

# Blood Flow Requirements During Cardiopulmonary Bypass in Children with Congenital Heart Disease

Theodore H. Stanley, M.D.\*

\*Associate Professor of Anesthesiology and Assistant Research Professor of Surgery

From the Department of Anesthesiology and Division of Artificial Organs, University of Utah College of Medicine, 50 North Medical Drive, Salt Lake City, Utah 84132

For the last five years work in our laboratories has been directed towards finding simply measured metabolic parameters of the adequacy perfusion during cardiopulmonary bypass.<sup>1-4</sup> Recent experiments have demonstrated that mixed venous oxygen tension ( $P_{V}O_2$ ) is an exquisitely sensitive index of the adequacy of tissue blood flow during bypass and that patients having  $P_{V}O_2$  maintained within a normal range (37-42 torr) during this period experience less metabolic acidosis, require less sodium bicarbonate and excrete greater volumes of urine than patients perfused via a fixed bypass flow rate.<sup>3-4</sup> These findings have resulted in the routine monitoring of  $P_{V}O_2$  and adjustments of pump flow rates to maintain this index within physiological normal limits in all patients undergoing cardiopulmonary bypass in our operating rooms. In the course of monitoring a number of children with cyanotic and noncyanotic congenital heart disease undergoing open-heart operations it was noticed that the former appeared to require higher bypass flow rates than the latter to maintain  $P_{V}O_2$  between 37-42 torr and avoid anaerobic metabolism. This study was undertaken to determine and compare bypass blood flow requirements and also oxygen uptake in a group of 40 children with atrial septal defects (ASD) or tetralogy of Fallot (TF).

## METHODS

All of the children were between 6 and 11 years of age and scheduled to have complete correction of a secundume type ASD or TF lesion. Each patient was randomly assigned preoperatively to receive halothane or morphine anesthesia. There were thus four groups of patients. Groups ASD I and TF I were given morphine and Groups ASD II and TF II halothane. Seven of the 15 TF patients had previous subclavian to pulmonary artery anastomosis, the remainder had never been operated on before. None of the 25 patients undergoing ASD repair had had previous cardiac operations.

Premedication for each patient included pentobarbital (1 mg/kg), morphine (1 mg/10 kg) and atropine (0.05 mg/10 kg) and was given 90 minutes prior to the operation. Before anesthesia was begun, two intravenous lines were started in the upper extremities, a central venous pressure catheter was placed in the internal jugular vein or antecubital fossa and threaded to the right atrium and a radial artery catheter was inserted. A catheter was also inserted into the urinary bladder and standard electrocardiograph leads applied to the extremities. Systolic, diastolic and mean arterial blood pressures were recorded every five minutes during induction and the entire operative procedure.

All patients received oxygen to breathe while morphine sulfate was given intravenously at a rate of 5-15 mg/min or halothane (0.5-1.5%) was slowly added to the inspired mixture. Respirations were first assisted and then controlled in order to keep arterial PCO<sub>2</sub> between 34-40 torr. Arterial blood samples for blood gas analysis were obtained every 15 minutes. When the patient became unresponsive succinylcholine (1.5 mg/kg) was given intravenously and the trachea intubated. Controlled ventilation was continued. When succinylcholine paralysis disappeared, the patient was given d-tubocurarine (0.5-0.75 mg/kg) over a period of 20 minutes and the operation started. Paralysis was maintained with 0.1 mg/kg doses of curare every 20 minutes. If additional anesthesia was considered necessary during the surgical procedure, patients in the morphine groups received 2-5 mg supplements of morphine and those in the halothane groups a higher concentration of halothane. During cardiopulmonary bypass 0.05% halothane was passed through the oxygenator in patients receiving halothane while those getting morphine received no other medication.

Ringer's lactate solution in 5% dextrose in water was administered at a rate of 10-15 ml/kg/hr during induction of anesthesia and 1-2 ml/kg/hr during the operative procedure. Whole blood was the only colloid routinely given intraoperatively and during the first two postoperative hours. During bypass blood was added to the oxygenator as required to maintain a blood flow of at least 50 ml/kg/min. After bypass blood was given to maintain preoperative central venous or intraoperative left atrial pressures. Urine output was measured hourly during the pre- and post-bypass periods and every half hour during bypass.

The extracorporeal system (Bentley\* oxygenator, Sarns\*\* roller pump) was primed with 18-24 ml/kg of fresh heparinized whole blood and 30-40 ml/kg of Ringer's lactate solution. Mixed venous blood samples were obtained from the common venous return line at the oxygenator every 5 minutes and analyzed on a Instrumentation Laboratories# acid-base analyzer for PO<sub>2</sub>, PCO<sub>2</sub> and pH. Blood samples were also analyzed for oxygenation saturation, oxygen content and hemoglobin. Bypass flows were regulated in order to keep mixed venous oxygen tension between 37-42 torr. Flows were therefore increased when P<sub>V</sub>O<sub>2</sub> was < 37 torr and decreased when P<sub>V</sub>O<sub>2</sub> was > 42 torr. Mean arterial blood pressure and extracorporeal flow rate were recorded every 5 minutes during bypass.

Arterial oxygen tensions were maintained between 130-170 torr during cardiopulmonary bypass via regulation of the flow rate of oxygen into the oxygenator. Oxygen uptake (VO<sub>2</sub>) during this period was determined from the Fick equation given below, using bypass flow rates as measured on the calibrated roller pump and calculated arterial and mixed venous oxygen contents.

$$VO_2 = (\text{bypass flow rate}) \times (\text{arterial oxygen content} - \text{mixed venous oxygen content})$$

Oxygen saturations were determined on an American Optical Company oximeter and bicarbonate and base deficits calculated using standard formulas. Base deficits greater than 4 mEq/L were half corrected with sodium bicarbonate every 10 minutes. Arterial and mixed venous oxygen contents were calculated on the basis of the hemoglobin-oxygen capacity studies of Theye<sup>s</sup> and measurements of PO<sub>2</sub>, and PCO<sub>2</sub>, oxygen saturation and the amount of physically dissolved oxygen as deter-

\*Bentley Laboratories, Inc., Irvine, California

\*\*Sarns Incorporated, Ann Arbor, Michigan

#Instrumentation Laboratories, Inc. Lexington, Massachusetts

mined by multiplying the measured  $PO_2$  by the constant 0.003. Serum hemoglobin was obtained from a Fisher Hemophotometer.

Intraoperative esophageal temperature was monitored with a Yellow Springs temperature probe. Patients were cooled to  $32^\circ$  during bypass and rewarmed to  $37^\circ$  C at its conclusion. Temperature corrections for blood gas analysis obtained during periods of hypothermia were made using standard normograms. At the conclusion of bypass, calcium chloride (100-600 mg) was routinely given. No other inotropic agents were needed either before or after bypass in any patient.

## RESULTS

Eight of the 15 children with TF received morphine (group TF I) and 7 were given halothane (group TF II). Ten patients with ASD received morphine (group ASD I) and 15 halothane (group ASD II). The mean preoperative age of all four groups was similar, Table 1, however, both ASD groups were significantly ( $P < 0.05$ ) heavier than either of the two groups of TF patients. Patients in group TF I received an average of 76 mg ( $2.8 \pm 0.4$  mg/kg) of morphine and those in group ASD I, 129 mg ( $3.4 \pm 0.5$  mg/kg).

Preoperative serum hemoglobins, the length of the operative procedures and intraoperative urine output were similar in groups ASD I and ASD II and TF I and TF II, Tables I and II. TF patients had significantly higher preoperative serum hemoglobins ( $P < 0.001$ ), longer operative procedures ( $P < 0.05$ ) and lower operative urine flow rates ( $P < 0.05$ ) than ASD patients. All groups had similar pre-and-post bypass arterial blood pressures except ASD I which had slightly but significantly higher mean arterial blood pressures ( $P < 0.05$ ) than the other three groups before bypass, Table II.

Bypass time, mean arterial blood pressure, urine flow rate, blood flow rate requirements and  $VO_2$  are given in Table III. ASD groups had much shorter ( $P < 0.001$ ) bypass times than TF groups. All groups except ASD I had similar mean arterial blood pressures and urine flow rates during bypass. ASD I bypass arterial blood pressures and urine flow rates were significantly ( $P < 0.025$ ) higher than those of patients in the other three groups. Bypass blood flow requirements and  $VO_2$  were markedly ( $P < 0.001$ ) higher in both TF groups than either of the ASD groups. Anesthesia had no significant effect on bypass blood flow requirements in either the TF or ASD patients. Bypass flow rates of all 15 TF children averaged 85.3 ml/kg/min versus 64.9 ml/kg/min for the 25 patients with ASD. The  $VO_2$  of TF and ASD children during bypass averaged 2.9 and 2.2 ml/kg/min respectively. Although ASD I and TF I groups had slightly higher  $VO_2$  than their halothane counterparts, this difference was not significant.

## DISCUSSION

The results of this study indicate that in order to insure aerobic metabolism during bypass, children with TF require cardiopulmonary bypass flow rates which average 31% higher than children of a similar age with ASD. Although weight and body surface area may be considered factors, the most important reason for this difference in bypass flow requirement appears to be a significant increase in  $VO_2$  in TF patients.

These data are not in agreement with a previous report by DeWalt and co-workers<sup>6</sup> in 1956 who showed that at equivalent bypass flow rates patients with cyanotic congenital heart disease had a lower oxygen uptake than patients with non-

TABLE I  
PREOPERATIVE DATA (MEAN ± S.D.)

	Anesthetic	Number of Patients	Age (years)	Weight (kg)	Hemoglobin (gm/100)
Group ASD I	Morphine	10	8	38	14.1
			±2.3	±5	±1.7
Group ASD II	Halothane	15	9	39	14.4
			±2.2	±4	±1.9
Group TF I	Morphine	8	9	37	18.38
			±1.6	±4	±3.2
Group TF II	Halothane	7	10	29	17.94
			±1.9	±3	±2.4

\*P < 0.05, Student's t-test when compared to Group ASD I or Group ASD II

#P < 0.001, Student's t-test when compared to Group ASD I or Group ASD II

TABLE II  
INTRAOPERATIVE DATA (MEAN ± S.D.)

Group	Anesthetic	Length of Procedure (hr)	Urine (ml)	Output (ml/min)	Mean Blood Pressure (mm Hg) Pre-Bypass	Post-Bypass
ASD I	Morphine	3.7	391	1.8	94*	86
		±0.6	±76	±0.4	±11	±18
ASD II	Halothane	3.6	310	1.6	76	81
		±0.5	±73	±0.2	±8	±13
TF I	Morphine	5.5	330	1.9	75	80
		±1.2	±89	±0.3	±12	±10
TF II	Halothane	5.7	342	1.0	72	79
		±1.0	±90	±0.3	±9	±8

\*P < 0.05, Student's t-test when compared to Group ASD I or ASD II

#P < 0.05, Student's t-test when compared to all of the other groups

TABLE III  
BYPASS DATA (MEAN ± S.D.)

Group	Time (min)	Mean Blood Pressure (mm Hg)	Blood Flow Rate (ml/kg/min)	Urine Flow Rate (ml/min)	VO <sub>2</sub> (ml/kg/min)	HCO <sub>3</sub> Require. (mEq)
ASD I	35	75#	64	2.1#	2.4	8
	±9	±8	±9	±0.3	±0.2	±11
ASD II	33	48	67	1.2	2.1	6
	±8	±7	±9	±0.4	±0.2	±9
TF I	74*	59	86*	1.0	3.0*	6
	±17	±11	±7	±0.2	±0.2	±14
TF II	73*	55	83*	0.9	2.9*	8
	±26	±14	±9	±0.3	±0.3	±12

\*P < 0.001, Student's t-test when compared to Group ASD I or ASD II

#P < 0.025, Student's t-test when compared to all of the other groups

cyanotic disease. An explanation of the difference in findings is probably related to the marked degree of metabolic acidosis that most of the former authors patients with cyanotic lesions experienced during bypass. Almost all of their cyanotic patients had arterial pH's below 7.25 while those with noncyanotic disease had more normal pH's. This, of course, is indicative of markedly inadequate perfusion during bypass in the cyanotic diseased patients which is well known to cause a reduction in VO<sub>2</sub>. In contrast, it was rare for any of our patients to have a pH below 7.35 and require sodium bicarbonate and none ever had an arterial pH below 7.32.

Patients with cyanotic congenital heart disease frequently have inadequate total body tissue perfusion and as a result are metabolically acidotic preoperatively.<sup>7,8</sup> Some of these patients are able to compensate through their respiratory systems, i.e. hyperventilation, and can have normal or close to normal arterial pH's while awake, however, during periods of relative respiratory inactivity, i.e. while asleep or during anesthesia, the respiratory compensation is lost and the metabolic acidosis becomes evident again. A number of authors<sup>9-11</sup> have shown that inadequate perfusion and metabolic acidosis is associated with a decrease in VO<sub>2</sub> because oxygen never gets to the tissues where it is needed due to low or no perfusion to these tissues. Nahas and colleagues<sup>12</sup> have demonstrated that VO<sub>2</sub> is increased in situations of inadequate perfusion or shock if pH is artificially maintained normal or if an animal is allowed to compensate using normal respiratory mechanisms. The latter authors postulate that the increase in VO<sub>2</sub> that occurs during inadequate perfusion states is due to stimulation of the sympathoadrenal system and catecholamine release which produces an accelerated turnover of free fatty acids. This calorogenic effect of the catecholamines is not observed in the presence of acidosis because the latter inhibits the metabolic actions of catecholamines.

Urinary catecholamines have been shown to be markedly higher in preoperative TF patients than ASD patients.<sup>13</sup> The latter combined with uncompensated metabolic acidosis and Nahas and co-workers findings may be an explanation why

Bing, et al<sup>14</sup> have found that patients with cyanotic heart disease have a lower than normal preoperative  $\text{VO}_2$ . It also might explain why bypass (a situation usually associated with increased circulating catecholamines) with a normal blood pH as in this study resulted in cyanotic patients having a higher  $\text{VO}_2$  than non-cyanotic patients while bypass at a low arterial pH as in DeWall, et al's<sup>6</sup> study caused  $\text{VO}_2$  to be lower in cyanotic than comparable non-cyanotic patients.

The accuracy of  $\text{VO}_2$  measurements in cyanotic patients during bypass as made in both DeWall, et al's study and in ours can be seriously questioned. The reason for this is the marked amount of bronchial artery blood flow that can occur in patients with cyanotic congenital heart disease. Indeed, Bing and colleagues<sup>14</sup> have reported preoperative bronchial arterial flow of two liters or more in patients with decreased pulmonary arterial flow and cyanotic congenital heart disease. During bypass most of this blood finds its exit to the operative field via the pulmonary veins and left atrium and is returned to the oxygenator separately from the rest of the venous return. The influence of bronchial flow on common venous return oxygen content is, therefore, not taken into account in any study accomplished during bypass. If the oxygen content of this blood was higher than the remainder of the common venous return, calculated  $\text{VO}_2$  would be lower, if it was lower or the same as the remainder of common venous return blood,  $\text{VO}_2$  would be respectively higher or the same as what was calculated not taking bronchial flow into account. Since neither the oxygen content nor volume of left atrial blood returned to the pump was measured during these studies nor in previous ones, it is impossible to say just how accurate our or other investigators calculated  $\text{VO}_2$  values are during bypass. Indeed, it is possible that an increase in bypass flow requirements of TF patients is not at all related to increased  $\text{VO}_2$ . Instead, increased bypass flow may be more directly related to bronchial blood flow, that is to say, the bronchial arteries in cyanotic patients represent a large drain from the systemic circulating and in order to maintain an adequate systemic blood flow much more blood may need to be perfused systemically to compensate for the large bronchial drain to the lungs.

Whether  $\text{VO}_2$  is increased, decreased or unchanged in cyanotic congenital heart disease as opposed to non-cyanotic disease is really not nearly as important as the realization that blood flow requirements appear to be higher in the former and that it is easy to optimize bypass blood flow, as we have previously reported,<sup>3,4</sup> by the simple technique of frequently measuring  $\text{PvO}_2$ . Current oxygenators and perfusion techniques allow us to provide almost any patient the amount of oxygen and blood flow that he or she requires for optimal metabolism. Our findings in this study reiterate a well known but often forgotten concept, and that is, that ideal flow is influenced but does not bear a constant relationship to body weight, surface area, temperature, muscular activity and perhaps other unknown factors. Our data demonstrates that another factor that should be considered is disease state. Perhaps more important our findings re-emphasize the simplicity of optimizing bypass flow by measuring  $\text{PvO}_2$  and adjusting flow to maintain the latter within normal limits.

#### SUMMARY

Blood flow and oxygen requirements of 40 children 6-11 years of age with secundum type atrial septal defects (ASD) or tetralogy of Fallot (TF) were compared during cardiopulmonary bypass. The two groups were similar with respect to age and all were perfused at 32° C with a bypass system primed with 18-24 ml/kg of blood and 30-40 ml/kg Ringer's solution. Bubble oxygenators were used and arterial  $\text{PO}_2$  kept at 130-170 torr during bypass. Oxygen consumption was determined from the Fick equation using bypass flow rates measured on a calibrated roller pump and

calculated arterial and mixed venous oxygen contents. Arterial and mixed venous blood were analyzed every 15 minutes for oxygen tension and content and bypass flow adjusted to maintain  $P_{V}O_2$  at 37-42 torr. TF children had preoperative hemoglobins that averaged 3.8 gms% higher than those with ASD. However, the former required significantly greater bypass flow rates than the latter (85.3 vs 64.9 ml/kg/min) to maintain  $P_{V}O_2$  levels and avoid metabolic acidosis. Bypass oxygen consumption of TF and ASD children averaged 2.9 and 2.2 ml/kg/min respectively. This difference was significant,  $P = .001$ . Our findings indicate that because of higher oxygen requirements children with TF require bypass blood flows that are approximately 20% higher than those with ASD to insure aerobic metabolism during bypass.

#### REFERENCES

1. Stanley, T. H., Volder, J. and Kolff, W. J.: Extrinsic Artificial Heart Control via Mixed Venous Blood Gas Tension Analysis. *Trans. Amer. Soc. Artif. Int. Organs* 19:258, 1973.
2. Stanley, T. H. and Kolff, W. J.: Metabolic Monitoring and Control of the Artificial Heart. *J. Thorac. Cardiovasc. Surg.* 67:434, 1974.
3. Stanley, T. H. and Isern-Amaral, J.: Periodic Analysis of Mixed Venous Oxygen Tension to Monitor the Adequacy of Perfusion During and After Cardiopulmonary Bypass. *Canad. Anaesth. Soc. J.* 21:454, 1974.
4. Stanley, T. H. and Isern-Amaral, J.: Mixed Venous Oxygen Tension: A Simple Metabolic Monitor of the Adequacy of Perfusion During Cardiopulmonary Bypass. *AMSECT Proc.* 2:41, 1974.
5. Theye, R. A.: Calculation of Blood  $O_2$  Content From Optically Determined Hb and  $HbO_2$ . *Anesthesiology* 33:653, 1970.
6. DeWall, R. A., Warden, H. E., Gott, V. L., et al: Total Body Perfusion for Open Cardiomy Utilizing the Bubble Oxygenator. *J. Thorac. Cardiovasc. Surg.* 32:591, 1956.
7. Gootman, N. L., Scarpelli, E. M. and Rudolph, A. M.: Metabolic Acidosis in Children with Severe Cyanotic Congenital Heart Diseases. *Pediatrics* 31:251, 1963.
8. Heins, H. L., Jr.: Metabolic Acidosis in Cyanotic Congenital Heart Disease. *Proc. Western Soc. Ped. Res.* 9:51, 1961.
9. McGoon, D. C., Moffitt, E. A., Theye, R. A., et al: Physiologic Studies During High Flow, Normothermic, Whole Body Perfusion. *J. Thorac. Cardiovasc. Surg.* 39:275, 1960.
10. Vetto, R. H., Winterscheid, L. C. and Merendino, K. A.: Studies in the Physiology of Oxygen Consumption During Cardiopulmonary Bypass. *Surg. Forum* 9:163, 1958.
11. Kay, J. H. and Gaertner, R. A.: A Simplified Pump Oxygenator with Flow Equal to Normal Cardiac Output. *Surg. Forum* 7:264, 1957.
12. Nahas, G. G., Lubos, T., Small, H. S., et al: Alterations in  $O_2$  Uptake Following Hemorrhage in Dogs. *Am. J. Physiol.* 210:1009, 1966.
13. Stanley, T. H., Liu, W. S. and Lathrop, G. D.: The Effects of Morphine and Halothane Anesthesia on Urine Norepinephrine During Surgery for Congenital Heart Disease. *Canad. Anaesth. Soc. J.* (In Press).
14. Bing, R. J., Vandam, L. D. and Gray, F. D.: Physiological Studies in Congenital Heart Disease: II. Results of Preoperative Studies in Patients with Tetralogy of Fallot. *Bull. Johns Hopkins Hospital* 80:121, 1947.