.

The predictability of mixed venous blood-gas composition over a wide range of altered acid base states.

Bieber (1979) questioned the assessment of acid-base status of systemic tissues with the use of arterial blood-gas composition by itself. Venous blood composition fluctuates in response to changing metabolic rates in various tissues. Therefore, venous blood-gas composition reflects the acid-base status of systemic cells. Bieber argued that blood from the pulmonary artery (mixed venous) reflects a true flow-weighted average of all blood returning to the heart. She states that mixed venous blood was a good source for obtaining venous blood for assessing acid-base status of systemic tissues. She hypothesized that both arterial and mixed venous blood are necessary to accurately assess acid-base status.

Using an animal model, mixed venous blood was withdrawn from the pulmonary port of a Swan-Ganz catheter. The femoral artery provided arterial blood.

Samples were drawn simultaneously and analyzed before and after infusion of NaHCO_3 and NH_4Cl . The pH ranged from approximately 7.0 to 7.7.

Bieber found that the pH and pO_2 of mixed venous blood was consistently lower than arterial blood. Mixed venous pCO_2 was consistently higher than arterial pCO_2 . The bicarbonate concentration of mixed venous blood was consistently higher than that of arterial blood during metabolic acidosis but was more variable during metabolic alkalosis. Bieber concluded that in both alkalotic and acidotic states over a wide range in pH, values change in mixed venous blood-gas composition appeared to mimic the pattern of change in arterial blood.

Griffith (1980) adapted the model used by Bieber (1979) and studied the manner in which mixed venous blood-gas composition compared with arterial blood-gas composition during respiratory acid-base disturbances.

Using an animal model, respiratory acidosis was attained by increasing the fractional concentration of CO_2 in the inspired air (FICO_2). Respiratory alkalosis was induced by changing the tidal volume on the respirator. Arterial and mixed venous blood was sampled simultaneously as each respiratory disturbance developed.

Griffith found that there was a predictable pattern between arterial and mixed venous blood-gas composition during respiratory disturbances. She concluded that

mixed venous blood can be used to predict pH, $p\text{CO}_2$, $[\text{HCO}_3^-]$ and the pH/ $[\text{HCO}_3^-]$ relationship of arterial blood during respiratory acid-base disturbances. In addition, Griffith concluded that mixed venous $p\text{O}_2$ may more accurately predict tissue oxygenation than arterial $p\text{O}_2$.

The effects of reduced cardiac output on arterial and mixed venous blood-gas composition.

Tung, Bettice, Wang and Brown (1976) investigated the difference between arterial and mixed venous blood-gas composition and intracellular pH changes when cardiac output was reduced in an animal model.

Twenty-two mongrel dogs were anesthetized and then hemorrhaged to reduce arterial blood pressure to a mean of 50 mmHg. This pressure was maintained for two hours through additional hemorrhage or infusion of blood as needed. The animal was allowed to stabilize and arterial, and mixed venous blood samples were obtained at regular intervals. The body temperature was monitored and decreased after hemorrhage from 37.9 ± 0.2 to 37.4 ± 0.2 degrees celsius.

Arterial and mixed venous blood-gas values revealed a difference in response to hemorrhagic shock. The plasma bicarbonate concentration decreased in both arterial and mixed venous blood, but the arterial $[\text{HCO}_3^-]$ fell more rapidly than that of mixed venous blood. Thus the arterial-venous $[\text{HCO}_3^-]$ difference increased. Mixed

venous $[\text{HCO}_3^-]$ remained higher than arterial $[\text{HCO}_3^-]$.

The arterial-venous pCO_2 difference also increased during hemorrhagic shock. The pCO_2 of mixed venous blood increased, but the pCO_2 of arterial blood decreased.

Mixed venous and arterial pH also decreased, however there was a more precipitous fall in pH of mixed venous blood. The pH of mixed venous blood remained lower than that of arterial.

Arterial pO_2 increased during hemorrhagic shock due to hyperventilation from metabolic acidosis. Oxygen saturation of hemoglobin was only slightly increased by this increase in pO_2 . Mixed venous oxygen tension fell rapidly from 36 to 16 torr. This resulted in a marked decrease in the oxygen saturation of mixed venous blood. The arterial pO_2 value was maintained during hemorrhage at about 85 torr, while the mixed venous pO_2 was markedly decreased (16 torr) due to tissue hypoxia.

In low cardiac output states, arterial blood-gas composition represented metabolic acidosis with respiratory compensation. The mixed venous blood-gas composition represented the inadequate perfusion to systemic tissues after hemorrhage reflecting both a metabolic and respiratory acidosis.

Tung et al. state that the combination of low $[\text{HCO}_3^-]$, low pH and elevated pCO_2 reflects inadequate alveolar ventilation if measured only in arterial blood.

In mixed venous blood, these values indicate inadequate perfusion. Therefore, the term "respiratory" is being used in its broad sense when the condition presented in mixed venous blood during hemorrhagic shock is described as "respiratory acidosis".

Murphy (1982) supported Tung's study and added evidence that mixed venous blood is a better indicator of systemic tissue oxygenation and acid-base status with low cardiac output. Adapting the model used by Griffith (1980), Murphy studied the manner in which mixed venous blood-gas composition varied in states of decreasing cardiac output.

Using an animal model, cardiac output was decreased with periodic bleedings from the femoral artery. Cardiac output was measured using a thermodilution technique. Arterial and mixed venous blood was sampled simultaneously as cardiac output changed.

Murphy found that arterial and mixed venous blood-gas compositions were significantly different with low cardiac outputs. Arterial blood-gas analysis showed a compensated metabolic acidosis, while mixed venous blood-gas analysis showed a combined metabolic and respiratory acidosis. From these results, Murphy concluded that mixed venous blood provides a more accurate source of blood for use in assessment of tissue acid-base status.

Conclusion

Studies in the literature have shown that mixed venous or arterialized venous blood can be used to adequately assess acid-base disturbances even in extreme ranges of pH, $p\text{CO}_2$, and $[\text{HCO}_3^-]$. Roos and Thomas (1967) suggested that mixed venous blood should be used for better assessment of respiratory acid-base disturbances in systemic tissues. Mixed venous blood has been compared to arterial blood in the assessment of metabolic and respiratory acid-base disorders. Bieber (1979) and Griffith (1980) demonstrated that over a wide range of pH values changes in mixed venous blood-gas composition mimicked the pattern of change in arterial blood. Both concluded that mixed venous blood can be used to predict pH, $p\text{CO}_2$ and $[\text{HCO}_3^-]$ of arterial blood during metabolic and respiratory disturbances. Murphy (1982) documented that mixed venous blood is a better and more accurate indicator of systemic tissue acid-base status and oxygenation than is that of arterial blood.

The importance of the mesenteric circulation has been discussed. It has been shown that a primary source of factors that lead to circulatory collapse and irreversible shock are lesions arising from the mesenteric vascular bed during prolonged shock.

Problem Statement

The question remains, how does mixed venous blood compare to mesenteric venous blood before and after changes in cardiac output in a controlled situation? Does mixed venous blood accurately predict the acid-base status of the ISF in the abdominal viscera?

In the following study I propose to compare the blood-gas composition of mesenteric venous blood and mixed venous blood after changes in cardiac output in an animal model. The cardiac output is decreased in steps via hemorrhage. The pH, pCO_2 , pO_2 , and $[HCO_3^-]$ of mixed venous blood and mesenteric venous blood is determined before and after changes in cardiac output are made.

Statement of the Variables

The independent variable is the change in cardiac output prior to sampling. The dependent variables are the pH, pCO_2 , pO_2 and $[HCO_3^-]$ in mixed venous and mesenteric venous blood. Mixed venous blood is the control for each cardiac output state. The experimental blood-gas value is obtained from mesenteric venous blood.

Hypothesis

1. The blood-gas composition of mixed venous and mesenteric venous blood will not differ significantly after changes in cardiac output.

2. A predictable pattern and correlation will be found between blood-gas compositions of mixed venous and mesenteric venous blood after changes in cardiac output.

3. There will be a significant decrease in pH, pO_2 and $[HCO_3^-]$ and an increase in the pCO_2 of mesenteric venous blood when cardiac output decreases.

Implications for Nursing

The role of the professional nurse is undergoing a dramatic expansion in relation to the delivery of health care services. Nurses in the intensive care unit (ICU) are assuming greater responsibilities in the management of patients in the acute care setting. Nurses are the only health care professionals present in the ICU at all hours. In this expanding role, the nurse functioning in the ICU requires not only a high level of proficiency, but also adaptability in dealing with the unpredictable changes in patient status. This demands the ability to make quick decisions and exercise proper judgment with interventions. The critical care nurse must accept the challenge of the difficulty and complexity of patient care and be accountable for the outcome of that nursing care.

In order to function as a competent member of the health care team, nurses must have intense, comprehensive education and must also keep up to date on current

practice in nursing in a variety of settings. Through participation in research, the nurse is also able to add to the development of new knowledge.

In the ICU, nurses are constantly confronted with the complexity of the acutely ill patient in multi-systems failure. It is one of the nurses' functions to be continually alert to impending crisis. The nurse is usually the first to assess a patient and suggest different modes of care. The intensive care nurse is the first to draw the blood, see the results, and convey them to the physician. She must also be able to integrate the laboratory results with other subjective and objective signs and symptoms from the patient.

Most of the patients in an ICU are critically ill and since many have multi-systems failure, acid-base disturbances are very common. A large percentage of these patients have Swan-Ganz flow directed catheters which will permit withdrawal of mixed venous blood. The benefits of obtaining mixed venous blood instead of arterial blood for blood-gas analysis have been discussed. There is also the aspect of patient comfort. Hematoma formation, nerve damage and bleeding complications from arterial puncture have been documented by many researchers (Sise, Hollingsworth, Brimm, Peters, Virgilio, and Shackford, 1981). Also important to the

patient is the pain involved with arterial sampling.

Abdominal pathology in the critically ill patient is a common problem. "Ischemic bowel" is often encountered in the post-trauma or post-surgical patient. Disseminated intravascular clotting (DIC) and other coagulopathies are cause for compromise in the mesenteric circulation. Sepsis may be yet another of the unending causes for low cardiac outputs and decreased flows to the abdominal viscera. Research into the use of mixed venous blood in comparison to mesenteric venous blood may show that mixed venous blood accurately reflects the acid-base status of the blood leaving the mesenteric region and thereby provide nurses with a new tool for assessing the status of mesenteric blood flow. In addition, new knowledge and insight in the area of physiology will increase the ability of nurses to accurately integrate data from the patient's biopsychosocial history, the physical examination and results from laboratory analysis. This will aid in establishing the nursing diagnosis with appropriate interventions.

Finally, the results of this study may demonstrate a different approach to the assessment of the acid-base status of systemic tissues along with the status of the mesenteric vasculature during states of shock. The physiological changes of the mesenteric tissues when

cardiac output is reduced has been discussed. It has been established that the irreversible factor in prolonged shock may be in part due to the release of toxic materials from the gut. An outcome from knowledge generated in this research, along with further laboratory and clinical testing will significantly affect not only the manner in which nurses obtain blood-gas samples, but the way they interpret the results. Close monitoring of physiological data in collaboration with other members of the health care team in regard to ongoing patient assessment will ensure optimum patient management. If a patient has a decreased cardiac output, assessment of mixed venous blood and prompt intervention may minimize the intestinal factor in the irreversibility of shock.

Chapter II

METHODS

Ten healthy dogs of either sex were anesthetized with sodium pentobarbital (30 mg/kg body weight). Sodium pentobarbital was given to maintain anesthesia throughout the study in 30-45 mg increments. Curare (0.25 - 1.0 cc) was given as needed to maintain muscle paralysis in order to control ventilation.

A tracheostomy was performed and an endotracheal tube inserted. Ventilation rate was controlled with a mechanical ventilator at a rate of 12-15 breaths/minute. Tidal volume was set at 14 ml/kg.

Body temperature of each animal was maintained at 37°C using a heat lamp when needed. Temperature was monitored using a rectal thermometer.

A catheter introduced into the carotid artery permitted arterial sampling. A pressure transducer was attached to the arterial catheter for monitoring blood pressure and heart rate. Pressure was recorded on a polygraph recorder (Grass, Model 7C). The right femoral vein was cannulated to permit infusion of anesthetics. A portion of the small bowel was isolated and a catheter introduced into a mesenteric vein for venous sampling.

A Swan-Ganz flow directed catheter was inserted into the pulmonary artery via the right jugular vein for withdrawal of mixed venous samples and measurement of cardiac output. A pressure transducer was attached for monitoring pressure in order to determine position and progression of the catheter. Position of the catheter was also confirmed by direct visualization and palpation on post mortem exam. Periodic infusions of heparinized saline was infused to maintain patency of the Swan-Ganz catheter.

The animal was allowed to stabilize for an hour after the surgical procedures. Baseline data for blood-gas parameters and cardiac output were obtained at the end of that hour. One ml blood samples were drawn from the carotid artery, mesenteric vein, and pulmonary artery and analyzed.

Cardiac output was obtained using a thermodilution technique. A cardiac output computer (Edwards Laboratories Model 9520A) was used to calculate cardiac output. Three ml of iced glucose solution was infused into the right atrial part of the Swan-Ganz catheter for each determination. The glucose solution prevents unnecessary expansion of plasma volume. Four to five determinations were made each time cardiac output was measured, and the average of the closest three values used as cardiac output.

In order to decrease cardiac output, blood volume was reduced by phlebotomy. The shed blood was stored in heparinized containers. The dog was allowed to stabilize for 40 minutes before repeating the measurement of the cardiac output. Samples of arterial, mesenteric and mixed venous blood were then obtained for blood-gas analysis.

Blood-gas samples were drawn simultaneously and anaerobically with heparinized glass syringes. The plunger and barrel of each syringe was lubricated with stopcock grease to eliminate contamination by air leakage between the barrel and plunger. A small amount of mercury (0.08 ml) was drawn up into the syringe to facilitate mixing of the blood after sampling.

A volume of blood equal to the catheter dead space was withdrawn prior to sampling. Each sample was drawn slowly to eliminate contamination from sources downstream. The syringes were capped and placed on ice to decrease oxygen consumption and metabolic rate of the red cells. Samples were analyzed in random order using a blood-gas analyzer (RADIOMETER Model BGA3, Mark 2). Calibration of the pH, $p\text{CO}_2$ and $p\text{O}_2$ electrodes were checked before analysis of each set of samples and periodically between samples as needed. On each sample,

pH readings were obtained until readings agreed within 0.005 pH units. The pO_2 and pCO_2 readings were recorded until three values were obtained that agreed within 1.0 mm Hg. Hematocrit and plasma protein concentration were measured from samples of arterial blood taken after the equilibration period following phlebotomy. Plasma protein was measured using a refractometer (Hitachi).

Blood volume was reduced in steps until cardiac output was decreased to less than 50% of control. Blood samples were obtained after each decrement. After obtaining the last set of blood samples at the minimum cardiac output, the shed blood was reinfused. Forty minutes after transfusion of the blood, a final set of blood samples were obtained.

The mean values of pH, pCO_2 and pO_2 were calculated. The Henderson-Hasselback equation was used to calculate $[HCO_3^-]$. The values obtained from arterial, mixed venous and mesenteric venous blood for pH, pCO_2 , pO_2 and $[HCO_3^-]$ were plotted against cardiac output. The slope, intercept and Pearson's r of these relationships were then calculated. The significance of differences between mixed venous and mesenteric venous blood-gas parameters were then determined from regression analysis.

Chapter III

RESULTS

General Description

Ten healthy mongrel dogs ranging in weight from 17.7 to 24.1 kg were used in this study. Cardiac output was reduced in steps by hemorrhage and the blood-gas composition of arterial, mixed venous and mesenteric venous blood was determined. Because cardiac output is a function of body mass and animals of different weights were used, changes in cardiac output are reported in terms of percent of control.

Temperature, heart rate and ventilatory rate were monitored continuously. Hematocrit and protein concentrations of blood were determined with each set of blood samples. Summary values for these parameters during control and final cardiac output measurements are shown in Tables I and II. In general, protein concentrations decreased with hemorrhage and ranged from 4.8 - 6.1 gm/dl. In four animals hematocrit concentration decreased slightly from control values to final values obtained after maximum hemorrhage. In eight animals, however, the hematocrit concentration actually increased even though hemorrhage had reduced cardiac output to less than 40% of control. Following hemorrhage, dogs are known to have profound splenic

contraction (Murphy 1982). Small spleens found on autopsy confirmed this fact.

Values for pH, $p\text{CO}_2$, $p\text{O}_2$ and $[\text{HCO}_3^-]$ in arterial, mixed venous, mesenteric venous and femoral venous blood are shown in Table III. Mean values and standard deviations for blood-gas parameters of each different type of sampled blood are shown in Table IV. Due to incorrect placement of the pulmonary catheter, data from dog 8 is not included in the graphic analysis.

To compare and present results clearly, specific blood-gas parameters are discussed under the following headings:

- 1) Comparison of mesenteric venous blood-gas composition with arterial and mixed venous blood-gas composition
- 2) Physiological comparison of pH, $p\text{CO}_2$ and $[\text{HCO}_3^-]$ of arterial, mixed venous and mesenteric venous blood using the pH/ $[\text{HCO}_3^-]$ diagram to assess acid-base status
- 3) The predictability of mesenteric venous blood-gas values based on mixed venous blood-gas values
- 4) Predictability of Mesenteric Venous pH and $p\text{CO}_2$ based upon femoral venous and arterial values

Comparison of Mesenteric Venous Blood-Gas Composition
with Arterial and Mixed Venous Blood-Gas Composition.

pH

The mean pH during control periods for arterial blood was 7.35. The mean pH for mixed venous and mesenteric venous blood were 7.34 and 7.33 respectively. The final value for arterial pH was 7.31 while the final values of mixed venous and mesenteric venous pH were 7.25 and 7.23 respectively (Table IV). The mean pH for arterial blood was consistently greater than that of mixed venous or mesenteric venous blood (Figure A). The mean values for pH in mixed venous blood correlated closely with the pH for mesenteric venous blood (≤ 0.01 pH units for cardiac outputs of greater than 41% of control). In the lowest range of cardiac output, i.e., less than 40% of control, the mean pH for mixed venous blood was 0.02 pH units less than the mean pH for mesenteric venous blood (Table IV). This close correlation is clearly illustrated in Figure 10.

pCO₂

The mean pCO₂ values during control periods for arterial, mixed venous and mesenteric venous blood were 39.0, 43.2, and 43.8 torr respectively (Table IV). Arterial pCO₂ decreased in all dogs after the final hemorrhage to a mean value of 36.5 torr (Table IV).

The $p\text{CO}_2$ of mixed venous blood increased in all animals as a result of hemorrhage (Table III). The final mean $p\text{CO}_2$ for mixed venous blood increased from a control mean of 43.2 to a final mean of 50.8 torr.

Mesenteric venous $p\text{CO}_2$ increased in all dogs except dog 3 where it decreased from 47.7 to 41.3 torr (Table III). The control mean $p\text{CO}_2$ in all dogs for mesenteric venous blood increased from 43.8 to a final value of 48.9 torr. The close relationship between mixed venous and mesenteric venous blood is shown in Figure 11.

$[\text{HCO}_3^-]$

The mean control values for $[\text{HCO}_3^-]$ in arterial, mixed venous, and femoral venous blood were 21.2, 22.5, and 22.6 mEq/L respectively (Table IV). Final mean concentrations were 17.9, 21.0, and 21.4 mEq/L in arterial, mixed venous and mesenteric venous blood, respectively. The $[\text{HCO}_3^-]$ of mesenteric venous blood was 0.4 mEq/L greater than the $[\text{HCO}_3^-]$ of mixed venous blood in all ranges of cardiac output except that of 51 - 60% of control where there was no difference (Table IV). These results are shown in Figure 12.

$p\text{O}_2$

The mean control $p\text{O}_2$ values for arterial, mixed venous and mesenteric venous blood were 84.4, 46.3, and 48.0 respectively. The mean $p\text{O}_2$ of arterial blood

progressively increased as cardiac output decreased to a mean final value of 87.1 torr. The mean pO_2 of mixed venous and mesenteric venous blood progressively decreased to mean final values of 30.6 and 34.2 torr, respectively. The pattern of change in the mean pO_2 of mesenteric venous blood closely paralleled the pattern of change in the mean pO_2 of mixed venous blood (Figure 13).

pH/[HCO₃⁻] Relationship

The pH/[HCO₃⁻] diagram in Figure 14 illustrates the pH and [HCO₃⁻] data points from each dog (1-10, excluding 8) in which cardiac output was less than 70% of control. This diagram is used to assess acid-base status based on the relationship between pH, pCO_2 and [HCO₃⁻] as expressed by the Henderson Hasselbalch equation. The pH/[HCO₃⁻] diagram can also be used to assess acid-base disturbances.

Approximately 9 of 25 arterial points (36%) fall within the category of a mixed metabolic acidosis and a respiratory alkalosis. Five arterial points (20%) fall within the category of a compensated metabolic acidosis. Eleven out of 25 arterial points (44%) are within the range of a combined respiratory and metabolic acidosis.

Twenty-two out of 25 mixed venous points (88%) fall within the category of combined respiratory and

metabolic acidosis. One mixed venous point is within the compensated respiratory acidosis range. This value was obtained from dog 2 at a cardiac output of 49% of control, with a $p\text{CO}_2$ of 50.1. The other two mixed venous points fell within the ranges of a metabolic acidosis and respiratory alkalosis and a compensated respiratory alkalosis, respectively.

Twenty-one (84%) of mesenteric venous points fell within a combined respiratory and metabolic acidosis range. Three values fell within a compensated metabolic acidosis range. The last mesenteric venous point fell within a range of a compensated respiratory alkalosis.

The Predictability of Mesenteric Venous Blood-Gas Values
Based on Mixed Venous Blood-Gas Values.

Figures 10-13 illustrate the close correlation between mixed venous and mesenteric venous blood-gas parameters over a wide range of values for cardiac output. A consistent pattern between mixed venous and mesenteric venous blood is evident. The mean pH value of mesenteric venous blood correlates with mixed venous pH within 0.01 pH units in cardiac output greater than 70%, 51-60% and 41-50% of control. In the range of 61-70% of control cardiac output there was no difference. After final hemorrhage, the pH of mixed venous and mesenteric blood differed by only 0.02 pH units. The mean $p\text{CO}_2$ value of mesenteric venous blood varied from the mixed venous $p\text{CO}_2$ by 0.6 to 1.9 torr, the latter value at 40% of control cardiac output. The mean $[\text{HCO}_3^-]$ for mesenteric venous blood was 0.2 to 0.4

mEq.L higher than the mean $[\text{HCO}_3^-]$ value for mixed venous blood. At 51-60% of control cardiac output, there was no difference in $[\text{HCO}_3^-]$ values. The mean values for mixed venous and mesenteric venous pO_2 differed by 0.5 to 2.7 torr when cardiac output was equal to or greater than 41% of control cardiac output. The mean pO_2 for mesenteric venous blood after final hemorrhage was greater than the mean pO_2 for mixed venous blood by 3.6 torr (Table IV).

Regression analysis for the measured blood-gas parameters is summarized in Table V. It is clear that there is a close correlation for pH of mixed venous and mesenteric venous blood with a correlation coefficient of 0.95. The relationship for the pCO_2 and pO_2 of mixed venous blood and mesenteric venous blood was also close with a correlation coefficient of 0.74 and 0.75 respectively.

Predictability of Mesenteric Venous pH and pCO_2 Based Upon Femoral Venous and Arterial Values.

Upon visual examination of Figures 10 and 11 a consistent pattern is evident. Mesenteric venous points for pH and pCO_2 are approximately midway between arterial and femoral venous points. If the mesenteric venous points are equidistant, then the mesenteric venous values may be predicted from the mean of arterial and femoral venous values. An average was calculated from arterial and femoral venous values for pH and pCO_2 and the close correlation is shown in Table VI. The predicted

mean values obtained were then plotted as a function of the actual mesenteric venous parameter (Figure 15). Because of the close correlation between actual and predicted values for mesenteric venous pH and pCO_2 , regression analysis was performed and the results reported in Table VII. The results of regression analysis showed that mesenteric venous pH and pCO_2 may be predicted from the mean arterial and femoral venous pH and pCO_2 .

TABLE I

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

Dog	Weight (Kg)	Respiratory Rate/ Ventilatory Setting (per min)	Hematocrit	Plasma Protein (Concentration) (gm/dl)	Cardiac Output (L/min)	Temperature (Rectal) (Centigrade)	Estimated Blood Volume ml
1	17.7	12/---	0.51	6	2.33	35.0	1240
2	18.2	12/255	0.41	6.8	2.99	37.5	1270
3	20.5	12/300	0.48	7.0	3.56	39	1430
4	20.5	12/315	0.48	6.4	3.24	38	1400
5	17.7	12-15/250	0.38	5.2	3.77	38	1240
6	20	12.5/300	0.34	5.2	5.6	40	1400
7	19	12/300	0.42	5.2	2.01	39	1300
8	27.3	12/380	0.51	6.2	5.03	40	1900
9	23.6	15/350	0.65	7.2	2.52	37.5	1650
10	24.1	12/350	0.48	6.0	3.31	38	1680

 $\bar{X}$

S.D.

Range

0.45	6.1	3.27	38
.09	0.85	1.05	1.39
.34-.65	5.2-7.2	2.01-5.6	35-40

TABLE II

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

Dog	Respiratory Rate/ Ventilatory Setting (per min)	Hematocrit	Plasma Protein (Concentration) (gm/dl)	Cardiac Output (4 min)	Temperature (Rectal) (Centigrade)	Estimated Blood Volume ml
1	12/---	0.55	5.8	1.02	36.0	605
2	12/255	0.49	6.1	1.75	37.5	835
3	12/300	0.49	6.0	0.99	--	900
4	12/315	0.50	5.2	1.89	37	825
5	12-15/250	0.30	4.8	1.22	--	500
6	12/300	0.36	5.4	1.38	39	500
7	12/300	0.45	5.0	1.00	--	500
8	12/380	0.47	4.8	1.90	40	800
9	15/350	0.59	6.1	1.01	36.1	650
10	12/350	0.54	6.0	1.64	37.5	500
$\bar{X}$		0.47	5.5	1.17	37.2	
S.D.		0.95	.55	.23	1.1	
Range		.30-.59	4.8-6.1	.99-1.90	36-40	

Table III

Summary of Data for Dogs 1 - 10

Cardiac Output	pH				pCO ₂ mmHg				[HCO ₃ ⁻] mEq/L				pO ₂ mmHg					
	$\bar{x}$	%control	A	MV	FV	SV	A	MV	FV	SV	A	MV	FV	SV	A	MV	FV	SV
Dog 1	2.33	100	7.308	7.282	7.276	7.287	39.5	46.2	46.7	45.3	19.19	21.15	21.08	20.97	104.5	46.7	45.9	54.0
	1.73	74	7.271	7.257	7.240	7.254	42.9	54.4	54.8	50.4	19.14	23.51	22.77	21.63	97.0	44.5	37.0	48.3
	1.32	57	7.261	7.243	7.244	7.240	41.2	48.1	50.2	41.2	17.97	20.12	21.05	17.12	98.3	43.2	44.1	46.7
	1.02	44	7.232	7.204	7.153	7.210	40.4	52.9	64.1	53.9	16.48	20.23	21.80	20.90	92.5	36.1	28.6	40.7
	2.71	116	7.289	7.273	7.251	7.278	33.1	37.0	39.9	38.0	15.40	16.6	17.0	17.2	113.3	56.6	45.6	55.9
Dog 2	2.99	100	7.348	7.350	7.349	7.355	45.1	48.1	47.5	46.0	24.0	25.8	25.4	25.0	81.6	50.4	40.3	53.5
	1.70	57	7.346	7.321	7.321	7.325	47.0	48.7	44.8	47.8	22.3	24.3	22.4	24.2	83.5	47.7	38.7	44.4
	1.48	49	7.355	7.333	7.310	7.348	41.8	50.1	54.9	44.5	22.6	25.8	26.8	23.7	85.4	43.5	38.3	43.4
	1.32	44	7.378	7.296	7.251	7.326	35.4	51.1	66.2	46.6	20.2	24.2	28.2	23.6	95.6	35.3	34.3	34.3
	1.00	33	7.304	7.211	7.116	7.195	33.3	51.3	71.0	54.6	16.0	20.0	22.2	20.5	89.5	30.6	20.6	26.8
Dog 3	3.10	104	7.307	7.291	7.280	7.295	42.4	46.2	48.3	46.9	20.6	21.6	22.0	22.1	96.6	52.6	53.9	55.5
	3.56	100	7.338	7.333	7.332	7.345	48.0	46.0	47.3	47.7	25.0	23.5	24.3	25.3	66.6	53.7	57.0	55.0
	2.07	58	7.323	7.303	7.308	7.320	44.8	47.8	44.8	46.5	22.5	23.0	21.8	23.2	66.7	56.5	44.3	52.2
	1.61	45	7.362	7.320	7.301	7.342	41.3	48.5	49.8	44.4	22.7	24.2	23.8	23.3	79.1	53.3	40.0	49.5
	1.53	43	7.373	7.323	7.294	7.361	38.3	49.4	52.2	43.4	21.6	24.9	24.6	23.8	89.4	46.1	38.0	48.3
Dog 4	0.99	28	7.370	7.283	7.248	7.353	35.5	51.0	56.3	41.3	19.9	23.4	28.8	22.3	92.0	45.2	28.3	46.6
	4.68	131	7.378	7.354	7.362	7.363	40.4	44.0	41.9	43.6	23.1	23.8	23.1	24.1	90.1	64.4	56.2	57.8
	3.24	100	7.429	7.415	7.385	7.391	35.3	37.0	43.7	41.5	22.7	23.0	25.4	24.4	90.3	50.6	42.0	43.3
	1.65	51	7.413	7.390	7.370	7.361	36.3	39.3	44.2	44.3	22.5	23.1	24.8	24.3	83.4	40.8	30.2	36.9
	1.65	51	7.398	7.350	7.306	7.329	33.6	43.4	51.4	47.3	20.1	23.2	24.9	24.1	80.0	35.3	32.1	33.3
Dog 5	1.55	48	7.368	7.302	7.272	7.290	34.5	44.6	55.1	52.2	19.3	21.4	24.6	24.3	93.9	37.4	35.8	35.3
	1.25	39	7.369	7.285	7.243	7.290	33.7	48.7	58.3	52.0	18.9	22.4	24.4	24.2	88.2	31.2	31.7	33.6
	1.89	58	7.371	7.330	7.302	7.339	36.9	45.8	50.7	45.2	20.7	23.4	24.3	23.6	93.9	38.8	41.2	43.4
	2.80	86	7.399	7.385	7.382	7.383	38.5	39.6	42.9	43.1	23.1	23.0	24.8	24.9	91.2	43.7	52.6	47.3
	3.77	100	7.317	7.293	7.290	7.289	46.4	50.5	54.3	52.4	23.0	23.7	25.3	24.4	59.6	33.0	33.6	44.7
Dog 6	2.27	60	7.325	7.284	7.254	7.261	42.3	50.6	58.5	55.9	21.4	23.3	25.1	24.4	68.2	25.9	22.7	32.9
	1.85	49	7.327	7.268	7.212	7.267	41.1	50.3	63.1	53.8	20.9	22.3	24.6	25.8	79.3	22.1	19.2	32.9
	1.22	32	7.286	7.236	7.193	7.252	41.7	54.5	62.8	52.8	19.3	22.4	23.4	22.6	79.6	16.3	22.6	37.5
	2.00	53	7.327	7.293	7.249	7.314	40.4	47.3	55.7	51.3	20.5	22.2	23.6	25.3	83.2	10.7	34.4	48.5
	3.50	93	7.337	7.321	7.303	7.326	43.4	45.9	49.6	46.0	22.6	23.0	23.8	23.3	78.6	37.8	41.4	52.6
Dog 7	5.60	100	7.376	7.346	7.338	7.322	38.2	43.0	40.9	43.2	21.7	22.8	21.3	21.7	70.5	42.4	43.0	46.4
	3.39	61	7.337	7.309	7.286	7.278	39.9	43.4	43.2	47.0	20.7	21.1	20.0	21.3	66.3	35.7	33.3	26.8
	1.38	25	7.200	7.135	7.074	7.148	38.8	50.4	53.6	47.0	14.7	16.4	15.2	15.8	79.1	28.5	22.2	23.4
	5.12	91	7.186	7.181	7.205	7.164	42.3	44.8	42.6	46.7	15.5	16.3	16.3	16.3	74.7	50.3	42.3	50.5

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

Table III (Continued)

Cardiac Output		pH				pCO ₂ mmHg				[HCO ₃ ⁻] mEq/L				pO ₂ mmHg			
		A	MV	FV	SV	A	MV	FV	SV	A	MV	FV	SV	A	MV	FV	SV
2.53	100	7.397	7.365	7.372	7.365	35.3	41.7	39.0	39.8	21.1	23.1	22.0	22.0	96.9	46.2	41.6	49.3
1.55	61	7.395	7.350	7.334	7.349	35.4	43.3	44.1	42.3	21.0	23.2	22.8	22.6	93.3	39.9	40.4	47.5
1.0	40	7.334	7.264	7.228	7.283	36.2	48.9	51.1	49.9	18.7	21.5	20.7	22.9	94.3	31.5	27.7	37.5
2.50	99	7.335	7.313	7.298	7.317	37.5	42.6	43.1	43.1	19.4	20.9	20.5	21.4	87.3	48.6	47.5	56.4
5.03	100	7.344	7.329	7.333	7.320	36.1	37.3	38.3	39.7	19.1	19.1	19.7	19.8	89.1	62.5	65.9	63.7
2.57	51	7.358	7.307	7.276	7.325	35.8	42.5	48.6	42.2	19.5	20.6	21.9	21.1	93.1	44.7	38.1	48.2
1.90	38	7.353	7.308	7.253	7.297	37.7	46.1	53.7	48.4	20.3	22.4	23.0	22.9	92.5	38.5	33.1	42.6
2.72	54	7.393	7.369	7.356	7.377	35.5	39.1	39.0	39.1	21.0	21.9	21.2	22.3	101.3	53.0	49.5	55.6
2.01	100	7.373	7.354	7.333	7.356	29.9	32.4	36.1	34.7	16.9	17.5	18.6	18.8	91.9	51.9	48.2	48.4
7.78	89	7.327	7.306	7.284	7.308	35.3	40.0	47.8	42.6	17.9	19.4	22.0	20.7	79.4	46.3	29.3	39.5
1.32	66	7.308	7.274	7.219	7.279	34.5	42.9	57.5	47.3	16.8	19.3	22.8	21.5	80.5	41.3	22.9	34.5
1.01	50	7.272	7.217	7.144	7.228	35.4	50.6	64.8	51.9	15.8	19.9	21.6	21.0	83.5	33.2	25.3	32.6
1.87	93	7.305	7.295	7.234	7.298	35.7	38.8	51.8	41.5	17.2	18.3	21.2	19.7	88.4	44.8	37.5	46.4
3.43	100	7.447	7.427	7.436	7.418	33.3	37.3	36.3	37.8	22.3	23.8	23.7	23.7	90.4	44.0	37.8	45.9
2.16	63	7.408	7.373	7.363	7.375	36.1	42.8	45.5	42.4	22.1	24.2	25.1	24.0	89.5	39.6	31.4	45.8
1.64	48	7.387	7.331	7.353	7.342	35.5	47.5	44.5	46.1	20.7	24.3	24.0	24.2	87.1	26.8	36.2	40.6
3.60	105	7.398	7.385	7.381	7.382	38.2	42.9	41.2	44.4	22.8	24.9	23.7	25.6	91.8	52.6	49.1	54.5

Table IV
Mean Values and Standard Deviations for
Blood-Gas Parameters of Dogs 1-7, 9, 10

Site	% Control	Cardiac Output	pH	pCO ₂	pO ₂	[HCO ₃]
art	>70%	$\bar{x}$	7.35	39.0	84.4	21.2
			+0.06	5.6	14.2	2.6
		SD	-0.05			
MV	>70%	$\bar{x}$	7.34	43.2	46.3	22.4
			+0.06	6.4	5.6	2.3
		SD	-0.05			
FV	>70%	$\bar{x}$	7.33	44.9	41.4	22.8
			+0.06	6.4	7.4	2.2
		SD	-0.05			
SV*	>70%	$\bar{x}$	7.33	43.8	48.0	22.6
			+0.05	5.3	4.8	2.0
		SD	-0.05			
art	61-70%	$\bar{x}$	7.36	36.4	82.4	20.2
			+0.05	53.	4.8	2.0
		SD	-0.05			
MV	61-70%	$\bar{x}$	7.32	43.1	39.1	22.0
			+0.05	0.2	2.4	2.2
		SD	-0.04			
FV	61-70%	$\bar{x}$	7.30	47.6	32.0	22.6
			+0.07	6.6	7.2	2.0
		SD	-0.06			
SV	61-70%	$\bar{x}$	7.32	44.8	38.6	22.4
			+0.05	2.8	9.8	1.2
		SD	-0.05			
art	51-60%	$\bar{x}$	7.34	41.8	80.0	21.1
			+0.06	4.8	11.6	1.8
		SD	-0.05			
MV	51-60%	$\bar{x}$	7.31	46.9	41.6	22.8
			+0.05	4.1	10.4	1.4
		SD	-0.05			
FV	51-60%	$\bar{x}$	7.30	51.2	38.4	23.4
			+0.05	7.8	9.67	1.6
		SD	-0.04			
SV	51-60%	$\bar{x}$	7.30	47.8	41.0	22.8
			+0.05	4.8	7.8	2.8
		SD	-0.04			

Table IV (cont'd)

Site	Cardiac Output		pH	pCO ₂	pO ₂	[HCO ₃]
art	41-50%	$\bar{x}$	7.34	38.2	87.3	20.0
			+0.06	3.0	6.0	2.4
		SD	-0.05			
MV	41-50%	$\bar{x}$	7.29	49.4	37.0	23.0
			+0.05	2.3	9.6	2.1
		SD	-0.05			
FV	41-50%	$\bar{x}$	7.25	57.2	32.8	24.4
			+0.08	7.6	7.0	2.1
		SD	-0.07			
SV	41-50%	$\bar{x}$	7.30	48.5	39.7	23.4
			+0.06	4.3	6.4	1.6
		SD	-0.05			
art	<40%	$\bar{x}$	7.31	36.5	87.1	17.9
			+0.07	3.2	6.4	2.1
		SD	-0.06			
MV	<40%	$\bar{x}$	7.23	50.8	30.6	21.0
			+0.06	2.1	9.2	2.5
		SD	-0.06			
FV	<40%	$\bar{x}$	7.18	58.8	25.5	22.4
			+0.08	7.2	4.4	4.4
		SD	-0.07			
SV	<40%	$\bar{x}$	7.25	48.9	34.2	21.4
			+0.08	4.2	8.3	2.9
		SD	-0.07			
art	trans	$\bar{x}$	7.35	38.9	90.6	19.8
			+0.07	3.1	10.4	2.9
		SD	-0.06			
MV	trans	$\bar{x}$	7.31	43.2	47.3	21.3
			+0.06	3.3	9.5	2.9
		SD	-0.06			
FV	trans	$\bar{x}$	7.29	46.2	45.6	21.8
			+0.06	5.2	6.9	2.8
		SD	-0.06			
SV	trans	$\bar{x}$	7.31	44.5	51.7	22.1
			+0.07	3.4	4.7	3.2
			-0.06			

*SV = mesenteric venous

TABLE V

Regression Analysis MV-SV* Differences

	pH	pCO ₂	pO ₂
MV X	7.30	45.77	41.57
S.D.	0.06	4.96	9.89
SV X	7.31	46.12	43.85
S.D.	0.06	4.75	8.68
Intercept	0.07	13.67	16.36
Slope	0.95	0.71	0.66
S.E.E.	0.02	3.22**	5.77**
r	0.95	0.74	0.75

*SV - Mesenteric Venous

**Standard Error of Estimate measured in torr

N=47

TABLE VI

Actual and Predicted Values
for Individual Dogs 1-10 for
pH and pCO_2

Dog	% control cardiac output	Actual SV pH	Predicted SV pH	Actual SV pCO_2	Predicted SV pCO_2
#1	100%	7.29	7.29	45.3	43.1
	74	7.25	7.25	50.4	48.8
	57	7.24	7.25	41.2	45.7
	44	7.21	7.19	53.9	52.3
#2	100%	7.36	7.35	46.0	46.3
	57	7.32	7.33	47.8	45.9
	49	7.35	7.33	44.5	48.3
	44	7.33	7.31	46.6	50.8
	33	7.20	7.21	54.6	52.2
#3	100%	7.34	7.34	47.7	47.7
	58	7.32	7.32	46.5	44.8
	45	7.34	7.33	44.4	45.6
	43	7.36	7.33	43.4	45.2
	28	7.35	7.31	41.3	45.9
#4	100%	7.39	7.40	41.5	39.5
	51	7.36	7.39	44.3	40.2
	51	7.33	7.35	47.3	42.5
	48	7.29	7.32	52.2	44.8
	39	7.29	7.30	52.0	46.0
#5	100%	7.29	7.30	52.4	50.4
	60	7.26	7.28	55.9	50.4
	49	7.27	7.27	53.8	52.1
	32	7.25	7.24	52.8	52.3
#6	100%	7.32	7.36	43.2	39.6
	61	7.28	7.31	47.0	41.6
	25	7.15	7.14	47.0	46.2

Table VI (cont'd)

Dog	%control cardiac output	Actual SV pH	Predicted SV pH	Actual SV pCO ₂	Predicted SV pCO ₂
#7	100%	7.37	7.38	39.8	37.2
	61	7.35	7.36	42.3	39.8
	40	7.28	7.28	49.9	43.7
#8*	100%	7.32	7.34	39.7	37.2
	51	7.32	7.32	42.2	42.2
	38	7.30	7.30	48.4	45.7
#9	100%	7.36	7.35	34.7	33.0
	89	7.31	7.31	42.6	41.6
	66	7.28	7.26	47.3	46.0
	50	7.22	7.21	51.9	50.1
#10	100%	7.42	7.44	37.8	34.8
	63	7.38	7.42	42.4	40.8
	48	7.34	7.37	46.1	40.0

* Data from Dog # 8 excluded from statistical analysis due to improper placement of pulmonary catheter

TABLE VII

Regression Analysis Values for Actual
and Predicted SV pH and pCO₂

	pH	pCO ₂
Actual X	7.30	46.6
S.D.	0.06	5.02
Predicted X	7.31	44.9
S.D.	0.06	4.96
Intercept	0.35	7.17
Slope	1.04	0.81
S.E.E.	0.02	2.89
r	0.96	0.82

N = 36

Figure 10

Mean Arterial, Mixed Venous,

Mesenteric Venous and Femoral Venous pH

as a Function of Percent of Control Cardiac Output

○ Arterial

● Mixed Venous

◆ Mesenteric Venous

□ Femoral Venous

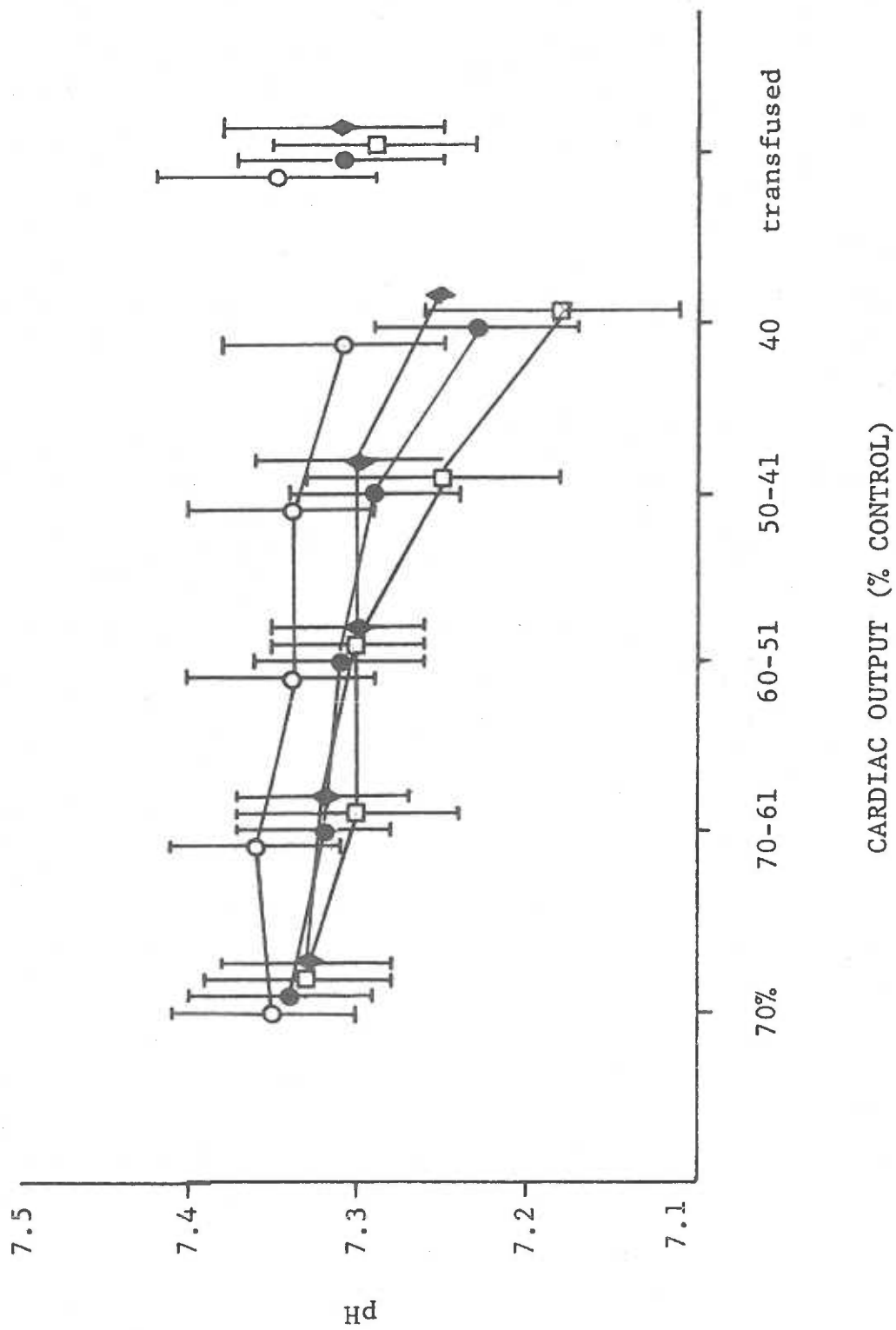


Figure 11

Mean Arterial, Mixed Venous,

Mesenteric Venous and Femoral Venous pCO_2

as a Function of Percent of Control Cardiac Output

○ Arterial

● Mixed Venous

◆ Mesenteric Venous

□ Femoral Venous

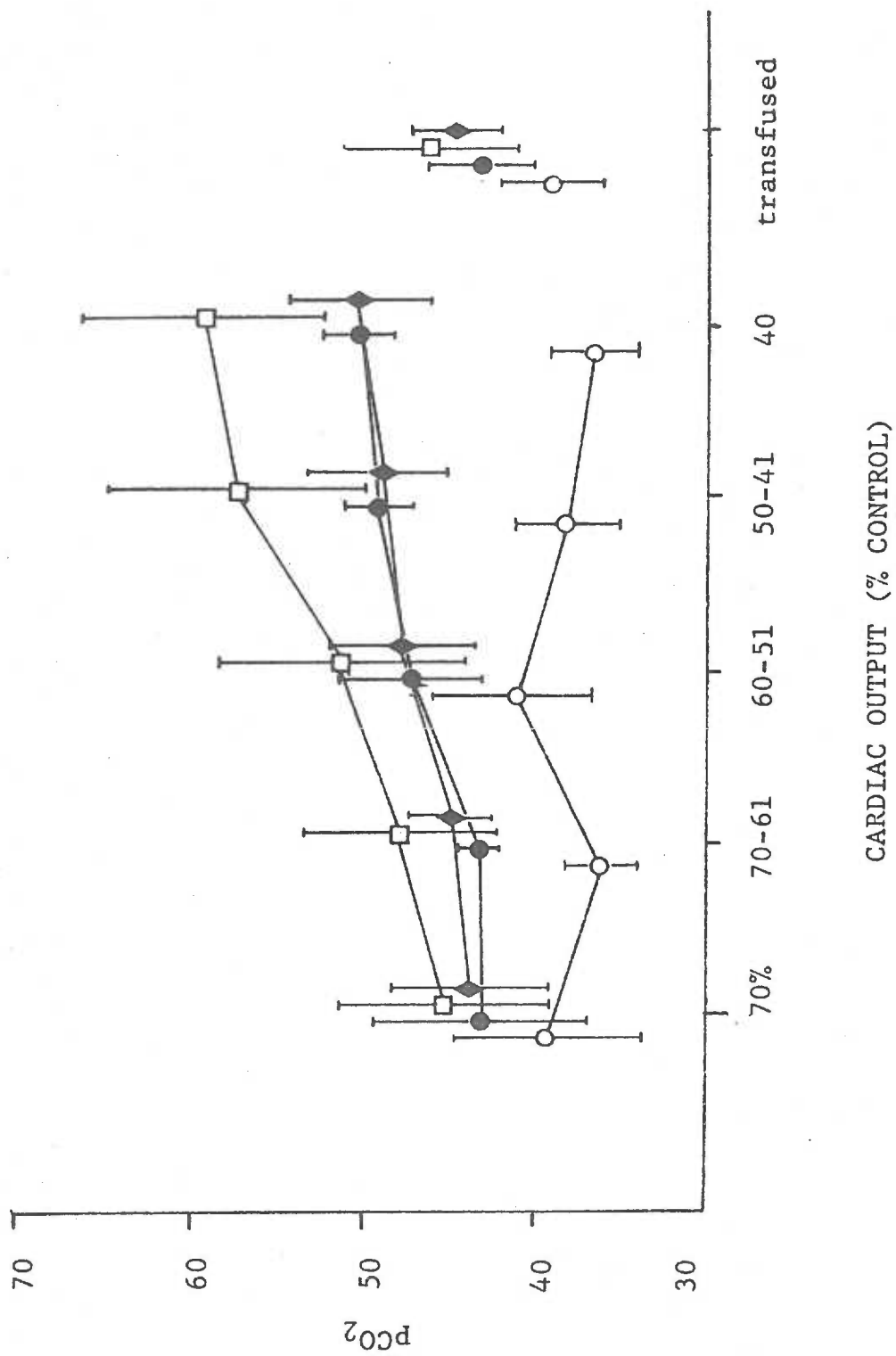


Figure 12

Mean Arterial, Mixed Venous,
Mesenteric Venous and Femoral Venous $[\text{HCO}_3^-]$
as a Function of Percent of Control Cardiac Output

- Arterial
- Mixed Venous
- ◆ Mesenteric Venous
- Femoral Venous

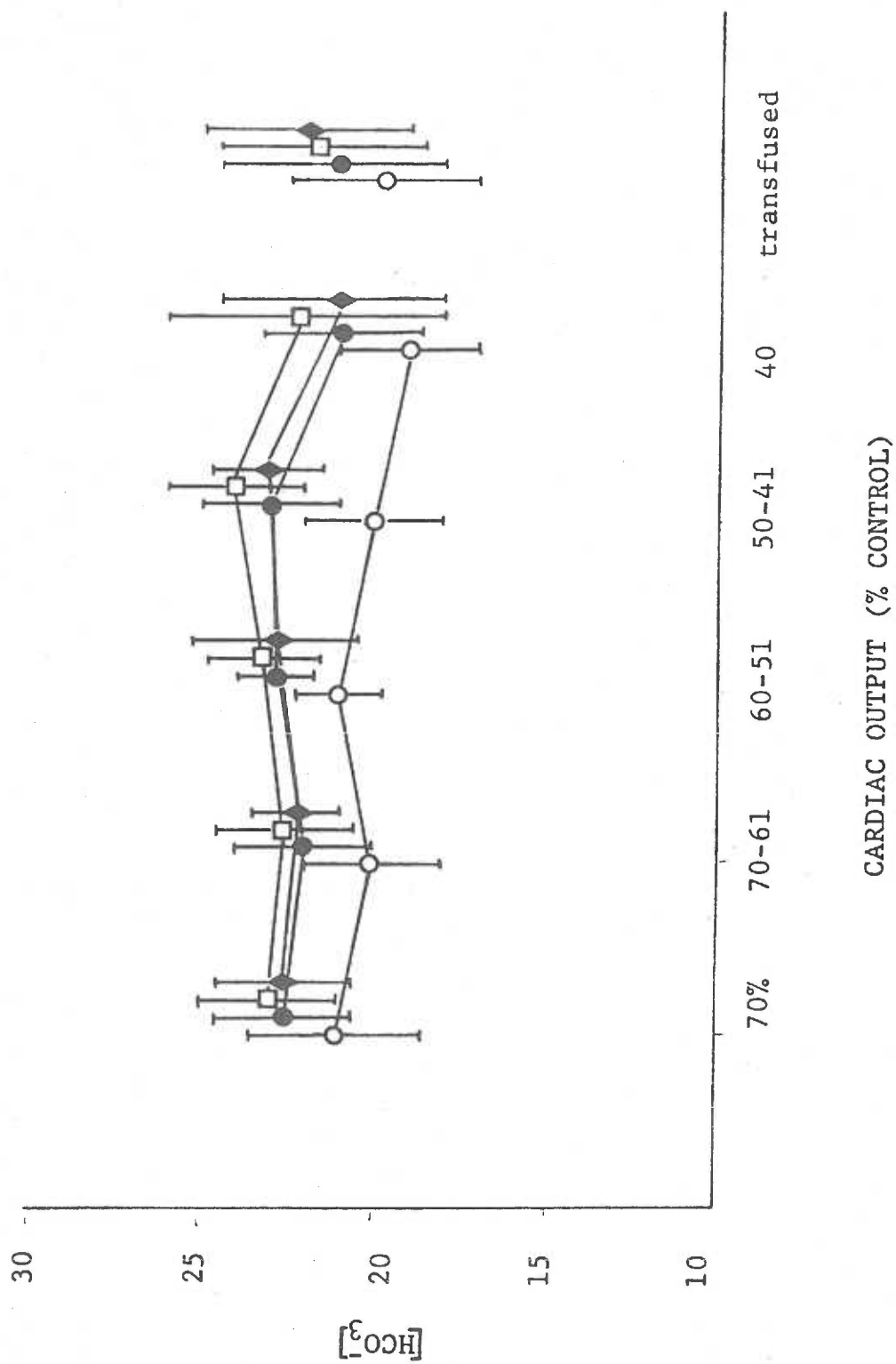


Figure 13

Mean Arterial, Mixed Venous,

Mesenteric Venous and Femoral Venous pO_2

as a Function of Percent of Control Cardiac Output

○ Arterial

● Mixed Venous

◆ Mesenteric Venous

□ Femoral Venous

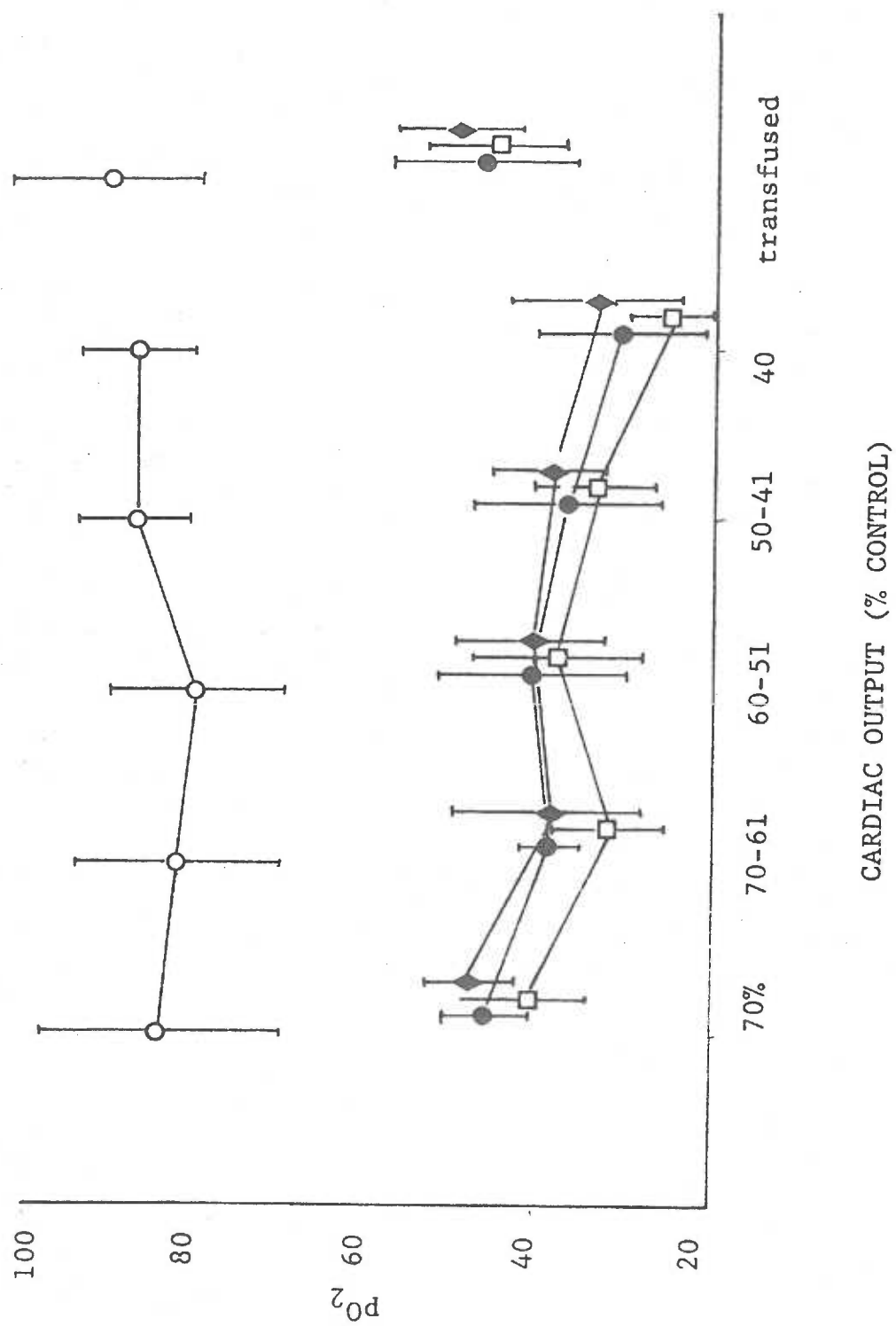


Figure 14

Arterial, Mixed Venous and Mesenteric Venous
Blood-Gas Parameters for Cardiac Outputs <89%
of Control Cardiac Output, Dogs 1-7, 9, 10

Plotted on a pH/ $[\text{HCO}_3^-]$ Diagram

○ Arterial

● Mixed Venous

◆ Mesenteric Venous

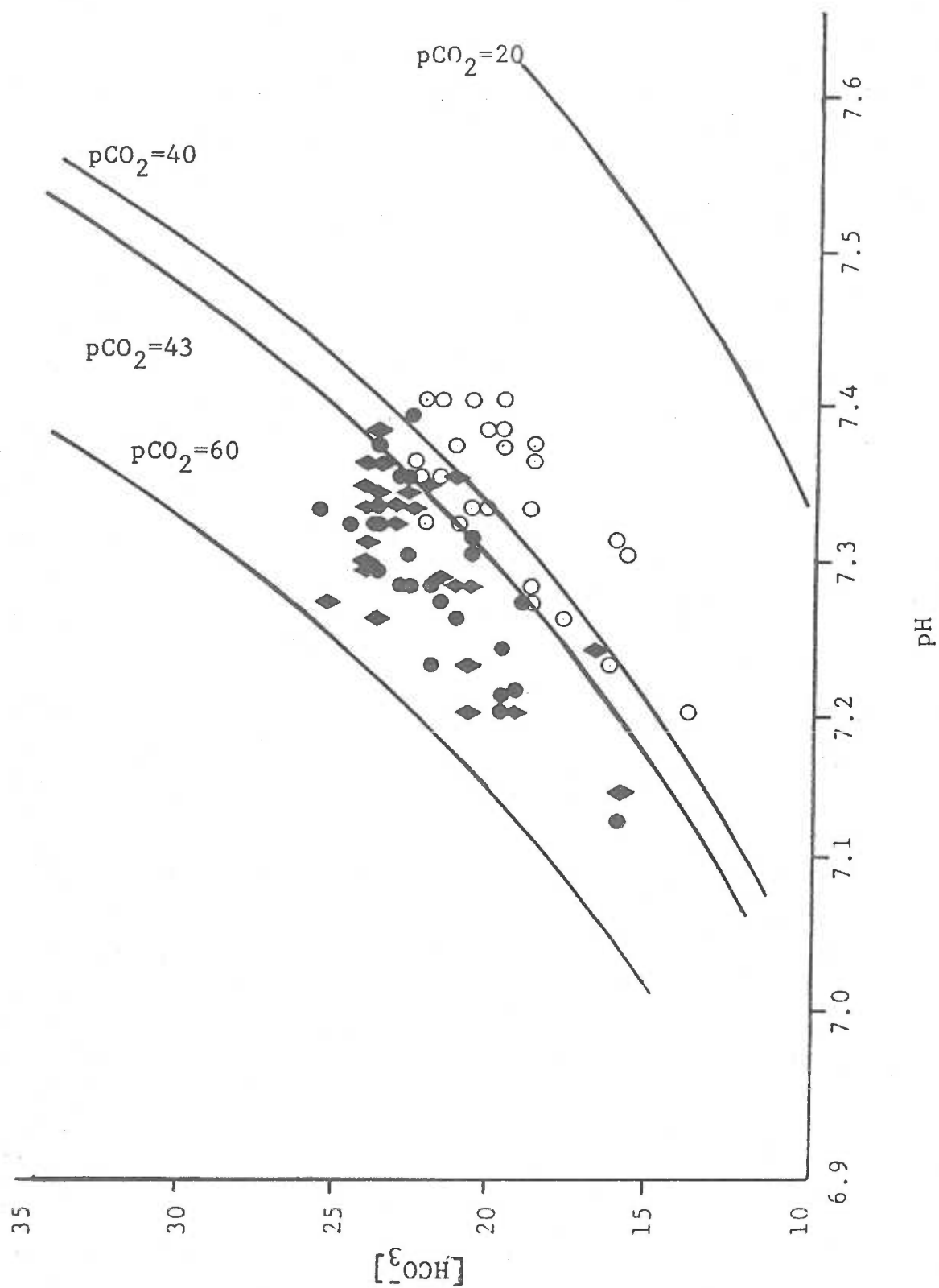
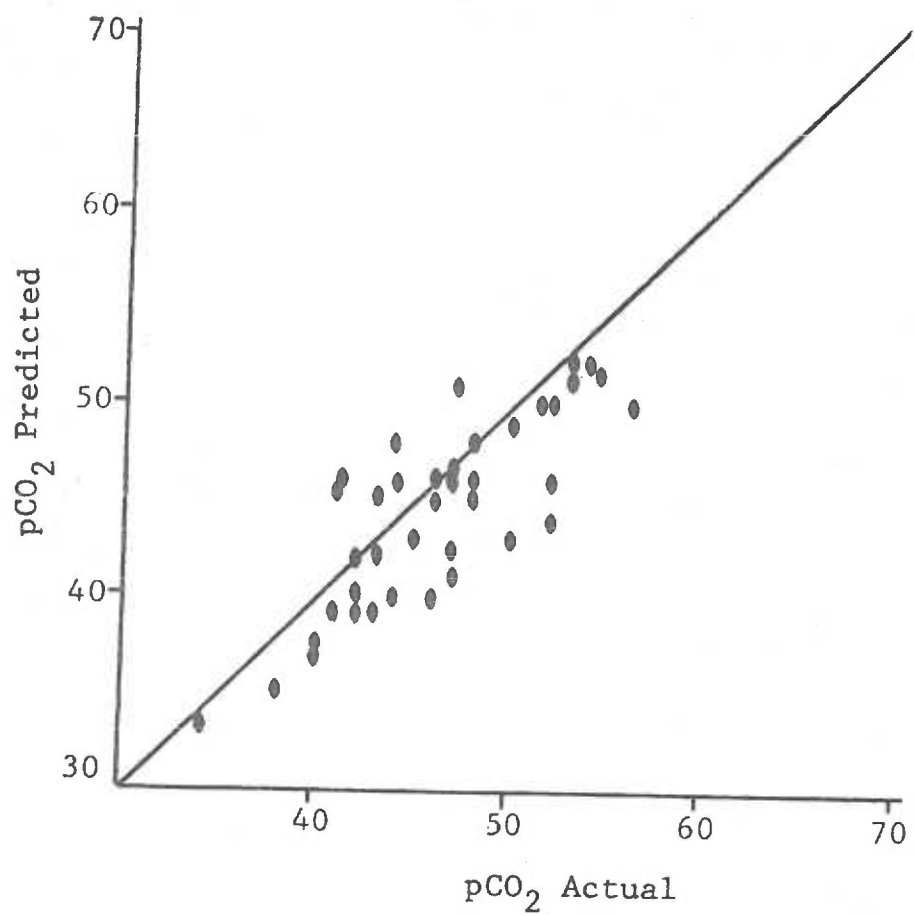
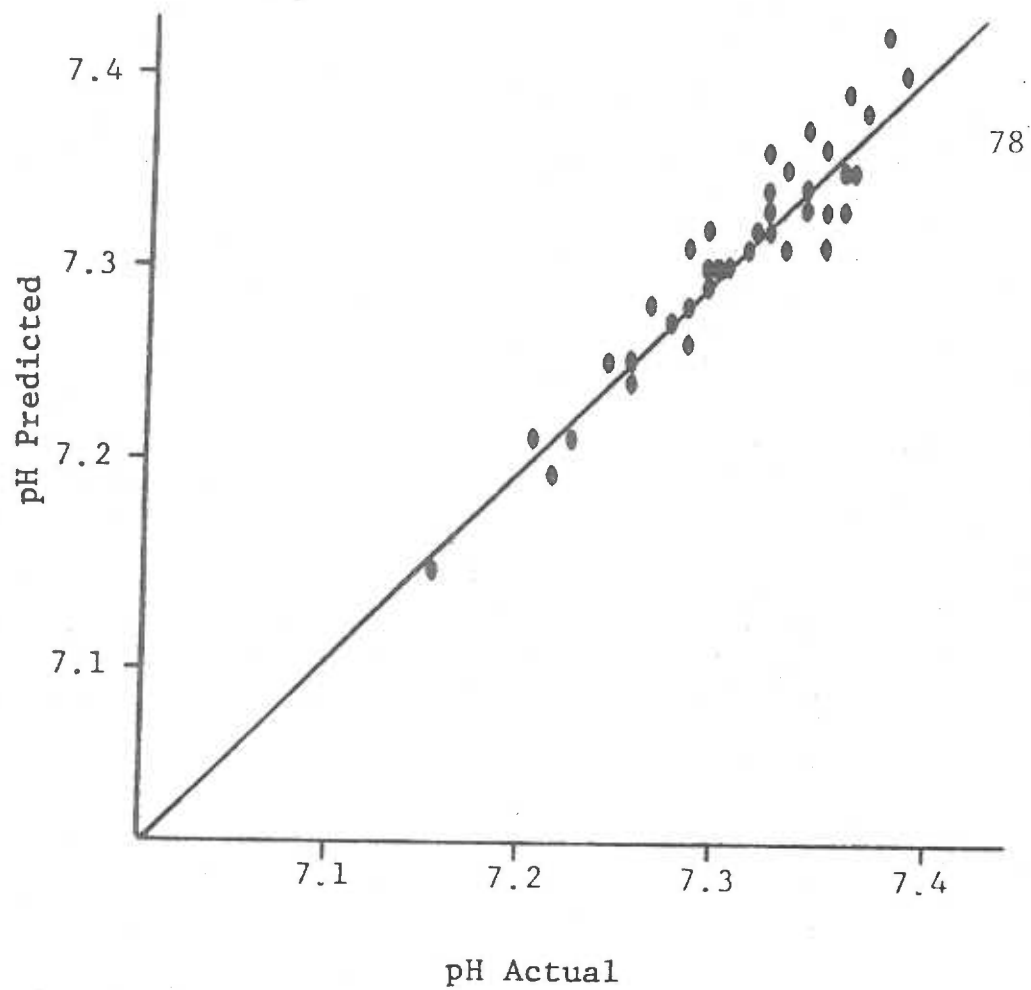


Figure 15
Identity Plots for
Actual and Predicted Values
for Dogs 1-7,9,10
for pH and pCO₂



Chapter IV

DISCUSSION

The discussion is organized under the following headings:

- 1) How does mesenteric venous blood-gas composition compare to mixed venous and arterial blood-gas composition when cardiac output is decreased?
- 2) Is the blood-gas composition of mesenteric venous blood predictable from femoral venous and arterial blood-gas values?
- 3) Clinical Implications

How Does Mesenteric Venous Blood-Gas Composition Compare to Mixed Venous and Arterial Blood-Gas Composition When Cardiac Output is Decreased?

In the theoretical framework and the review of the literature it was established that the blood-gas values obtained from mixed venous blood represent the true acid-base status and oxygenation of the tissues. From the model (Figure 4) it was suggested that the status of the mesenteric tissues would be better represented by the blood-gas composition of mixed venous blood.

In this study, arterial, mixed venous and mesenteric venous blood-gas compositions were compared after cardiac output was decreased. To clearly present the relationships

between arterial, mixed venous, and mesenteric venous blood-gas composition each blood-gas parameter is discussed separately.

pH

The mean initial pH for mixed venous and mesenteric venous blood was less than that for arterial blood (Figure 10). This result is consistent with prediction derived from the model (Figure 4). Cell metabolism continues to produce acids which diffuse into capillary blood which in turn flows into the veins causing a lower pH in venous blood compared to that of arterial blood.

After cardiac output was decreased the mean final value for pH decreased from control values in arterial, mixed venous and mesenteric venous blood. At the lowest values of cardiac output the decrease in the mean pH of both mixed venous and mesenteric venous blood was greater than the decrement in the mean pH of arterial blood (Table IV & Figure 10). The more precipitous decrease in the pH of mixed venous and mesenteric venous blood is due to tissue hypoxia and anaerobic metabolism which causes an increase in production of lactic acid. In addition, CO_2 accumulated in capillary and venous blood shifting the reaction in equation 3 to the right, increasing $[\text{H}^+]$. Arterial pH decreased due to those reasons stated above but was reduced less than the change in pH of venous blood due to an increase in the ventilation/perfusion ratio ($\dot{V}_A/\dot{Q}_C$), relative to the increase in mixed venous pCO_2 when cardiac output

was decreased. Ventilation remained the same whereas perfusion decreased causing reduced delivery of CO_2 to the lungs for excretion. The resultant decrease in arterial pCO_2 minimized the fall in pH (Equation 3).

There was a strong correlation between the pH values of mixed venous and mesenteric venous blood over the entire range of cardiac output tested ($r=0.95$, Table V). From those data it is concluded that the pH of mesenteric venous blood can be predicted from the pH of mixed venous blood.

pCO_2

The mean arterial pCO_2 decreased from a control value of 39 torr to a final mean value of 36.5 torr following hemorrhage. This can again be explained by an increase in the $\dot{V}_A/\dot{Q}_c$ ratio. As blood flow decreased from hemorrhage both acids and low blood pressure stimulated the animals to breathe. Even though the animals' respirations were controlled via mechanical ventilation a small decrease in arterial pCO_2 was evident. Part of this decrease was caused by reduced delivery of CO_2 to the lungs for excretion. With constant alveolar ventilation, reduced delivery of CO_2 will cause a corresponding decrease in arterial pCO_2 . In other words, the $\dot{V}_A/\dot{Q}_c$ ratio increased producing an apparent respiratory compensation.

The mean values for pCO_2 of mixed venous blood and mesenteric venous blood increased during hemorrhage (Table IV & Figure 11). This was due to accumulation of CO_2 in ISF and

reduced blood flow. The $p\text{CO}_2$ of MV blood was closely related with that of mesenteric venous blood ($r=0.74$, Table V). It can be concluded that the $p\text{CO}_2$ of mesenteric venous blood can be predicted from the $p\text{CO}_2$ of mixed venous blood.

$p\text{O}_2$

The mean arterial $p\text{O}_2$ increased from an initial value of 84.4 torr to a final value of 87.1 torr (90% saturation). The change in oxygen saturation is minimal at these values of $p\text{O}_2$ (Figure 16). This slight increase in $p\text{O}_2$ in response to hemorrhage can be accounted for by an increase in the V_A/Q_C ratio. If the animals had not been anesthetized and respirations controlled, the increase in $p\text{O}_2$ after hemorrhage due to compensatory hyperventilation might have even been greater.

The mean $p\text{O}_2$ of mixed venous blood decreased from an initial value of 46.3 torr (slightly greater than 50% saturation). Acute tissue hypoxia must have been present when cardiac output was reduced as reflected by the reduced $p\text{O}_2$ of mixed venous blood (Tables III & IV). Arterial blood does not reflect this tissue hypoxia and, in fact, increased while tissue $p\text{O}_2$ decreased. This finding is consistent with that reported by Tung, et al. (1976) and Murphy (1982).

The mean $p\text{O}_2$ of mesenteric venous blood decreased from an initial value of 48.0 torr (approximately 75% saturation) to a final value of 34.2 (approximately 60% saturation). At $p\text{O}_2$ values in the range of 20 to 60 torr, the oxyhemoglobin

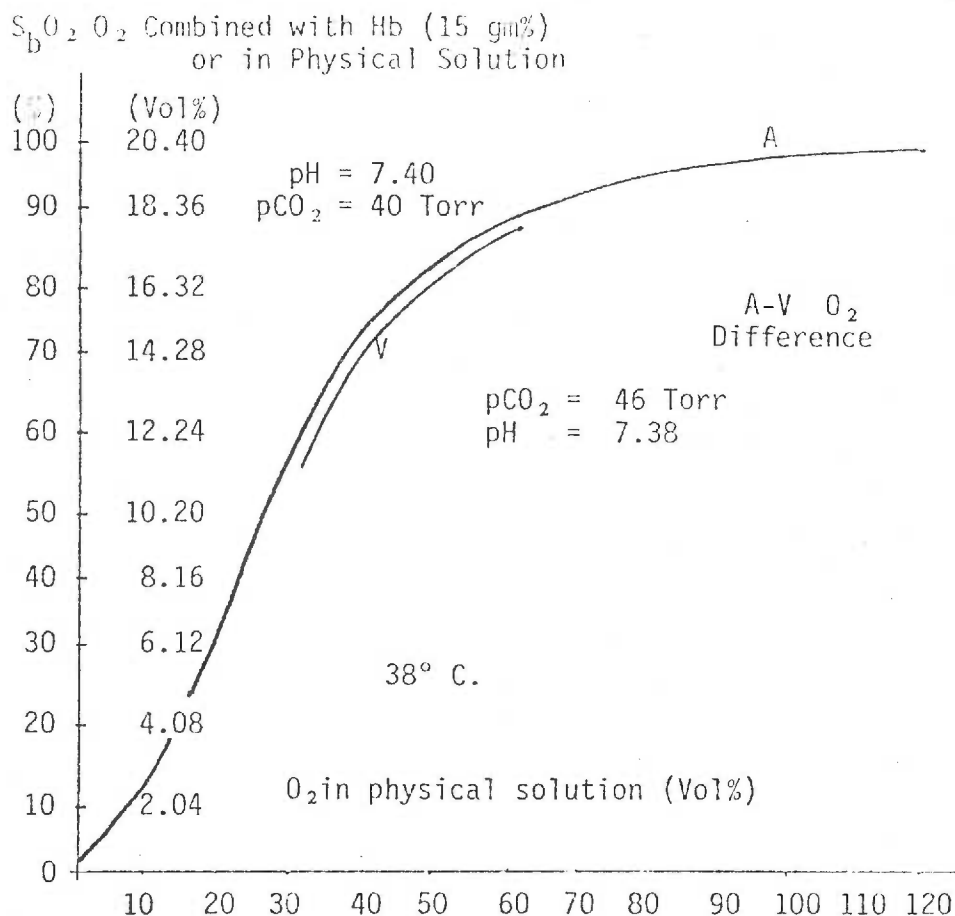


Figure 16

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

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

curve has a steep slope and is reasonably linear (figure 16). Because of this steep slope, at low pO_2 values, even a small decrement in pO_2 has a pronounced effect on oxygen saturation. Mesenteric venous pO_2 reflected a state of acute tissue hypoxia even though arterial pO_2 was within normal limits.

The mean pO_2 of mesenteric venous blood was slightly greater than the mean pO_2 of mixed venous blood when cardiac output was less than 50% of control (Figure 13). As is apparent from the theoretical framework, when the oxygen availability to demand ratio decreases, increased sympathetic activity causes vasoconstriction of the mesenteric vascular bed, enhancing interstitial hypoxia. The metabolic feedback system opposes neurogenic vasoconstriction via an autoregulatory escape mechanism, which tends to increase flow and oxygenation (Figure 3). It is hypothesized that the autoregulatory escape mechanism became prominent at values of cardiac output less than 50% of control when mesenteric pO_2 values slightly exceeded those for mixed venous blood. In addition, it may be hypothesized that hypoxia at the tip of the intestinal villi was enhanced when cardiac outputs were less than 50% of control due to the countercurrent exchange system (Figure 1 & 2).

Nevertheless, over the entire range of cardiac outputs, the pO_2 of mixed venous blood was reasonably closely related with that of mesenteric venous blood ($r=0.75$, S.E.E.=5.8 torr, Table V). It may be concluded that the pO_2 of mesenteric venous blood can be predicted from the pO_2 of mixed venous blood.

HCO_3^-

The mean values for $[\text{HCO}_3^-]$ of mixed venous and mesenteric venous blood were greater than the mean values for $[\text{HCO}_3^-]$ in arterial blood (Table IV and Figure 12). Final mean values for mixed venous and mesenteric venous blood were approximately the same (Table IV and Figure 12). The low arterial $[\text{HCO}_3^-]$ may be explained from the analysis of equation 3. As $[\text{CO}_2]$ decreases the reaction shifts to the left, decreasing the HCO_3^- concentration in the blood. In venous circulations however, a decrease in cardiac output causes an accumulation of CO_2 which shifts the equation to the right, increasing the $[\text{HCO}_3^-]$. The mean $[\text{HCO}_3^-]$ of mesenteric venous blood was slightly higher than that of mixed venous blood in all ranges except one (51-60% of control cardiac output). It is possible that the generation of HCO_3^- by the parietal cells of gastric mucosa contributes to the slightly higher $[\text{HCO}_3^-]$ in mesenteric venous blood over that found in mixed venous blood.

Over a range of decreasing cardiac outputs, the $[\text{HCO}_3^-]$ of mixed venous blood was closely related to that of mesenteric venous blood (Table III & IV). It may be concluded that the $[\text{HCO}_3^-]$ of mesenteric venous blood can be predicted from the $[\text{HCO}_3^-]$ of mixed venous blood.

pH/ $[\text{HCO}_3^-]$ Relationship

The results of plotting mesenteric venous data on the

pH/[HCO₃⁻] diagram also shows a pattern predicted by the theoretical framework. Almost all of the mesenteric venous points plotted in Figure 14 fall within the category of a combined respiratory and metabolic acidosis. Approximately 88% of the mixed venous points are in the same category (Figure 14).

Arterial points fall in different acid-base categories with only 11 (44%) in the range of a combined metabolic and respiratory acidosis (Figure 14). Arterial blood reflects pulmonary gas exchange and the acid-base status of pulmonary tissues while venous blood represents systemic tissue acid-base status. Arterial blood-gas composition provides an erroneous picture of the acid-base status of the mesenteric tissues. Mixed venous blood, however, correctly reflects the profound tissue hypoxia and combined acidosis exhibited in the mesenteric tissues during hemorrhagic shock.

It is apparent from the raw data (Table III) that the blood-gas values of mixed venous blood reflect those of mesenteric venous blood even at values of cardiac output of only 25% of control. The close correlation in the blood-gas composition of mixed venous and mesenteric venous blood when cardiac output was reduced is clearly shown in Figures 10-13. Therefore it is concluded that the blood-gas composition of mixed venous blood accurately reflects the blood-gas composition of mesenteric venous blood.

Is the Blood-Gas Composition of Mesenteric Venous Blood Predictable from Femoral Venous and Arterial Blood-Gas Values?

Mesenteric venous data points for pH and $p\text{CO}_2$ are approximately midway between arterial and femoral venous data points for the same blood-gas parameters (Figures 10 & 11). Therefore an average was calculated from arterial and femoral venous pH and $p\text{CO}_2$ values (Table VI). The predicted mean values obtained for pH and $p\text{CO}_2$ were then plotted as a function of the actual mesenteric venous parameters (Figure 15). Regression analysis of these data showed a strong correlation between predicted and actual values (Table VII). Actual mesenteric venous pH and $p\text{CO}_2$ values were found to be predicted from the average of simultaneously drawn samples of femoral venous and arterial blood (Table VI & Figure 15).

The $[\text{HCO}_3^-]$ of mesenteric venous blood also fell between arterial and femoral venous data points for HCO_3^- (Figure 12). It is important to note that $[\text{HCO}_3^-]$ was calculated according to the Henderson-Haselbalch equation from values of pH and $p\text{CO}_2$. Since mesenteric venous pH and $p\text{CO}_2$ can be predicted from femoral venous and arterial values a mesenteric venous $[\text{HCO}_3^-]$ can also be calculated from predicted values.

Both mesenteric venous and femoral venous values for $p\text{O}_2$ decreased in response to hemorrhage (Figure 13). Changes in femoral venous $p\text{O}_2$ values can, therefore be monitored as an

indicator of mesenteric venous pO_2 .

Femoral venous pO_2 was consistently less than the pO_2 of mesenteric venous or mixed venous blood. Because of shunting produced by sympathetic induced vasoconstriction and the countercurrent exchange system in the villi, it is likely that the pO_2 of femoral venous blood is closer to the actual mesenteric tissue pO_2 that is the pO_2 of mesenteric venous blood. As a result, femoral venous pO_2 may prove to be a more reliable indicator of mesenteric tissue oxygenation than even the pO_2 of mixed venous blood.

In summary, the following conclusions can be made:

- 1) The blood-gas composition of mixed venous blood accurately assesses the status of mesenteric venous blood when cardiac output is reduced.
- 2) Femoral venous blood-gas composition can be used as a predictive tool in assessing mesenteric tissue status when mixed venous blood is not available.

Clinical Implications

It has been established that mixed venous blood is a better indicator of the acid-bas status and oxygenation of systemic tissues than is arterial blood. The results of this study showed that mixed venous blood may be used to assess mesenteric tissue status when cardiac output is decreased. Considerations for nursing practice regarding this conclusion are addressed below:

- 1) Nurses who use acid-base assessment need to be

knowledgable about the various methods for assessing acid-base status. This knowledge must include the purpose for blood-gas assessment and the type of blood that would best assess a particular condition.

2) If the patient already has a pulmonary artery catheter in place, the nurse may advocate the use of mixed venous blood in assessing mesenteric tissue status. Nurses need to be knowledgable about the use of mixed venous blood and its advantages. If pulmonary function is to be assessed, it must be remembered that arterial blood must be used for blood-gas analysis.

3) Nurses need to be properly trained in the correct technique for obtaining arterial, mixed venous and femoral venous blood. Protocols need to be established if there are no current standards.

4) Continued nursing research is necessary regarding mesenteric tissue status under a variety of conditions.

5) Nurses need to use their knowledge to educate other members of the health care team to make proper judgements regarding source of blood, interpretation of acid-base balance and correct techniques.

Limitations of the Study

The major limitation of this study is that it is with a small number of animals (9). It should be noted that I found no other documented research regarding the use of mixed venous blood to assess the status of mesenteric tissues during shock

with which to compare and contrast results. The rationale and predictions are logical however, and the results support current theory regarding mesenteric tissue status in shock.

Chapter V

SUMMARY, CONCLUSIONS, RECOMMENDATIONS

Summary and Conclusions

Reduced blood flow in the mesenteric circulation due to low cardiac output threatens the integrity of the intestinal tissues. The small intestine is particularly vulnerable to mucosal lesions in low flow states due to a countercurrent exchange system in the villi. There is accumulating evidence that intestinal mucosal lesions of the mesenteric vascular bed may be a primary source of factors leading to circulatory collapse during prolonged shock. It is difficult to know from current assessment techniques when a low cardiac output is compromising intestinal oxygenation and acid-base status. Mixed venous blood is proposed to be a source that can be used to predict mesenteric venous pH, $p\text{CO}_2$, and $[\text{HCO}_3^-]$. Mixed venous $p\text{O}_2$ can also be used to accurately monitor mesenteric tissue hypoxia.

Ten mongrel dogs were used in this study. The dogs were anesthetized, intubated and mechanically ventilated. Cardiac output was progressively decreased by periodic hemorrhage. Arterial, mixed venous, mesenteric venous and femoral venous blood-gas samples were obtained simultaneously with each cardiac

output determination.

Results showed that mesenteric venous blood-gas composition is accurately reflected by mixed venous blood-gas analysis. Mesenteric venous pH, $p\text{CO}_2$ and $[\text{HCO}_3^-]$ can be also accurately predicted from femoral venous and arterial blood-gas values. Changes in femoral venous $p\text{O}_2$ values can be monitored as an indicator of mesenteric tissue hypoxia.

Mesenteric venous and mixed venous blood-gas parameters fall within the same category of combined metabolic and respiratory acidosis with decreased cardiac output. Arterial blood showed different acid-base disturbances from those obtained for venous blood during hemorrhage. Mixed venous blood reflected the acute mesenteric tissue hypoxia whereas arterial $p\text{O}_2$ increased after hemorrhage.

Based on these results it can be concluded that mixed venous blood accurately predicts mesenteric venous pH, $p\text{CO}_2$, $[\text{HCO}_3^-]$ and $p\text{O}_2$ when cardiac output is decreased. Therefore, mixed venous blood-gas analysis can be used as a better assessment tool for determining mesenteric tissue perfusion than blood-gas analysis of arterial blood.

Recommendations for Furthur Study

Because the research was based on an animal model in a laboratory situation and the findings regarding mixed venous blood and mesenteric venous blood were highly positive, further recommendations are as follows:

- 1) Continued laboratory research comparing mixed venous blood and mesenteric venous blood-gas compositions during states of decreased cardiac output due to other shock states, e.g., cardiogenic, septic, etc.
- 2) Both laboratory and clinical research on changes in mesenteric venous blood-gas composition in states of severe and irreversible shock. Results from these kinds of studies may lead to a more reliable indicator of impending irreversibility during shock.

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AN ABSTRACT OF THE THESIS OF
SUSAN VAUGHN

For the MASTER OF NURSING

Title: THE USE OF MIXED VENOUS BLOOD IN ASSESSING MESENTERIC
TISSUE STATUS DURING CHANGES IN CARDIAC OUTPUT

Approved: 

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

The integrity of the intestinal tissues may be severely compromised when blood flow is reduced in the mesenteric circulation due to low cardiac output. It is difficult to know however, from current assessment techniques, when a low cardiac output is compromising mesenteric tissue perfusion. Mixed venous blood has been proposed to have a composition that accurately reflects the acid-base status and oxygenation of mesenteric tissues when cardiac output is decreased. The following questions were asked in this study:

- 1) How does mesenteric venous blood-gas composition compare to mixed venous and arterial blood-gas composition during decreased cardiac outputs?
- 2) Can mixed venous blood-gas composition be used to predict mesenteric tissue status when cardiac output is reduced below 40% of control values?

Ten mongrel dogs were used in this study. The dogs

were anesthetized, the trachea intubated and mechanically ventilated. Cardiac output was reduced by periodic hemorrhage and determined via the thermodilution technique. Arterial, mixed venous, mesenteric venous and femoral venous blood-gas samples were obtained simultaneously with each decrement of cardiac output. The pH, $p\text{CO}_2$ and $p\text{O}_2$ were measured and $[\text{HCO}_3^-]$ was calculated for each sample from the Henderson-Hasselbalch equation.

Results showed that mixed venous blood-gas composition accurately reflected mesenteric venous blood-gas composition. Mesenteric venous blood-gas parameters also fell within the same category of acid-bas disturbance as mixed venous blood during hemorrhage. Arterial blood-gas parameters showed various patterns of acid-bas disturbances during hemorrhage. In addition, arterial blood-gas analysis erroneously reflected adequate perfusion and oxygenation.

From the results it can be concluded that mixed venous blood accurately predicts mesenteric venous pH, $p\text{CO}_2$, $[\text{HCO}_3^-]$ and $p\text{O}_2$ when cardiac output is decreased. Therefore, mixed venous blood-gas composition provides a more accurate assessment of mesenteric tissue perfusion than that of arterial blood especially when cardiac output is decreased.