Direct Measurement of Intracardiac Blood Flow in Dogs with Experimental Ventricular Septal Defects

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ABSTRACT

Experimental ventricular septal defects (VSD's) were produced in dogs under general anesthesia by excising a 9-mm core of tissue from the septum with a cylindrical cutting tool. A specially designed electromagnetic flow transducer was wedged into the defect compressing the septal tissue around it, thus causing all of the shunted blood to pass through the lumen. The sensing electrodes were in direct contact with the blood stream, allowing the transducer to be calibrated externally, and to be used as a primary standard of measurement. When left-to-right shunts were measured by the Fick technique, the average error was 57% (2% to 154%). When pulmonary arterial oxygen saturation exceeded 85%, measurements using the Fick method showed errors greater than 30% (61% to 154%) in 9 of 11 animals. The VSD's were of moderate size and resulted in right ventricular systolic pressures between 4 and 5 of systemic. The flow pattern and the interventricular pressure difference were remarkably similar in contour. Delay in right ventricular activation occurred in most animals as a result of surgical disturbance of the conduction system. Diastolic shunting, which varied between 15% and 25% of the total, was noted in animals with or without changes in conduction pattern. The sequence of ventricular activation was an important factor in controlling systolic shunting and may be an important factor in the distribution of myocardial work.

ADDITIONAL KEY WORDS electromagnetic flow transducer congenital heart disease Fick method diastolic shunting cannulating flow transducer ventricular shunts

Phasic flow transducers have been used extensively for measurement of aortic, pulmonary, and regional blood flow both in man and experimental animals. In contrast, intracardiac shunts have been estimated by indirect methods that at best yield average flow rates. To establish a primary standard for measuring shunts and to determine the effects, if any, of phasic flow on myocardial performance in an animal model of ventricular septal defect, the most common variety of congenital heart disease, electromagnetic flow transducers were adapted for use within the interventricular septum itself. The decision to use this type of transducer was made primarily on the basis of proven accuracy, availability, familiarity, and convenience. There is no reason to suppose that the equally accurate ultrasonic transit-time technique would not work as well. The emphasis of this report is therefore on the feasibility of making these measurements rather than on the superiority of a particular transduction principle.

The timing of intracardiac shunts has occupied the interest of several previous investigators. Using an hydraulic model of the circulation, Brostoff and Rodbard (1) predicted that diastolic shunting might occur in ventricular septal defect (VSD) with primar-
illy left-to-right shunting if the opening was sufficiently large. This was confirmed in patients with this lesion by Sissman and Abrams (2) using selective cineangiography. Combining the latter technique with hemodynamic observations, Levin and associates (3) clearly showed the dependence of the timing and direction of shunt flow upon the temporal variation of the interventricular pressure difference, and the further dependence of this variable on the size of the communication between the ventricles. Unfortunately, none of the methods used by these investigators yielded a quantitative estimate of shunt flow in vivo. This difficulty has now been overcome. Development of the intracardiac transducer has not only provided a primary standard for assessing the accuracy of indirect measurements of left-to-right shunts, but has also made possible a correlation of shunt flow patterns with other physiological events. Additional determinants of flow through ventricular septal defects and their probable effect on long-term cardiac performance have been uncovered as a result of these investigations.

Methods

Mongrel dogs weighing 18 to 35 kg were studied with the chest open during general anesthesia produced with pentobarbital (30 mg/kg, iv). Ventricular septal defects were produced in 44 dogs by inserting a cylindrical cutting tool of 9 mm external diameter into the cavity of the right ventricle through an incision made within a purse-string suture in the free wall. The purse-string was placed midway between the annulus of the pulmonary valve and the apex of the right ventricle, equidistant to the major branches of the right and left coronary arteries. With rapid rotation of the cutter and the application of suction, a 9-mm core of septal tissue was excised. The position of the boring tool against the interventricular septum was critical in avoiding the aortic valve and the papillary muscles of the tricuspid valve. The mitral valve was easily spared. Seventeen additional ventricular septal defects were produced in a second series of experiments using the right atrial appendage as the portal of entry into the heart. In 39 of the total of 61 animals satisfactory flow tracings were obtained by inserting a flow transducer into the defect.

Insertion proved to be the most crucial and difficult part of the procedure. Using stay sutures attached to the periphery of the purse-string suture initially used for introducing the cutting tool, the hole in the free wall of the right ventricle (or the remains of the atrial appendage in the second series) could be enlarged momentarily to permit passage of the transducer into the heart. The transducer, positioned on a flanged push-rod, and held by its cable, was then gently pushed into the VSD. The latter could be located by probing with the rounded end of the push-rod which extended about a quarter of an inch beyond the transducer. Compression of myocardial tissue by the probe prevented leakage around it, and caused all the shunted blood to flow through the lumen. At first many animals died because of ventricular fibrillation, but with increasing experience, the survival rate improved.

Prototype transducers having a rigid, cylindrical, plastic lumen of 9 mm internal diameter and the push-rod device for inserting them into defects were designed and constructed in this laboratory (4). The various prototypes were all of coreless design. Since no tissue was interposed between the lumen of the probe and the blood stream, the device could be externally calibrated by measuring the time for 1 liter of fluid to pass through it. Timing accuracy was insured by high speed (100 mm/sec) recordings of electrical pulses generated as the fluid passed over two electrodes on the measuring cylinder. The transducer was linear over the entire range used (0 to 25 liter/min) and the difference between saline and blood calibration (Fig. 1) was less than 1% for the same probe. The calibration was stable over short periods of time and in subsequent chronic experiments (not reported here) was within 2% of the original value after implantation for 1 to 6 weeks.

Since the first prototype could be pushed through the septum into the left ventricular cavity, it was redesigned with a wide flange on the proximal side. To facilitate insertion into the defect, the current model (Fig. 2) includes both a flange on the proximal side and a conical section on the leading edge. ECG artifacts seen on early records were eliminated by additional insulation of the external surface of the electrodes to prevent conduction of myocardial potentials. Intraluminal electrocardiographic potentials, being symmetrical about both sensing electrodes, were therefore rejected by the balanced input circuitry of the flowmeter amplifier. The probes were energized by a gated, sine-wave device of commercial manufacture (Biotronics BL 410). The amplitude response of the system was flat to 50 Hz and fell 3 db at 100 Hz.

In 25 animals, simultaneous right and left ventricular and arterial pressures were recorded.
MEASUREMENT OF INTRACARDIAC BLOOD FLOW

**Figure 1**

Representative transducer calibration curve. Each point represents the average of four runs at the same flow rate. Output was linear over the entire range of flow velocity. Observations with blood(•); observations with saline(+) Calibration factor was identical for both in this instance and often differed by less than 1%.

Electromagnetic, intracardiac flow transducer and instrument used for inserting it into ventricular septal defect. Core of transducer was made of Teflon to prevent clotting of blood on inner surface, and leading edge was beveled to facilitate insertion in septum.

by implanting no. 6 NIH-style catheters in each ventricle, and connecting them to strain-gauge transducers (Electrodyne X-4000). Stiff connecting tubing filled with degassed saline solution was used to minimize damping. The undistorted amplitude response of the catheter-transducer combination varied between 20 and 40 Hz with a registration delay of 2 to 4 msec. Static hydraulic calibrations were performed at the beginning of each experiment. Zero reference pressure and electrical calibration were obtained at the end of individual pressure recordings. Oxygen consumption was determined by collecting expired air in a Douglas bag for a period of 5 minutes, beginning and ending at the same point in the respirator cycle. Since the animals were being ventilated artificially with a Harvard piston-type pump, caution was taken to prevent loss of air around the cuffed endotracheal tube and the slide valve of the pump. The latter was checked regularly for O-ring wear and sealed with silicone grease. Great care was taken during surgery to avoid puncturing the surface of the lungs. Inadvertent puncture was detected by wetting the surface of the lungs with saline and looking for bubbling. Minor punctures usually subsided with time and mild compression; occasionally a tear had to be sutured. Inspired gas was fresh air with an oxygen concentration between 20.93 and 20.95%. A value of 20.94% was assumed for all experiments. Expired gas was analyzed for oxygen and carbon dioxide concentration by the Scholander technique (5). Three samples were taken from the Douglas bag immediately upon completion of the collection and the total volume was determined with a Collins gas meter. Corrections were made for ambient room temperature and barometric pressure. Three-milliliter samples of blood for oxygen saturation were obtained in rapid succession from catheters securely placed by Rudolph’s method (6) in the following sites: (1) the superior vena cava, between the azygous vein and the right atrium; (2) the inferior vena, just proximal to the level of the diaphragm; (3) the right atrium, at the mid-lateral border; (4) the right ventricle, in the infundibular zone; (5) in a branch of the pulmonary artery (usually the right), at least 3 cm distal to the pulmonary valve; (6) in one of the right pulmonary veins; and (7) the ascending aorta (via the right internal mammary artery). Samples were withdrawn slowly (approximately 15 seconds per sample over 4 respiratory cycles) into heparinized syringes, but all samples were obtained within 30 to 45 seconds of the start of collection. Samples were iced until analyzed. Oxygen saturation and capacity were determined spectrophotometrically in triplicate with a Beckman DU spectrophotometer according to Gordy and Drabkin’s method (7) as modified by Nahas (8). Systemic (Qs)
pulmonary (Qp), and left-to-right shunt flow (QLR) were calculated as follows:

\[ Q_s = \frac{V_{O_2}}{C_{S A O_2} - C_{M V O_2}} \]

\[ Q_p = \frac{V_{O_2}}{C_{P V O_2} - C_{P A O_2}} \]

\[ Q_{L R} = Q_p - Q_s \]

where \( C_{O_2} \) = ml \( O_2 \) per 100 ml blood; \( SA \) = systemic arterial, \( MV \) = mixed venous; \( PV \) = pulmonary venous and \( PA \) = pulmonary arterial.

All data were recorded both on a direct-writing oscillograph (Offner Dynograph) and a magnetic tape recorder (Ampex SP300). Differential interventricular pressures and flow rates were computed after digitizing the analog records on the Stanford ACME computer (IBM 1800, 360/50). Left-to-right shunt flow measured by the transducer was obtained by integration of flow in this direction during the 1-minute period overlapping the collection of the blood samples for the Fick determination. Graphs of pressure, flow, and electrocardiographic data were produced on a digital plotter (Calcomp).

Results

A. VSD FLOW PATTERNS

Two distinctive flow patterns were observed. Not only were these dependent on the pressure relationships between the ventricles, but also upon the QRS pattern, the cardiac rhythm, and the relative size of the defect. These aspects will be described in greater detail in the ensuing sections. These common patterns observed are illustrated in Figure 3. Velocity in the left-to-right direction has been defined as positive. Thus the area below the curve and above the zero flow line represents the volume of blood which passes left-to-right per cardiac cycle. Similarly, the area above the curve and below zero represents the right-to-left shunt per cycle. Integration of these areas over a known length of time yields average volume flow rates. Since zero flow velocity could not be established electronically by shutting off the magnets, it was determined by producing a short period of cardiac arrest with acetylcholine (Fig. 4). Since flow in the positive direction was initiated by left atrial contraction, the first initial wave of low amplitude is termed the a-wave. The zero flow point (or directional reversal point) occurred just before the a-wave. Following a short electromechanical lag, a rapid rise in flow velocity occurred due to the onset of ventricular contraction, and is called the c-wave. Peak velocity was reached early and preceded or followed the opening of the pulmonary valve. Throughout the remainder of systole, velocity decreased relatively slowly until aortic valve closure occurred. Velocity decreased rapidly during ventricular diastole. In animals with delayed conduction, not only did the flow fall to zero, but it also reversed, producing a small right-to-left shunt. In one animal (no. 17) the right-to-left shunt was approximately one-fourth of the shunt in the other direction, but in the others this did not result in a significant decrease of systemic arterial oxygen saturation. No changes in flow pattern with respiration were noted in defects of 9.3 mm whether or not block was present or absent.

B. PRESSURE AND ECG-FLOW RELATIONSHIPS

Right ventricular and pulmonary arterial systolic pressures averaged one-third of the comparable systemic pressures. In no instance did either exceed half the systemic pressure as might be expected in defects of moderate size. Pulmonary arterial pressure was 39/17 with a mean of 24 (SD 5) mm Hg. Aortic pressure was 121/96 with a mean of 100 (SD 9) mm Hg. The animals with the highest pulmonary arterial oxygen saturations, and consequently the highest pulmonary flow rates, were evenly distributed in the range of RV/LV and PA/AO systolic pressure ratios (.27 to .50). When the QRS interval following creation of the VSD was greater than 150% of the initial value, a marked delay in the development of right ventricular pressure was observed (Fig. 3). This was a natural result of damage to the conduction system during production of the VSD. Interestingly, in many dogs a conduction delay was noted after the incision of the free wall, before the core of the septal tissue was removed. When the right atrial appendage was used as a portal of entry, severe damage to the conduction system with the production of right ventricular activation delay was less frequent. In animals with
Phasic flow patterns of intracardiac shunts through VSD's showing relationships with ECG and ventricular and arterial pressures. Left-to-right flow along positive axis of ordinates. Left-to-right shunt per cardiac cycle represented by area above zero flow axis. Area below zero flow axis is small right-to-left shunt (delayed conduction only). Left: Normal RV conduction and activation. RV and LV pressures rise nearly synchronously. Abrupt change in VSD flow velocity is coincident with aortic dicrotic notch (right vertical broken line). Left-to-right shunt commences before either aortic or pulmonary valve opens (left vertical broken line), and continues through most of diastole. There is no isovolumetric contraction interval for either ventricle since shunt flows throughout cardiac cycle. Right: Delayed RV conduction and activation. RV pressure rises unopposed by RV producing large early systolic left-to-right shunt. Note long QRS and delayed opening of pulmonary valve. RV pressure exceeds LV pressure in diastole producing small right-to-left shunt. RV pressure has characteristic triangular shape. VSD = ventricular septal defect; RV = right ventricle; LV = left ventricle.

delayed right ventricular activation and subsequently delayed relaxation, the left ventricular pressure was unopposed during early systole and resulted in the passage of a large fraction of the shunt during early left ventricular systole (Fig. 3). However, during
the relaxation phase of the left ventricle, there was a period during which right ventricular pressure exceeded the left, and resulted in a reversal of flow. The dependence of flow upon differences in pressure between the left and right ventricles was easier to appreciate when this interventricular pressure difference was correlated with the pattern of VSD flow (Fig. 5, left). In many instances this was more striking when a train of normal beats was followed by an ectopic beat (Fig. 5, right). Disappearance of right-to-left shunting during an ectopic beat in which left ventricular pressure always exceeded the right, further emphasizes the primary dependence of flow on the interventricular pressure difference. There was commonly an easily observable lag between shunt flow and pressure difference. This can probably be attributed to inertia. In all of the animals with an unchanged pattern of ventricular depolarization (QRS interval increased less than 50% of preoperative value), the shape of the flow velocity curve showed distinctive features which could also be correlated with the interventricular pressure difference (Fig. 3). Flow in the left-to-right direction generally persisted through more of diastole, right-to-left shunting was frequently absent, and since right and left ventricular pressures rose promptly together, early systolic shunting was diminished considerably.

That a sizeable pressure difference existed between the two atria, sufficient to allow flow across the septum during late ventricular diastole, was suggested by simultaneous recordings from these two sites in animal 17. The maximum interatrial pressure difference favoring flow from the left to the right side occurred shortly after the onset of the P-wave of the electrocardiogram when both atrioventricular valves were presumably open.

C. TIMING OF SHUNTS IN VSD

The left-to-right shunt during each cardiac cycle can be divided into three distinct components (Fig. 6). Fraction S1, the early systolic shunt represents shunting from the LV to RV before the pulmonary valve opens. This occurs during what would ordinarily be the isovolumetric contraction period. Fraction S2, the late systolic shunt occurs between pulmonic opening and aortic closure. Fraction D is the diastolic shunt. When the group of animals was subdivided depending upon whether delayed RV activation (block) was

FIGURE 4
Zero flow velocity following injection of 20 μg of acetylcholine. Flow velocity in liter/min.

FIGURE 5
Left: Comparison of interventricular pressure difference (labeled “gradient”) with VSD flow velocity. Difference is positive when LV pressure exceeds RV. The general shape of both curves is similar. Reversal of VSD flow when LV pressure is lower than RV is not immediate. Right: Dependence of VSD flow upon interventricular pressure difference (labelled “gradient”) is clearly demonstrated during the ectopic beat. Note disappearance of right-to-left shunt when LV pressure is higher than RV throughout the cardiac cycle. Pressure in mm Hg; flow velocity in liter/min. Abbreviations as in Figure 3.
Timing of left-to-right shunts in VSD. Left-to-right shunts can be divided into three fractions. S1: Early systolic shunt; volume transferred from LV to RV before opening of pulmonary valve (P). S2: Late systolic shunt; volume transferred during ejection from both ventricles. D (diastolic shunt) commences with aortic valve closure (A) and continues into mid-diastole. Fraction S2 is dominant systolic fraction during normal RV activation. Fraction D shows little variation dependent on QRS pattern. Abbreviations as in Figure 3.

present or absent, a clear relationship emerged between the presence of block and the volumetric proportions of the first two fractions, S1 and S2. In animals with normal conduction and consequently normal coordination of RV and LV pressure development (post-operative QRS interval of 0.040 to 0.060), fraction S1, the early systolic left-to-right shunt, ranged between 5% and 18% of the total and fraction S2, the late systolic shunt, varied from 61% to 74% of the total. When RV activation was delayed (QRS 0.090 to 0.133) the marked pressure difference favoring the left ventricle in early systole resulted in fraction S1 values from 32% to 54% of the total, and fraction S2 values from 26% to 47%. Thus the fraction of the left-to-right shunt which occurred in early systole was exquisitely sensitive to the pattern of ventricular activation. Quite unexpectedly, the diastolic shunt (fraction D) ranged from 15% to 25% regardless of the presence or absence of block. This distribution of flow during the cardiac cycle has obvious implications in terms of myocardial work distribution between the ventricles.

In one animal, the effect of a change in the cardiac rhythm on the shape of the flow trace was quite striking. When sinus rhythm was present, (Fig. 7) prominent atrial flow waves (a) were observed, but when a nodal tachycardia ensued these promptly disappeared. Increases in rate alone did not result in such a marked change in the flow pattern in other animals during sinus tachycardia.

D. COMPARATIVE MEASUREMENTS OF LEFT-TO-RIGHT SHUNTS

Results of studies in 25 animals are summarized in Table 1. Left-to-right shunts, measured using the Fick technique, were calculated as the difference between total pulmonary and effective pulmonary blood flow since one animal manifested a significant degree of systemic arterial desaturation. When there was no significant right-to-left shunt (all except animal 17), systemic and effective pulmonary flow rates were identical. The latter was calculated from the difference in...
oxygen content between pulmonary venous and mixed systemic venous blood samples. Taking the right atrial samples as representatives of mixed systemic venous return, which is commonly done in calculating flow rates in ventricular septal defects, the errors in measuring the shunt averaged 57% with a range of 2 to 154%. Since tricuspid reflux was suspected in 13 animals with delayed right ventricular activation (QRS > 100 msec), because each had a systolic thrill over the right atrium and dilatation of this chamber, calculations were repeated using values for superior and inferior vena caval blood to represent those of mixed venous blood. This did not decrease the average error, and the averages actually increased, although there was considerable overlap among the three groups of calculations (Table 1).

Comparison of data from the individual animals using the two methods (Fig. 8) shows that 13 of the 25 animals had errors exceeding ±30%. The distribution of errors in the two groups of animals with and without block was not significantly different either at the 1 or 5% level using the two-tailed t-test. However, errors in estimating the shunt flow were closely related to the absolute level of the pulmonary arterial saturation (Fig. 9). When the latter was under 85%, 11 of 14 Fick measurements were within 30% of the true value. In only two of 11 animals with a saturation above 85% was similar accuracy achieved.

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**FIGURE 8**

Left-to-right shunt measured by Fick technique on vertical axis compared with transducer measurement of shunt on horizontal axis. Solid line at 45°C is line of identity. Broken lines at plus and minus 30% error. Thirteen of 25 animals had errors exceeding these limits. Asterisks denote animals with block. Distribution of errors in the two subgroups was not significantly different.

**FIGURE 9**

Error in measurement of left-to-right shunts by Fick method plotted on ordinates. Overestimate (+). Underestimate (*). Eleven of 14 measurements with Fick method were within 30% of true value (horizontal line) when pulmonary arterial saturation (abscissa) was less than 85% (vertical line). Only 2 of 11 animals with saturation higher than 85% were within 30% error.
Comparison of Shunts Measured by Transducers with those Calculated by the Fick Method

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The relationship of the time of left-to-right shunt in the cardiac cycle to the duration of intraventricular electrical conduction is shown. MV = mixed venous; RA = right atrium; SVC = superior vena cava; IVC = inferior vena cava.

Detailed tables of original data from which material presented in Table 1 was taken will be provided by the author on request.
**Discussion and Conclusions**

**A. PATTERNS OF INTRACARDIAC SHUNTS IN VENTRICULAR SEPTAL DEFECTS**

The feasibility of measuring intracardiac blood flow directly by inserting an electromagnetic flow transducer into experimentally created VSD's has been demonstrated in 39 dogs. Observations by Gamble and his co-workers (9) on the variation in optical density of blood within or near interventricular septal defects using fiber-optic techniques suggest that the pattern of blood flow in human VSD is similar to those observed with the directly implanted transducer. Since most naturally occurring VSD's are located in the membranous interventricular septum, changes in size of the defect during the cardiac cycle are not likely to be significant. If this is true, the flow patterns described here are probably similar to those that exist in most human hearts with VSD. Until such time that VSD flow patterns are studied in man, possibly with catheter-tip flow sensors now available, flow patterns obtained with the septal transducer should not be extrapolated in all details to those occurring naturally in humans or animals.

**B. PRESSURE-FLOW RELATIONSHIPS**

The conclusion drawn by Levin and his co-workers (3) on the relationship between the interventricular pressure difference and the timing of intracardiac shunts in ventricular septal defects have been confirmed. That the shape of the flow curve can be matched by the computed interventricular pressure differences has also been confirmed in VSD's of moderate size, and lends credence to this method for studying the shape of flow patterns in man. Since the physical system is one with both reactive and resistive components, allowance must also be made for the inertial lag between the onset of pressure and the onset of flow. The most important factor which influences the magnitude of the interventricular pressure difference is undoubtedly the size of the defect as previously shown by Savard et al. (10). To this must be added the phase relationships between left and right ventricular pressures, which is controlled by the pattern of myocardial depolarization, the forcefulness and phase of atrial contraction, heart rate, and the cardiac rhythm. As useful as the interventricular pressure difference may be for timing the various fractions of shunt flow, it is apparent from a few basic quantitative considerations that estimates of flow cannot be derived by this method. Since there is an inverse relationship between VSD size and the magnitude of the interventricular pressure difference, the orifice size and changes in orifice size during the cardiac cycle would have to be known with exactness. Moreover, the interventricular pressure difference would have to be measured precisely at the orifice on both right and left sides. Neither of these conditions can be met in man with current technology.

Prominent LV-aortic systolic pressure differences ranging from 15 to 35 mm Hg were noted in 10 animals. These differences could not be attributed to left ventricular outflow obstruction since the transducer position was checked carefully at autopsy and was found to lie well below the aortic valve. More likely, the LV catheter may have impinged upon the flange of the transducer producing an artifact in the recording.

**C. ECG-FLOW RELATIONSHIPS**

Although most children with naturally occurring VSD's do not have abnormalities of ventricular activation, the results of this investigation may clarify the behavior of two small groups of VSD that often do: VSD of endocardial cushion origin and residual post-operative VSD. The occurrence of right heart failure in the absence of severe pulmonary arterial hypertension in these two groups may be a reflection, in part, of the unusual distribution of myocardial work and energy expenditure. Unlike the situation in patent ductus arteriosus wherein the left ventricle carries the entire volume overload (11), the distribution of volume work in VSD is complex because both ventricles handle the load. When VSD is present, not only must the right ventricle eject its output at higher pressure, it must also discharge a greater stroke volume into the pulmonary artery. Thus any disturbance such as an alteration in impulse conduction which requires the right
ventricle to handle an even larger share of the volume overload in VSD could predispose it to early decompensation. Even in the absence of right ventricular activation delay, as much as one fourth of the total left-to-right shunt may occur during diastole relieving the left ventricle and overloading the right. But when intraventricular conduction block is present and the major fraction of the shunt occurs in early systole, the right ventricle may be required to handle as much as 75% of the total volume overload by itself. The notion that the left ventricle ejects blood directly into the pulmonary artery thus taking the major burden away from the right ventricle is refuted here by the combined magnitude of the diastolic plus early systolic shunt that enters the right ventricle before the pulmonary valve opens. That the right ventricle may thus be in a precarious state of compensation if conduction is delayed is readily understandable. With larger defects, competition of the early systolic shunt with normal right ventricular filling from the right atrium may occur and lead to elevated ventricular filling pressure and infringement on the normal reserve of myocardial function in the acute state. This hypothesis cannot be confirmed on the basis of experiments conducted thus far with defects of moderate size.

Delayed right ventricular activation did not result in a large negative pressure difference in early diastole in most animals but in dog 17 this was sufficient to produce a right-to-left shunt of sufficient volume to result in systemic arterial desaturation. This observation is consonant with the occasional occurrence of right-to-left shunting in children with VSD and right bundle branch block in whom no obstruction to the right ventricular outflow can be demonstrated (personal observation). The infrequent occurrence of this phenomenon in the experimental animals was probably related to the moderate size of the defect and may have occurred more often had they been larger.

D. EVALUATION OF FICK METHOD FOR MEASURING LEFT-TO-RIGHT SHUNTS

These results are in general agreement with the only previous comparison of electromagnetic flowmeter and Fick methods for measuring left-to-right shunts (12), wherein were found errors in excess of 25% in six of 12 animals. Unfortunately, noncannulating transducers were used in their study, and since the same transducer was used to measure both aortic and pulmonary blood flow in an acute preparation, it is possible that the potential accuracy of the flowmeter method was not achieved.

Our observations indicate an even greater divergence between the Fick method and the method utilizing a cannulating flow transducer in the septum. Errors as great as 154% can arise in measuring shunts by the Fick method since the individual errors in measuring pulmonary and systemic flow may be compounded. Inaccurate assessment of pulmonary blood flow is most likely to occur when the pulmonary arteriovenous oxygen difference is small and variation from sample to sample due to streaming may often exceed severalfold the potential accuracy of the method of measurement of oxygen content. Errors in measuring systemic flow arise primarily from inaccurate estimation of the oxygen content of mixed systemic venous blood. As noted previously, tricuspid insufficiency was suspected when thrills were present over an enlarged right atrium. That this can be quite marked in animals with intraventricular conduction disturbances is suggested by preliminary angiocardio graphic studies in chronic animals with VSD in our laboratory. Although tricuspid reflux may contribute to the imperfect mixture of the various sources of systemic venous return, right atrial samples obtained at the mid-lateral area represented the best compromise even when delayed right ventricular activation occurred. Thus when pulmonary arterial oxygen saturation was less than 85%, the difficulty in obtaining a true sample of mixed systemic venous blood was probably offset by more accurate measurement of pulmonary blood flow. Though reasonable, these explanations are largely hypothetical. Our observations would suggest, however, that extreme caution be used in interpreting
individual measurements of shunt flow by the Fick technique.

E. RIGHT-TO-LEFT SHUNTS

A systematic study and comparison of right-to-left shunts was not attempted because it was not possible to quantify this shunt accurately with the transducer unless the flow was large (as it was in animal 17). An error in determining the baseline (zero flow) affecting the L→R shunt by no more than ±5% would have been sufficient to over or underestimate the R→L shunt by 50 to 150% since most of the R→L shunts were very small. The average difference in $O_2$ saturation between systemic arterial and pulmonary venous blood in animals with block was only 0.2%. In animal 17, the R→L shunt measured 0.66 liter/min, approximately one-fourth of the left-to-right shunt. Given that RA saturation is true mixed venous saturation, and that pulmonary flow is accurate (a reasonable assumption since PA saturation was low, 76%), then the systemic arterial saturation would be 86%. This agrees quite well with the observed value of 84.6% (see appendix for calculations).

**Appendix**

Calculation of systemic arterial saturation given the following:

- $Q_P = 4.64$ liter/min (Fick).
- $Q_{LR} = 2.52$ liter/min (Transducer).
- $Q_{RL} = 0.66$ liter/min (Transducer).
- $PV_{sat} = 95%$.
- $MV_{sat} = 56.6%$ (RA).

1. $Q_{EP} = Q_P - Q_{LR} = 4.64 - 2.52 = 2.12$ liter/min.
2. $Q_S = Q_{EP} + Q_{RL} = 2.12 + 0.66 = 2.78$ liter/min.
3. $(Q_{EP} \times PV_{sat}) + (Q_{RL} \times MV_{sat}) = Q_S \times SA_{sat}$.

Solving for $SA_{sat}$,

$$SA_{sat} = \frac{(Q_{EP} \times PV_{sat}) + (Q_{RL} \times MV_{sat})}{Q_S} = \frac{(2.12 \times 95) + (0.66 \times 56.6)}{2.78} = 86\%$$

$SA_{sat} = 84.6\%$ observed


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Direct Measurement of Intracardiac Blood Flow in Dogs with Experimental Ventricular Septal Defects
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