THE HEMODYNAMIC EFFECTS OF PATENCY OF THE DUCTUS ARTERIOUSUS IN COMPLETE TRANSPOSTION OF THE GREAT ARTERIES

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ABSTRACT

Quantitative assessment of hemodynamics parameters, in particular blood flow, in neonates with complete transposition of great arteries has been difficult and noninvasive data has been limited to pressure estimation. Two dimensional directed pulsed echocardiography was used for the measurements of both aortic valve (right ventricle) and pulmonary valve (left ventricle) flow velocities in 5 neonates with TGA . The measurements were carried before and during a one hour PGE_1 infusion at 0.1 mcg/kg/min following ballon atrial septosomy. Ductus arteriosus (DA) size by 2D imaging increased in all patients. Left and right stroke volume changes were estimated by the product of the Doppler time-velocity integral and heart rate (TVI*HR). During PGE_1 infusion left ventriclular stroke volume decreased while the right ventricular stroke volume increased. Hence PGE_1 in neonates with TGA results in decreasing the LV to RV stroke volume ratio. Enhanced intraatrial mixing in TGA with PGE_1 is midiated, in part, by decreased LV filling and exchanging LV output for PDA shunt.

INTRODUCTION AND BACKGROUND

The circulatory system may be generally divided into two major circuits : the systemic circuit and the pulmonary circuit Fig (1). In normal circulation the oxygenated blood is pumped by the left ventricle to the aorta and its branches and their final subdivisions into the arterioles. Interchange of substances takes place in capillaries and venules and then the unoxygenated blood is collected in small and larger veins which drain into the right atrium. The pulmonary circuit similarly begins with the right ventricle which pump the unoxygenated blood through the pulmonary artery to the lungs where the exchange of gasses takes place and oxygenated blood drains back into the left atrium. The entire system is one complete loop or a SERIES CIRCUIT.

In transposition of great arteries (TGA), which is one of the most common congenital heart diseases, occuring in about 15% of neonates with congenital heart defects, the sytemic and pulmonary circuits form TWO SEPARATE PARALLEL blood-flow circuits Fig (2).

This malformation is characterized by origin of the aorta from the right ventricle and origin of the pulmonary artery from the left ventricle [1]. In such cases the oxygenated blood is directed to the pulmonary circuit and the unoxygenated blood is inappropriatly directed to the body. Unless there is some communications between the two circuits life after birth is not possible. In about half of the cases there is a shunt between the left and right ventricles (ventricular septal defect VSD). A usual common communication is also in the form of an open duct between the pulmonary and the aorta (Patent ductus arteriosus). In the absense of such communications a shunt is created between the left and right atriun (shunt no. 1 in Figure 2) as an emergency procedures shortly after birth to allow mixing between oxygenated and unoxygenated blood.

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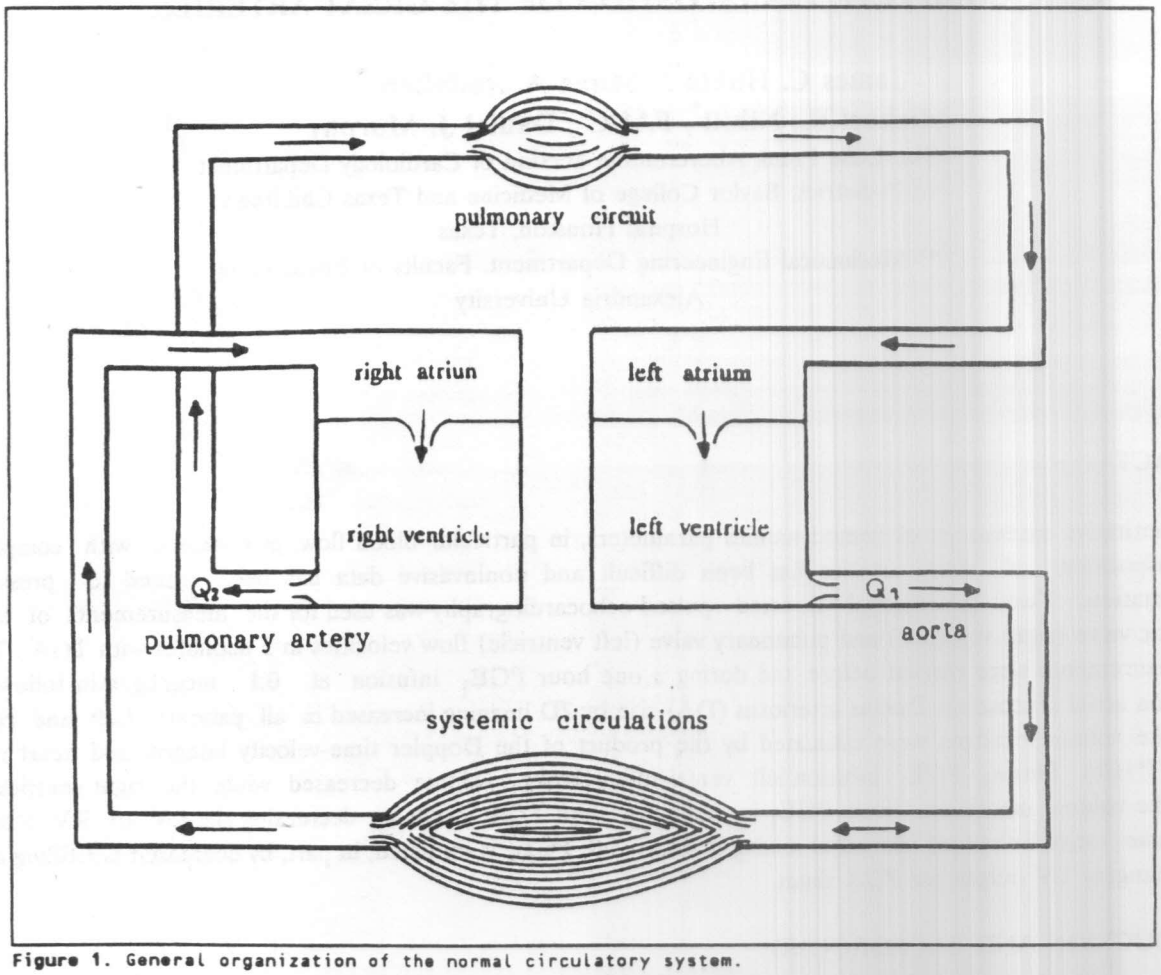

Figure 1. General organization of the normal circulatory system.

Prostaglandin E1 (PGE_1) is currently used for the treatment of cynosis (lack of oxygen in the arterial system) in neonates with TGA [2],[3]. The beneficial effect of this agent is believed to be related to its effect on the dimensions of the ductus arteriosus (shunt no. 2 in Figure 2), and on the resistanse of the pulmonary and systemic circuits [4]. However little information is available concerning the quantitative changes in hemodynamics in neonates with TGA after treatment with PGE_1 . This is due to the fact that cathetarization is impractical and hazardous for longitudinal studies due to the risks of repeated transport to the catheterization laboratory in newborns and the risks of catheter manipulations and vascular diseases.

From a fluid mechanics point of view the problem is that a shunt is to be created between two separate flow circuits with different impedence and different pressure levels. Obviously a bidirectional shunt must be present since unidirectional shunting would results in a progressive drain of the blood from one circuit to another. The advent of noninvasive techniques including two-dimensional echocardiography and directed pulsed doppler echocardiography now allows measurements of flow parameters within the cardiac chambers and great blood vessels [5],[6],[7]. The aim of this work is to apply this technique to answer the following questions: 1) What is the effect of the patency of the ductus arteriosis (i.e the shunt between the aorta and the pulmonary artery) on the flow rate pumped by the left ventricle, (Q_1). 2) How does prostaglandin E1 infusion palliate TGA and increase the systemic arterial saturation.

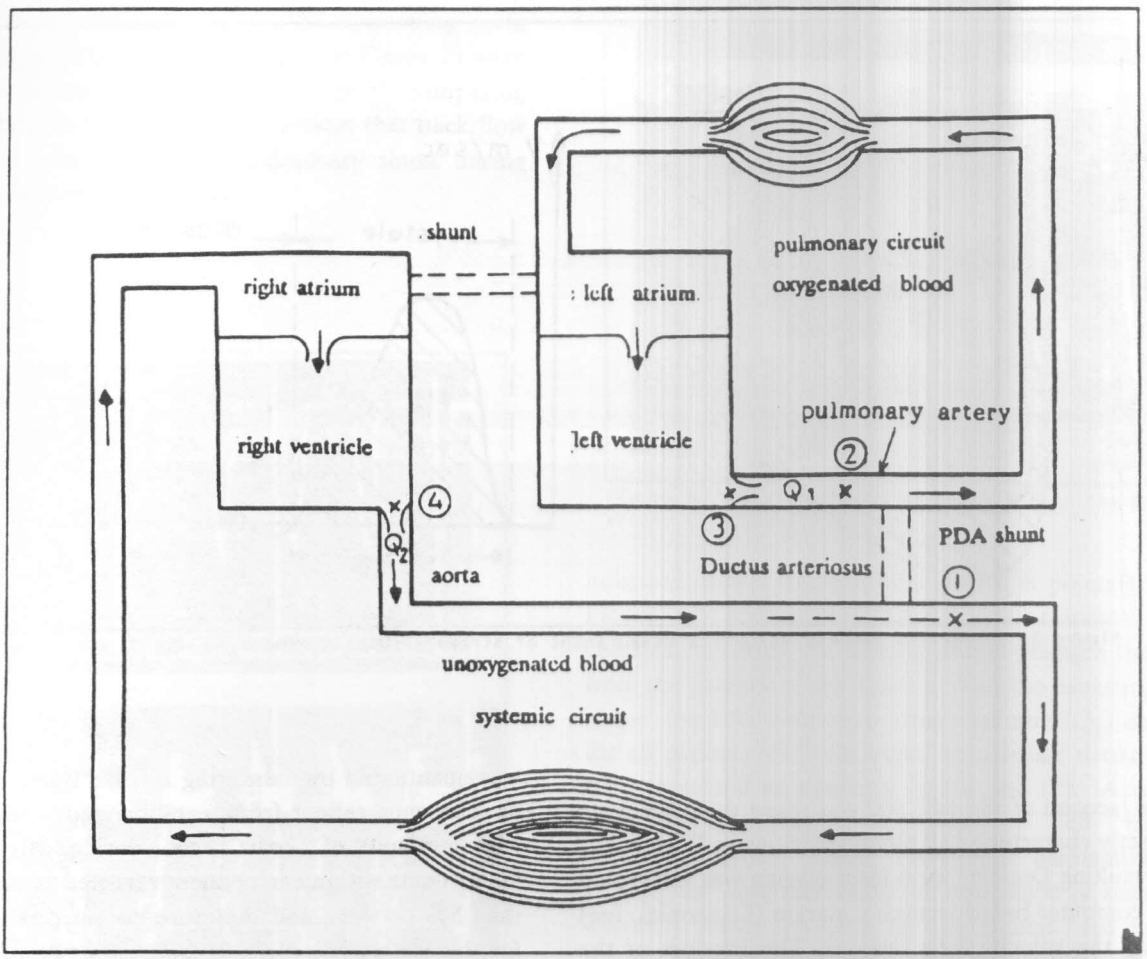

Figure 2. General organization of the circulatory system in transposition of great arteries (TGA).

INSTRUMENTATION AND MEASUREMENTS

Two dimensional echocardiography examinations including segmental analysis of intra and extracardiac anatomy were performed on all patients entered in this study. Special attention were given to image the left and right ventricular outflow tract, the ductus arteriosus and the septum between the left and right atria to evaluate the presence or absence of a shunt. All examinations were done with 7.5 megahertz imaging. To determine the blood velocity the equipment were switched to Doppler mode and the transducer is stopped along any image line and Doppler sample volume is positioned at the selected depth allowing accurate localization of the site where velocity is to be determined. The fast fourier spectral output Doppler shift is automatically converted to velocity of flow in cm/second according to the equation:

$$\text{velocity} = \frac{\text{Doppler frequency shift} \times \text{Velocity of sound}}{2 \times \text{transmitted frequency} \times \cos\theta}$$

where θ is the angle between the direction of blood flow and the Doppler beam. A positive velocity curve indicates flow towards the transducer and a negative curve indicates flow away from the transducer. Efforts were made to obtain as close to a zero axis with the flow of blood as possible in all measurements. Recording of the velocity signal were made simultaneously on video tapes and on heat sensitive paper at 100 mm/second. All Doppler examinations were performed with a MK 600 ATL equipment with 5 megahertz crystal (mid focus). The depth setting were minimized and the other equipment setting were as follows : Wall filter, 400 Hertz; Energy output, 6 db; sample volume size, 5 mm; dynamic range, 35 db; maximum depth, 5 cm; maximum frequency, 12.6 Khz. The maximum detectable velocity

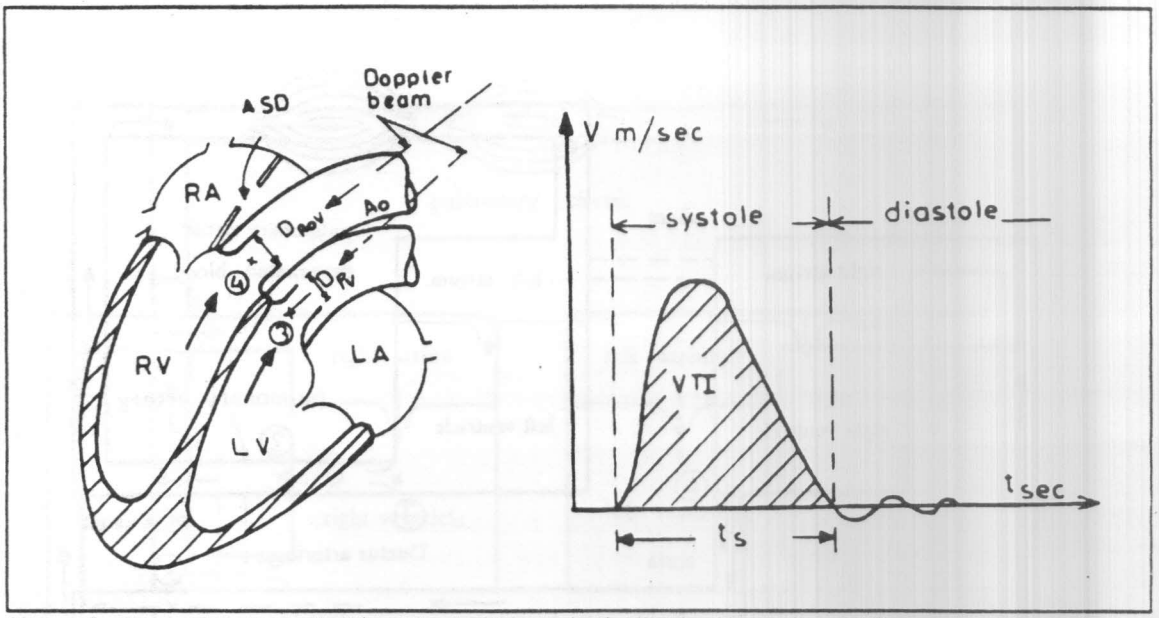

Figure 3. Schematics demonstrating the measurement of stroke volumes Q_1 and Q_2.

of 2.6 m/second of the MK 600 was more than adequate to accuretly characterize all blood velocities in TGA cases.

The resulting Doppler wave form tracing was integrated using a computer based analysis program (Digisonics, Inc) to obtain the velocity time integral. The product of the time velocity integral and the estimated cross-sectional area obtained from two-dimensional echocardiograms yielded an estimate of stroke volume as shown in Fig. (3). i.e Stroke volume = orifice area × velocity time integral

$$\text{left ventricle stroke volume } (Q_1) = \frac{\pi}{4} D^2_{pv} \times \int_0^{t_s} V_3(t)\, dt$$

$$\text{Right ventricle stroke volume}(Q_2) = \frac{\pi}{4} D^2_{Aov} \times \int_0^{t_s} V_4(t)\, dt$$

The ductus arteriosus in TGA could be readily visualized from the suprasternal and high parasternal locations in neanates [8] .Hence simultaneous two-dimensional echocardiographic assessment of the ductus arteriosus was performed during Doppler echocardiography measurements for the purpose of confirming changes in its dimensions. The pulmonary end of the ductus arterious was quantitated by measuring a feeze frame image using an electronic caliper from a standarized window. Measurements of heart rate during stroke volume assessments within each patient revealed variations of less than 5% or less, and therefore no correction was made for this factor.

RESULTS

During (PGE_1) progressive withdrawal, from infussion rate of 0.1 to 0.006 mcg/kg/min and then off, the ductus arteriosus diameter simultaneously decreased until it is totaly closed as visualized by 2-D imaging. The left ventricular stroke volume (Q_1) showed a progressive increase with the prostaglandin discontinued as shown in table(1).

At varrying intervals following ballon atrial septosomy, PGE_1 infussion was instituted for one hour period.

Table 1. LV stoke volume during PGE_1 infusion withdrawal.

PGE_1 dosage (mcg/kg/min)	0.1	0.025	0.012	0.006	OFF
Q_1 (cc)	7.6	9.8	11.5	12.0	13.3

Measurements of aortic velovcity in the descending aorta downstream of shunt no. 2 (point no. 1 in Figure 2) were performed before and after PGE_1 infusion. By comparing the velocity patterns in fig.(4), it is evident that back flow exists as a result of aortic to pulmonary shunt during diastole in case of open ductus.

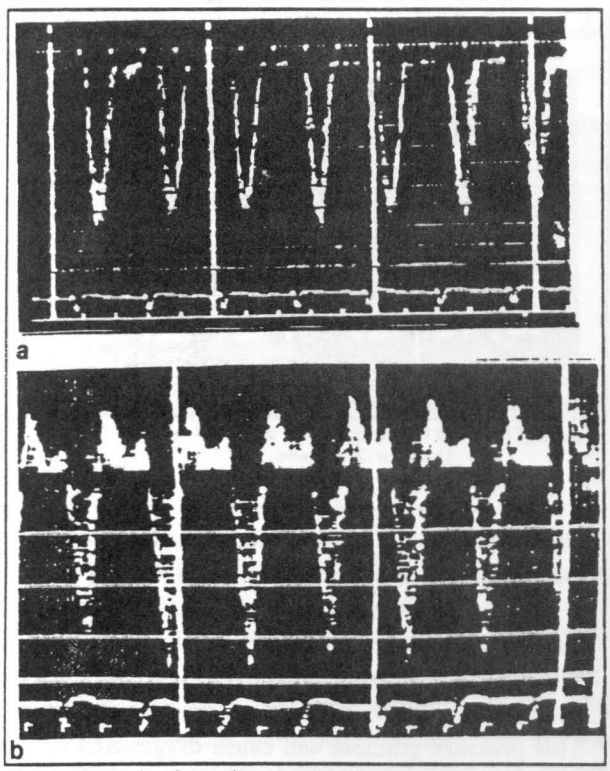

Figure 4. Velocity signal at point 1
a. with shunt # 2 closed.
b. with shunt # 2 open.

The flow of blood through the ductus was also confirmed by Doppler sampling of the main pulmonary artery (point no. 2 in Figure 2). In case of an open ductus a reversed ductus flow directed away from the transducer was noted as shown in fig.(5). Measurements of left and right ventricular stroke volume (Q_1 and Q_2 respectively) were performed prior and after one hour

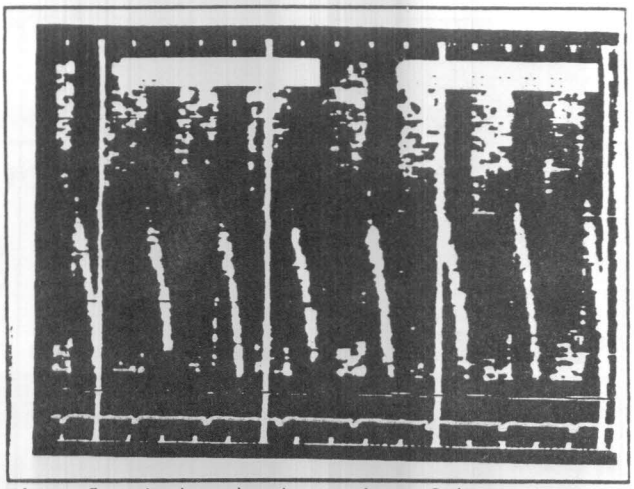

Figure 5. Velocity signal at point # 2 in the pulmonary artery with shunt # 2 open.

infusion. Sample volumes were placed at points 3 and 4 in Figure (2) respectively. These measurements and its changes reflected the hemodynamic changes that result from the patency of the ductus. With the existence of the shunt the left ventricular stroke volume (Q_1) decreased for all patients while the right ventricular stroke volume (Q_2) increased as shown in fig.(6) and (7). Accordingly there was a consistent decrease of left to right ventricular stroke volume ratio with administration of PGE_1 , i.e with increasing the dimension of shunt no. 2. Table(2) shows the data of one patient and table (3) shows the average results for all patients.

DISCUSSION

Little information is available concerning the effects of patent ductus arteriosus in complete transposition of the great arteries with intact ventricular septum in neonates. It is known that prostaglandin E_1 infusion results in patency of the ductus arteriosus and may be useful for palliation of such neonates. The effect of ductus patency has been presumed to be due to supplemental increase in pulmonary blood flow due to aortic to pulmonary shunting through the ductus arteriosus. The data from this study suggest that this in not the case. Left ventricular stroke volume, rather than being maintained during prostaglandin E_1 infusion, decreases .

The mechanism of the increase of the arterial oxygen saturation which results from PGE_1 infusion in TGA is likely to be the result of the following hemodynamic changes;

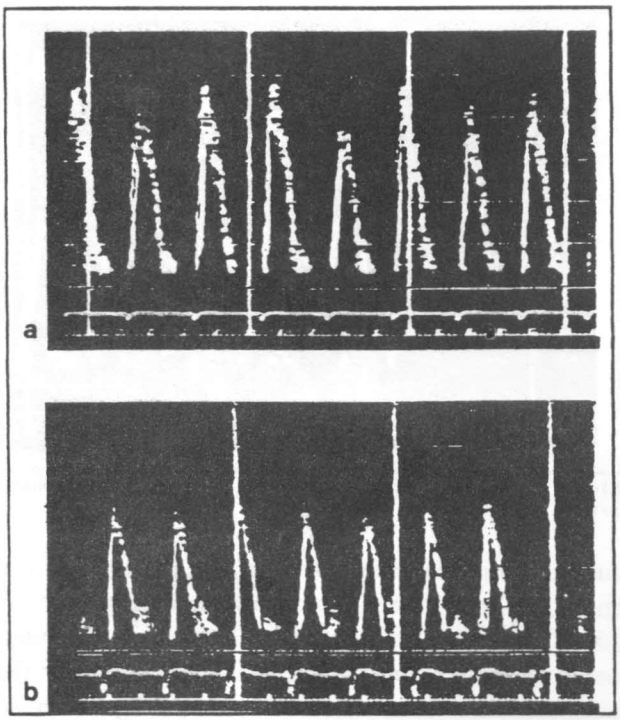

Figure 6. Velocity signal at point # 3
a. shunt # 2 closed.
b. shunt # 2 open.

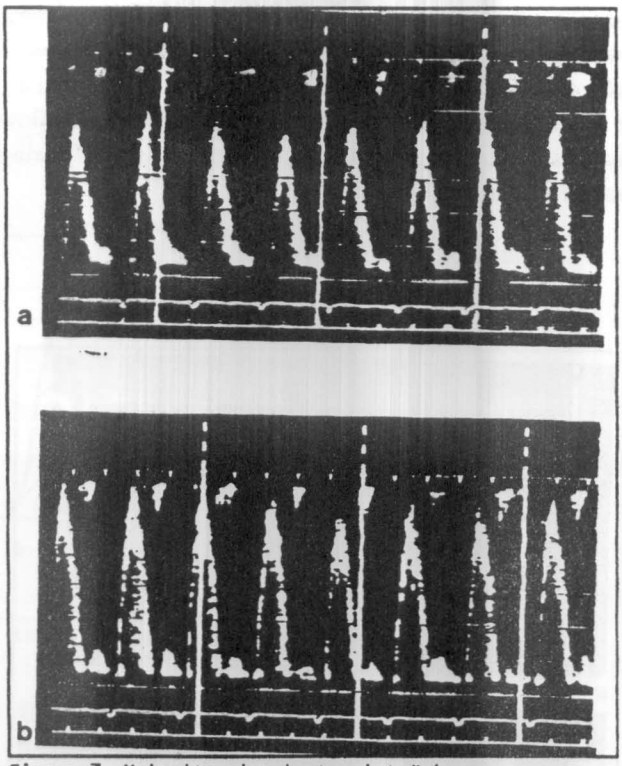

Figure 7. Velocity signal at point # 4.
a. shunt # 2 closed.
b. shunt # 2 open.

1. Communication between the pulmonary and the systemic flow circuits is created with PGE_1 infusion (shunt no. 2).
2. Since the pressure in the systemic circulation is higher than that of the pulmonary circuit, the existence of the shunt will cause the flow of unoxygenated blood from the aorta to the pulmonary artery. The amount of the shunted flow will be governed by the pressure difference between the two circuits and the cross sectional area of the shunt i.e.

$$Q_{(shunt)} = C\, A_{sh} \sqrt{\Delta P / \rho}$$

This shunt flow will be primarily during the diastolic plase of the cardiac cycle, since the high inertia of the forwardly moving blood will prevent it from changing its direction to enter the ductus during systole.

3. As a result of the pulmonary circuit being partially filled during diastole, less pressure gradient across the pulmonary value will be expected during systole. Hence the amount of blood pumped to the lungs by the left ventricle (Q_1) will be diminished. This reduction in the left venticle stroke volume is dependent on the amount of the shunt flow which in turn is a function of the dimensions of the ducts as stated previously.
4. Decreased left ventricle stroke volume (Q_1) results in a decreased lift ventricular filling. The oxygenated blood entering the left atriun will thus accummulate causing the left atriun pressure to increase creating a pressure gradient between the left and right atrium.
5. This pressure gradient will cause oxygenated blood to flow the right atrium through shunt no. 1. The findings that right ventricle stroke volume (Q_2) increases support this concept. Mixing of oxygenated with unoxygenated blood in the right atrium will eventually increase the oxygen concentration in the systemic circulation.

Accurate measurements of pulmonary blood flow in neonates with transposition of the great arteries have not been performed. We speculate that it is feasible for palliation of these neonates with prostaglandin E_1 to be effective without an absolute increase in total pulmonary blood flow. Enhanced mixing results with decrease in left ventricular stroke volume. Each increment of left ventricular stroke volume decrease results in a similar increment in intraatrial mixing. Further research is necessary in order to investigate the

Table 2. Data of one patient showing Q_1 and Q_2 variations with PGE_1 infusion at different time interval.

	LV Stoke Volume (Q_1) (cc)		RV Stroke Volume (Q_2) (cc)		Q_1/Q_2	
	Before PGE	On PGE	Before PGE	On PGE	Before PGE	On PGE
24 hours	14.4	10.3	3.9	5.0	3.7	2.1
48 hours	10.4	8.3	4.2	5.7	2.5	1.5
72 hours	13.3	7.6	4.2	3.7	3.2	2.1
averages	12.7	8.7	4.1	4.8	3.1	1.9

Table 3. Effect of ductus patency on LV to RV stroke volume ratio.

n=8	HR	TVI × HR LV	TVI × HR RV	$TVI_{LV} \times HR$ / $TVI_{RV} \times HR$
Off PGE	135	2122	1125	1.89
On PGE	148	1767	1466	1.21
p value	< 0.05	<0.005	<0.005	<0.005

effects of opening the ductus arteriosus on pulmonary artery pressure and flow.

Potential difficulties with this study relate primarily to the methodology. It was necessary to use extreme care in establishing the same Doppler sampling angle at the pulmonary and aortic valve orifice before and after any intervention. From the suprasternal approach this was possible in all patients.

The unique parallel circulations in transposition of the great arteries with intact ventricular septum result in hemodynamic changes which have no parallel in the usual circulation. The finding that dramatic changes in stroke volume can take place in the left and right ventricular in this situation alter previous concepts in this lesion. This understanding may also have important implications for understanding the fetal circulation where the ventricular outputs are in parallel rather than in series. It is likely that left and right ventricular outputs are independently controlled by their respective preload and afterload and must be measured individually in such situations.

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