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Reversed Shunting Across the Ductus Arteriosus or Atrial Septum In Utero Heralds Severe Congenital Heart Disease

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Objectives. **This study was performed to define the significance of Doppler color flow mapping in demonstrating reversal of the direction of the normal physiologic flow across the atrial septum and ductus arteriosus in the human fetus.**

Background. **Reversal of the physiologic shunting across the ductus arteriosus or atrial septum in utero (i.e., left to right) can be readily identified by Doppler color flow mapping, complemented by pulsed and continuous wave Doppler information.**

Methods. **We reviewed echocardiograms recorded at our three institutions from 1988 to 1993, which displayed reversal of flow by Doppler color flow in 53 fetuses of gestational age 18 weeks to term. The diagnoses were confirmed by postnatal echocardiography, operation or autopsy. Reversal of shunting was consistently associated with severe heart disease.**

Results. **Reversed atrial shunting was found with severe left heart obstructive lesions, including 19 with hypoplastic left heart syndrome, 3 with critical aortic stenosis, 2 with double-outlet right ventricle and 1 each with an interrupted aortic arch, atrioventricular septal defect and severe left ventricular dysfunction due to dilated cardiomyopathy. Reversed ductus arteriosus shunting was found with severe right heart obstructive lesions, including nine fetuses with pulmonary atresia, six with severe obstructive tricuspid valve abnormalities, five with severe tetralogy of Fallot, four with Ebstein's anomaly and two with single ventricle and pulmonary stenosis. Associated cardiac lesions were common in both groups. Only 3 of the 15 infants who were delivered alive from the reverse ductus arteriosus shunt group and 4 of 12 from the reverse atrial shunt group still survive.**

Conclusions. **The finding of reversed flow by Doppler color flow mapping during fetal life provides a key to subsequent accurate diagnosis and denotes a spectrum of diseases with a very poor prognosis.**

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Advances in ultrasound technology, including the addition of Doppler waveform and color flow modalities, have provided accurate information about fetal heart structure, function and hemodynamics. Accurate prenatal echocardiographic diagnosis of congenital heart disease in the fetus is a crucial factor in management decisions. Reversal of the normal shunting patterns (i.e., left to right) through the fetal foramen ovale or ductus arteriosus can be identified rapidly by Doppler color flow mapping. Reliance on Doppler color flow as a diagnostic method is enhanced in the presence of suboptimal imaging found in some fetal cardiac examinations. Such a finding may be a strong discriminator of prognosis or the presence of a major abnormality. The diagnosis can be further refined by pulsed and continuous wave Doppler modalities, which may then further target and refine the two-dimensional imaging. A reversal of the physiologic shunting at either level is associated with serious disturbances of the fetal circulation (1–3); because of the fetal circulatory pathways, reversed atrial shunting is found primarily with severe left heart obstructive lesions, whereas reversed ductal shunting is found with severe right heart obstructive lesions. We pooled the experience from three institutions between 1988 and 1993 using Doppler color flow mapping to define the impact of detecting reversed shunting on diagnosis and outcome.

Methods

A retrospective review of all abnormal fetal echocardiograms performed between January 1, 1988 and December 31, 1993, was undertaken in the fetal cardiac diagnosis laboratories at the University of California, San Francisco; Children's National Medical Center, Washington, D.C.; and the Oregon Health Sciences University, Portland, Oregon. These prenatal studies were performed on patients referred for known congenital heart disease risk factors, including family history, an abnormal or suspicious obstetric scan, maternal diabetes, fetal hydrops and abnormal chromosomes by amniocentesis or chorionic villus sampling. The outcome of each fetus identified as having congenital heart disease was determined. Confirma-

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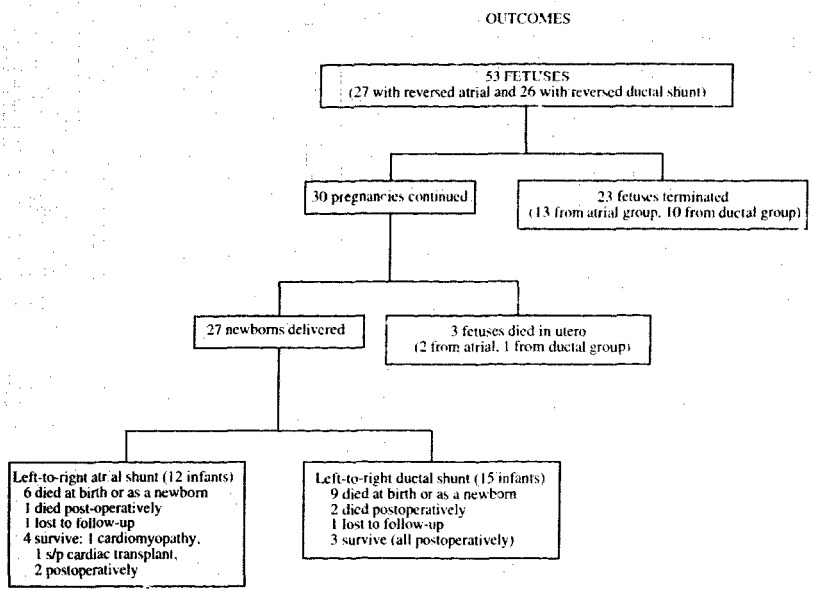

Figure 1. Outcomes of fetuses identified by Doppler color flow mapping as having a reversal of physiologic shunting pathways. s/p = status post.

tion of the prenatal cardiac diagnosis was obtained by autopsy (when available), surgery or routine postnatal follow-up, including clinical, echocardiographic and cardiac catheterization data and surgical reports.

Initial fetal echocardiographic studies were obtained between 15 and 34 weeks of gestation (average estimated gestational age at examination was 24.4 weeks). Repeat studies were performed when possible. All studies included complete high resolution cross-sectional imaging with 3.5-, 5.0- and 7.0-MHz transducers using Acuson or Hewlett Packard ultrasound systems. Four-chamber, long-axis, short-axis and arch views were obtained using previously described two-dimensional imaging techniques (4,5). Doppler color flow signals were carefully obtained at all cardiac levels, including the ductus arteriosus and foramen ovale, using a low Nyquist limit (generally, 10 to 30 cm/s) to provide increased sensitivity to the low velocities of fetal flow. Direction of flow was confirmed with pulsed and continuous wave Doppler modalities when possible.

All patients were informed of the fetal diagnosis at initial presentation and counseled regarding treatment options.

Results

Between 1988 and 1993, a total of 3,250 fetal echocardiograms were obtained at the three centers. From these studies, an estimated 300 studies revealed structural heart disease; 53 fetuses were identified by Doppler color flow mapping as having a reversal of the physiologic shunting pathways—27 with a reversed atrial and 26 with a reversed ductus arteriosus shunt (Fig. 1).

Reversed atrial shunt. All of the patients in the reversed atrial shunt group had severe left heart obstruction, frequently including a variation of the hypoplastic left heart syndrome (19 patients) (Table 1, Fig. 2 [top left and right]). A single fetus had dilated cardiomyopathy, whereas another had an interrupted aortic arch and valvular aortic stenosis. Two fetuses had a double-outlet right ventricle, one associated with mitral atresia and the other with aortic stenosis. Finally, one fetus had an unbalanced atrioventricular septal defect associated with aortic atresia. We found 13 of 27 fetuses in whom the Doppler color flow information clearly indicated reversal of atrial flow, which would not have been suspected by other modalities of ultrasound because the shunt was small or interrogation of the flow disturbance perpendicular to flow (Fig. 2, top left) would have been difficult to interpret.

Reversed ductal shunt. Similarly, all of the patients in the reversed ductal shunt group had some form of severe right heart obstruction. Pulmonary atresia, either as a primary or a secondary lesion, was the most common obstruction (nine fetuses had pulmonary atresia as their primary lesion) (Table 2). However, severe pulmonary stenosis in association with other cardiac lesions, such as with tetralogy of Fallot, was also common (five patients). The remaining fetuses had tricuspid atresia (six patients), Ebstein's anomaly (four patients) or a single ventricle with pulmonary stenosis (two patients). The latter two lesions were always associated with a severe degree of right heart outflow obstruction (Fig. 2, bottom). In 8 of 26

Table 1. Left-to-Right Atrial Shunt

Pt No.	EGA at Echo (wk)	Shunt Velocity (m/s)	Prenatal Diagnosis		Postnatal Diagnosis	Outcome
			First	Second		
1	25		HLHS	Hypo asc aorta	Hypo asc aorta	Died as newborn
2	33	0.5–1.0	HLHS	Aortic atresia	Aortic atresia	Died DOL 1
3	30		Cardiomyopathy		Cardiomyopathy	Survived
4	35	0.4	HLHS	Aortic atresia	Aortic atresia	Died preop
5	26		DORV	Mitral atresia		TOP
6	30	0.6	Valvular AS	Hypo LV		Lost to follow-up
7	20		DORV	AS		TOP
8	34	0.4	HLHS	Aortic atresia	Aortic atresia	Died postop
9	25		HLHS	CoA	CoA	Died DOL 7
10	22	0.5	HLHS	Aortic atresia	Aortic atresia	TOP
11	28		HLHS	EFE	EFE	TOP
12	24		Interrupted arch	Valvular AS		TOP
13	22	0.95	HLHS	Hypo asc aorta		Died as newborn
14	21	0.4	HLHS	EFE	EFE	TOP
15	18	0.4	Single ventricle	Mitral atresia		TOP
16	22	> 1.0	HLHS	Aortic atresia		TOP
17	15	0.25	Critical AS	Hypo asc aorta		TOP
18	28	0.6	AVSD-unbal	Aortic atresia	Aortic atresia	Died as newborn
19	22		HLHS	Hypo asc aorta		TOP
20	24		HLHS	Aortic atresia		TOP
21	24		HLHS	Aortic atresia		TOP
22	23		HLHS	Aortic atresia	Aortic atresia	Survives postop
23	22		HLHS	Hypo asc aorta	Hypo asc aorta	Survives postop
24	23		HLHS	Aortic atresia		TOP
25	24		Critical AS	EFE		Stillborn
26	27	> 1.0	Critical AS	EFE		Stillborn
27	31	> 1.0	HLHS		HLHS	Survives transplantation

AS = aortic stenosis; asc = ascending; AVSD-unbal = atrioventricular septal defect–unbalanced; CoA = coarctation of the aorta; DOL = day of life; DORV = double-outlet right ventricle; Echo = echocardiography; EFE = endocardial fibroelastosis; EGA = estimated gestational age; HLHS = hypoplastic left heart syndrome; Hypo = hypoplastic; LV = left ventricle; postop = postoperatively; preop = preoperatively; Pt = patient; TOP = termination of pregnancy.

fetuses, a ductus right-to-left shunt was recognized initially by the Doppler color flow modality.

Outcome. Of the 53 pregnancies in which the fetus was identified as having a reversed shunt, 23 were terminated electively after discussion with families and referring physicians. Of the remaining 30 fetuses, 3 were delivered stillborn. The other 27 fetuses (51%) were delivered, including 12 with a reversed atrial shunt (44% of the original reversed atrial shunt group) and 7 with a reversed ductal shunt prenatally (27% of the original reversed ductal shunt group).

The prognosis for both groups was uniformly poor. Of the 12 infants born from the reversed atrial shunt group, 6 died in the newborn period, including 1 who died postoperatively and 1 who was lost to follow-up. Only four infants survived (15% of the original 27 in the reversed atrial shunt group), including one with dilated cardiomyopathy, two who are status post stage 1 Norwood procedure for hypoplastic left heart syndrome and one who underwent cardiac transplantation for hypoplastic left heart syndrome.

Of the 15 infants born from the reversed ductal shunt group, 8 died in the newborn period without intervention, 3 died postoperatively and 1 survived initially and was later lost to follow-up. Only three infants have been verified as surviving (12% of the original 26 fetuses in the reversed ductal shunt group).

Discussion

Value of color flow imaging. Reversed shunting through the fetal atrial or ductus arteriosus communications is quickly and easily defined by Doppler color flow mapping during fetal echocardiography. It is most important to realize that the quality of imaging may be suboptimal because of maternal factors, fetal lie or the overall nature of the disease and the minute sizes of the structures to be imaged. It is in these areas that the addition of Doppler color flow mapping adds immeasurably to the overall examination. The recognition of a structure by the flow signal within a chamber or vessel focuses the examination on the abnormal structure and vice versa, making separation and value of the modality subjective. This finding has been observed frequently since Doppler analysis of blood flow characteristics became standard practice during fetal echocardiographic evaluations (6–9). Reversal of normal fetal flow direction results from blood flow bypassing a left- or

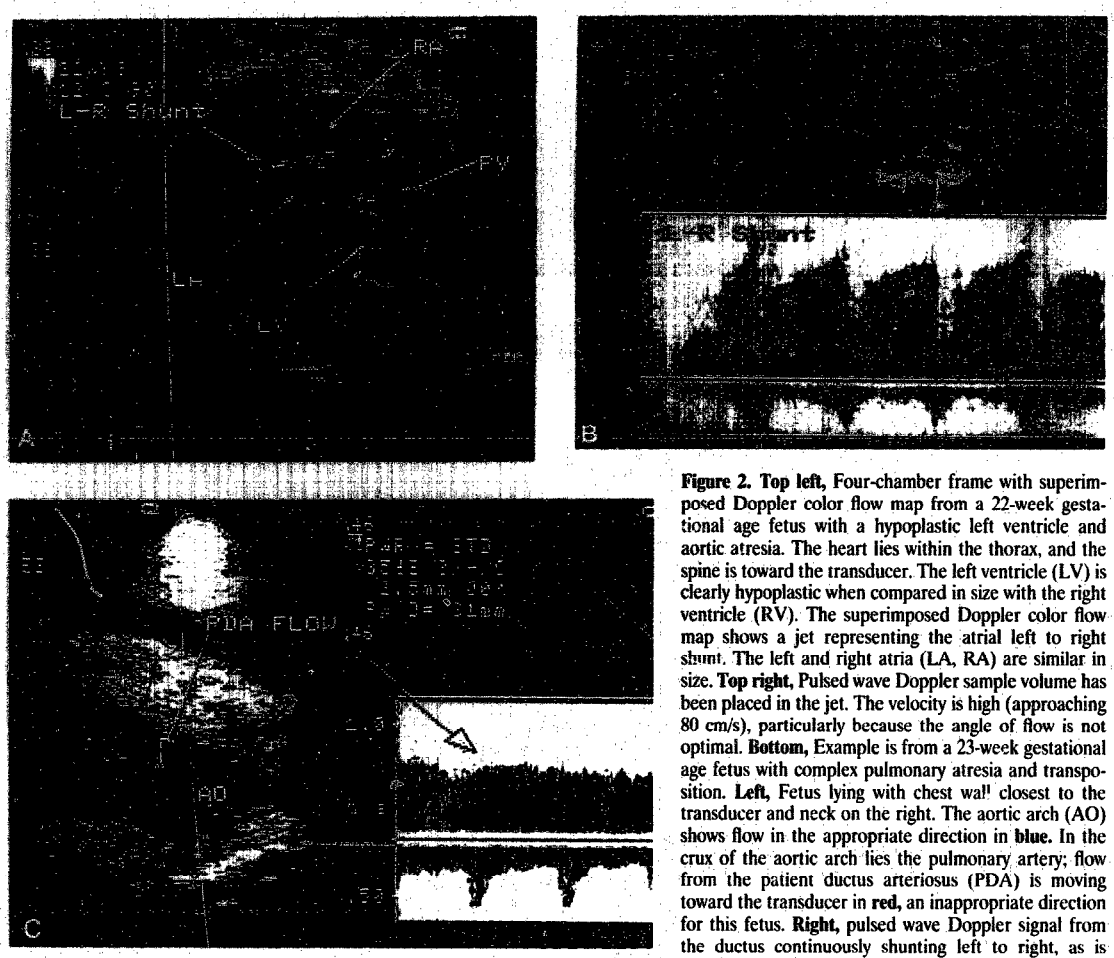

Figure 2. Top left, Four-chamber frame with superimposed Doppler color flow map from a 22-week gestational age fetus with a hypoplastic left ventricle and aortic atresia. The heart lies within the thorax, and the spine is toward the transducer. The left ventricle (LV) is clearly hypoplastic when compared in size with the right ventricle (RV). The superimposed Doppler color flow map shows a jet representing the atrial left to right shunt. The left and right atria (LA, RA) are similar in size. **Top right,** Pulsed wave Doppler sample volume has been placed in the jet. The velocity is high (approaching 80 cm/s), particularly because the angle of flow is not optimal. **Bottom,** Example is from a 23-week gestational age fetus with complex pulmonary atresia and transposition. **Left,** Fetus lying with chest wall closest to the transducer and neck on the right. The aortic arch (AO) shows flow in the appropriate direction in **blue.** In the crux of the aortic arch lies the pulmonary artery; flow from the patient ductus arteriosus (PDA) is moving toward the transducer in **red,** an inappropriate direction for this fetus. **Right,** pulsed wave Doppler signal from the ductus continuously shunting left to right, as is typically observed after birth.

right-sided obstructive lesion. On the left side, diminution of mitral forward flow, due to obstruction or ventricular dysfunction, yields an atrial left-to-right shunt. On the right side, diminished flow across the pulmonary valve causes pulmonary blood flow to be supplied through the ductus. Because the pulmonary vascular resistance is high, the velocity may be low and difficult to detect unless the Nyquist limit is low; however, some fetuses have disturbed flow, which is easier to detect. The Nyquist limit was set for maximal ranges of 10 to 30 cm/s, as described above.

Primary recognition of shunting by Doppler color flow imaging. Reversed shunting, as defined by Doppler color flow mapping, is therefore an indirect but readily detectable sign of obstruction. The presence of atrial left-to-right shunting was the point of recognition by Doppler color flow imaging in 13 of the 27 fetuses, whereas in 8 of 26 fetuses, this modality was the point of recognition of ductus right-to-left shunting. In the rest of the examinations the structural anomaly could be identified primarily. Reversed atrial shunting provided diagnostically valuable information, particularly in those fetuses with aortic stenosis and cardiomyopathy. Recognition of the ductus left-to-right shunt provided important information about the ductus-dependent nature of several of the lesions, including the patients with Ebstein's malformation and five fetuses with tetralogy of Fallot and pulmonary atresia or transposition with pulmonary stenosis.

Implications. It is clear that the prenatal finding of reversed atrial or ductus arteriosus shunting implies complex congenital heart disease, with major diminution of forward blood flow to the corresponding great vessel. Based on detection of flow patterns by Doppler color flow, the survival of fetuses in this series was very poor (7 [13%] of 53), and even

Table 2. Left-to-Right Ductal Shunt

Pt No.	EGA at Echo (wk)	Shunt Velocity (ms)	Prenatal Diagnosis		Postnatal Diagnosis	Outcome
			First	Second		
1	28		PS	VSD	Pulm atresia	TOP
2	18	0.5	Tricuspid atresia	VSD		TOP
3	21	0.6	Pulm atresia	Dandy-Walker		Died at birth
4	29		TOF	Pulm atresia		TOP
5	20	0.8	PS	VSD	VSD	TOP
6	24	< 1.0	DILV (SV)	PS	PS	Died postop
7	23	0.75	D-TGA	Hypoplastic PA		TOP
8	22		Pulm atresia	Trisomy 13	Trisomy 13	Died DOL 1
9	19	0.5	AVSD-unbal	Pulm atresia		TOP
10	22	0.8	Ebstein's anom	Pulm atresia	Pulm atresia	TOP
11	32	< 1.0	Ebstein's anom	Critical PS	Critical PS	Died postop
12	22	0.87	Pulm atresia	D-TGA	D-TGA	TOP
13	26		Severe PS		Tricuspid atresia	Died at birth
14	24	1.75	TOF	D-TGA	D-TGA	TOP
15	24		TOF	Severe PS		Lost to follow-up
16	31		Ebstein's anom	PS	PS	Died as newborn
17	27		Ebstein's anom	Pulm atresia	Pulm atresia	Died as newborn
18	30		TV dysplasia			Died as newborn
19	29		Unguarded TV		Unguarded TV	Stillborn
20	28		SV	PS	SV	Survived
21	32		DORV	PS	DORV/PA	Died at birth
22	30		PS	VSD	Pulm atresia	Survived
23	24		Pulm atresia	Hypo RV	Hypo RV	Died at birth
24	22		Tricuspid atresia	VSD		TOP
25	26		Pulm atresia	Hypo RV	Hypo RV	Survived
26	23		Pulm atresia	Asplenia syndrome	Asplenia syndrome	Died as newborn

anom = anomaly; DILV = double-inlet left ventricle; D-TGA = dextro transposition of the great arteries; PA = pulmonary artery; PS = pulmonary stenosis; Pulm = pulmonary; RV = right ventricle; SV = single ventricle; TOF = tetralogy of Fallot; TV = tricuspid valve; VSD = ventricular septal defect; other abbreviations as in Table 1.

worse than found in previous studies of fetuses referred for similar prenatal risk factors for congenital heart disease (5,10–13). These previous studies relied heavily on two-dimensional imaging and the standard four-chamber view, which may have limited the ability to diagnose abnormalities of the great vessels (10,14). The majority of fetuses in this series had lesions that frequently involved abnormalities of the great vessels. Doppler color flow mapping may more readily demonstrate abnormal flow patterns commonly associated with the abnormalities described in this series of fetuses (6,9,15–18) than actual imaging of the primary lesion responsible for the abnormality. If the pregnancies that were electively terminated are disregarded, however, the survival of the remaining fetuses is similar to previous studies (7 [23%] of 31).

The merits and limitations of Doppler color flow mapping have been described (6–9). However, the increased ability to diagnose congenital heart disease using Doppler color flow mapping, combined with the standard two-dimensional views, would explain the lower rate of survival of these fetuses than predicted by earlier studies.

Conclusions. We found reversed shunting through the atrial septum or ductus arteriosus in utero, as defined rapidly and effectively by Doppler color flow mapping, to be associated consistently with severe structural, and less commonly, functional congenital heart disorders. Routine evaluation in the fetus suspected of having structural heart disease, including defining flow in these fetal pathways, may focus attention on the abnormal morphology and provide documentation of disordered fetal cardiac physiology associated with left- or right-sided cardiac obstruction. In addition, the technique may have added benefit to those clinicians primarily concerned with fetal diagnosis. The use of Doppler color flow mapping may be of particular benefit for focusing attention on a targeted fetal cardiac examination.

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