In view of the need for a more basic understanding of the nature of shunting mechanisms in many types of congenital heart disease, a method of studying such phenomena has been developed in our laboratory. This investigation was designed primarily to delineate the mechanisms and timing of shunting across the ventricular defect in a situation where systemic systolic pressures are present in both ventricles. This communication is concerned with pressure-flow dynamics in patients with tetralogy of Fallot. It is generally considered that the right-to-left shunt occurs as the right ventricle ejects blood into the aorta; however, the exact nature of shunting across the ventricular defect has not been delineated, and this formed the main purpose of the present investigation.

Methods

Twenty-nine clinically cyanotic children between the ages of 3 and 14 years were studied at the time of preoperative cardiac catheterization under light nitrous oxide anesthesia in the supine position. Biplane cineangiocardiology demonstrated all patients to have infundibular pulmonary stenosis and a ventricular septal defect.

The magnitude of the right-to-left shunt was calculated by the use of blood oxygen saturation data (Fick principle).

Oxygen content of inspired air and blood was measured with an Instrumentation Laboratories 113 pO₂, pCO₂, and pH meter. The inspired air was sampled intermittently to maintain the oxygen concentration between 20.5 and 21.0 vol%.

Pressure Recordings

The study was designed to measure the instantaneous pressure differences between the two ventricles and between the right ventricle and the ascending aorta just above the aortic valve. This was done by using two matched catheter systems; the right ventricular catheter was passed to the heart via the saphenous vein and the catheter to the left ventricle via the femoral artery. To ensure the validity of the varying pressure gradients throughout the cardiac cycle and to exclude the possibility of artificial pressure gradients, each recording was repeated following reversal of the catheter positions. In each instance, similar gradients were obtained. No. 6 and 7 catheters with lateral holes and the ends sealed were employed. Prior to each study, the catheters were matched for equal length, volume, and transmission time. The entire catheter-recording systems included Statham P23Gb pressure transducers connected to Sanborn 350-1100 preamplifiers. The static unbalance of both systems was evaluated to be no greater than ±0.1% over the range of 0 to 300 cm of water. The dynamic response of the entire system was found to be over-damped and flat to 7 cycles per second as determined with the use of a sinusoidal pressure generator. The catheter impulse transmission time was 5 to 15 msec. The characteristics of the entire system approached the dynamic response criteria for pressure gradient determinations as outlined by Greenfield and Fry. To determine the continuous pressure differences, the output of the preamplifiers was connected to a Heathkit EC-1 analog computer. The analog computer was programmed to subtract the right ventricular from the left ventricular pressure. The difference was fed back to the recording system and was recorded photographically and on tape simultaneously with the electrocardiogram and both ventricular pressures (fig. 1).

Prior to and after each recording, zero base-line
conditions referenced to the midchest position were checked to ensure that there were no baseline shifts.

**Determination of Flow**

To study the timing of the bidirectional shunt across the defect, biplane cineangiography was chosen because of the rapid response time it provided with 5 msec frame exposures at the rate of 60 frames per second. This method allows for determination of changing events within a period of less than 20 msec. In order to relate the timing of the shunt to the cardiac cycle, a special photocell device was used in the beams of both the anteroposterior and lateral image amplifier tubes. The outputs of the photocells were simultaneously recorded with the electrocardiogram graphically and on magnetic tape. The latter was replayed for expansion of the time scale in order to relate the individual cine pulses to the electrocardiogram in real time (fig. 2 A and B). Further studies were performed to determine the delay time of (a) the onset of x-ray exposure of each cine pulse to the inscription of the recorded impulse through the timing device system; and (b) the onset of the x-ray impulse to the appearance of the image on the output phosphor of the image amplifier tube. No time delay was found (less than 1 micro-second). Contrast studies utilized sodium diatrizoate (75% Hypaque-M), 1 ml per kilogram of body weight. Each injection was made with an Amplatz injector which delivered the bolus over a period of 1 sec. Injections into the left ventricle were used to study the left-to-right shunt and into the right ventricle to study the right-to-left flow across the defect. Great care was taken in positioning the catheters in their respective ventricles to avoid the production of premature beats. Rarely premature beats occurred, and such injections were excluded from analysis for timing of the shunt.

To determine that the injection of contrast media did not significantly alter the timing and direction of the shunt, right ventricular pressures were measured during the time of injection in 13 patients. Additionally, in six patients, left and right atrial injections of contrast media were done while both ventricular pressures and their pressure differences were recorded. Coincident with the injection, the ventricular systolic pressures remained stable, or increased the peak systolic pressure a maximum of 4 mm Hg (fig. 2A). With atrial injections, the pattern of flow across the ventricular defect and the simultane-

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**Figure 1**

*Pressure gradient relationships throughout the cardiac cycle in moderate tetralogy of Fallot. The simultaneously recorded electrocardiogram (above), instantaneous pressure gradient (center), and left (LV) and right (RV) ventricular pressures are shown. (A). Period favoring left-to-right gradient. The left ventricular pressure remained slightly higher than the right during diastole with accentuation of the left-to-right pressure gradient during isovolumic ventricular contraction. (B). Period favoring the right-to-left gradient. Asynchronous fall of the pressures during isovolumic ventricular relaxation, with the left ventricle leading the right, resulted in a right-to-left gradient during this period.*

**Figure 2**

*Data recorded during biplane cineangiography. All data were recorded photographically at a low paper speed (A) and simultaneously on magnetic tape for playback with expansion of time scale (B). The arrow indicates the onset of injection. (A). Type of data recorded during cine studies. The anteroposterior and lateral cine units photocell timing device outputs (top), the aortic pressure (middle), and the simultaneous right ventricular pressure (bottom) during injection of contrast material into the right ventricle (arrow). Coincident with the injection, right ventricular systolic pressure remained stable, or rose a maximum of 4 mm Hg as indicated here. (B). Replay from magnetic tape with expansion of time scale. This demonstrates the 60 per second individual cine spikes of the photocell timing device for the anteroposterior and lateral image amplifier tubes which could accurately be related to the electrocardiogram (top) and right ventricular pressure tracing (bottom).*

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ously recorded pressure gradient remained unaltered when compared to the ventricular injections. None of these patients showed a right-to-left shunt at the atrial level. Because of the possible influence of respiration, all patients were studied during periods of apnea.

**Correlation of Flow with Instantaneous Pressure Gradients**

The correlation of the onset and direction of flow across the defect with the pressure gradient was performed in the following manner: The selected cine frames were related to their cine spikes as obtained from the photocell device previously described, and their time relationship to the electrocardiogram was noted (fig. 2). After previously determining the catheter response delay time, this point on the electrocardiogram was, in turn, related to the recorded pressure gradient tracing through its simultaneously recorded electrocardiogram. Thus, each cine frame could be related in real time to the pressure gradient (fig. 3). Care was taken in this correlation to ensure that the heart rate remained constant by measurement of the R-R intervals.

It should be emphasized that no attempt was made to quantitate the flow across the defect during this study; the above correlation was merely concerned with the timing of the onset of a pressure gradient favoring either ventricle and the onset of flow across the defect in the direction suggested by such a gradient.

**Results**

Twenty-seven children, in whom the right-to-left shunt ranged between 21% and 45% of systemic flow and who were categorized as having moderate Fallot’s complex, constituted a homogeneous hemodynamic group of patients. Two patients, aged 3 and 12 years, fell into a more severe group with their right-to-left shunts comprising 66% and 75% of systemic flow. Heart rates ranged between 80 and 130 beats per minute.

In correlating the pressure dynamics with the direction of flow across the ventricular defect as visualized by cineangiocardiography, detailed analysis of cine frames showed an excellent correlation between these two parameters. The onset of flow in either direction across the defect commenced simultaneously with the occurrence of a pressure

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**Figure 3**

Timing of the right-to-left shunt across the ventricular defect in moderately severe tetralogy of Fallot. The boxed-in area B of figure 1 is illustrated at the top. Below are the cine frames coinciding in time with various points of the gradient curve. The right-to-left shunt across the defect during the period of isovolumic ventricular relaxation is illustrated.
gradient favoring the ventricle (that is, the pressure being greater in that ventricle) from which flow occurred. No delay was detected between the occurrence of a pressure gradient and the actual onset of flow across the defect.

Moderate Tetralogy of Fallot

In the 27 patients constituting the moderate group of the Fallot complex, a consistent pressure gradient pattern was found throughout the cardiac cycle (Fig. 1). During ventricular diastole, the left ventricular pressure remained slightly higher than that of the right with the pressure gradient favoring the left ventricle. Isovolumic ventricular contraction was characterized by asynchronous rise in the pressures with marked accentuation of the left ventricular pressure gradient. After the opening of the aortic valve and the commencement of systolic ejection, the right ventricular pressure exceeded that of the left for a short period. This resulted in a transient pressure gradient favoring the right ventricle during early ejection. For the remainder of the ejection period, there were small pressure differences between the two ventricles. Subsequently, isovolumic relaxation (that is, the period from aortic valve closure to the beginning of diastole) was characterized by asynchronous fall of the ventricular pressures. The period of isovolumic relaxation was characterized by a large pressure gradient (18 to 20 mm Hg) favoring the right ventricle. This gradient rapidly reversed as isovolumic relaxation came to an end and favored the left ventricle during the period of rapid filling and the remainder of diastole. Thus, there were two periods during the cardiac cycle in which the pressure gradient favored the right ventricle, namely (a) the early ejection phase of ventricular systole, and (b) the period of isovolumic ventricular relaxation. However, a left ventricular pressure gradient occurred during late systolic ejection and the entire period of diastole, the latter being accentuated during isovolumic ventricular contraction.

Dynamics of the Right-to-Left Shunt (Fig. 3)

The boxed-in area B of the pressure gradient shown in Figure 1 is reproduced in Figure 3 with the time related individual cine frames demonstrating the timing of the right-to-left shunt across the ventricular defect during the period of isovolumic ventricular relaxation. As noted, this period was characterized by a large pressure gradient favoring the right ventricle. Cine studies demonstrated that all patients had right-to-left shunting across the defect during this interval. Although the period of early ventricular ejection revealed a pressure gradient favoring the right ventricle, cine studies revealed the absence of shunting across the defect during this interval when both ventricles were ejecting blood into the aorta.

Dynamics of the Left-to-Right Shunt (Fig. 4)

Cine frames related to the reproduction of the boxed-in area A of Figure 1 are shown in Figure 4 to depict the left-to-right shunt across the defect during the period favoring the left ventricular gradient. During the latter part of isovolumic relaxation, the pressure gradient favored the right ventricle and no left-to-right shunting was noted on biplane cineangiography. With the commencement of diastole and the appearance of a left-to-right ventricular pressure gradient, shunting of blood in this direction occurred across the defect, as depicted on the cine frames related to the pressure gradient. The shunt was noted to accentuate coincident with the increase in the left ventricular pressure gradient during isovolumic ventricular contraction. During the latter period of ventricular ejection, although there was a pressure gradient favoring the left ventricle, there was no flow across the defect.

Discussion

Shunting mechanisms and the pressure-flow dynamics in patients with tetralogy of Fallot have been the subject of much thought and speculation among investigators for many years. Although a vast literature pertaining to the Fallot complex exists, no detailed study of the pressure-flow dynamics across the ventricular defect has been noted. Kjellberg and associates considered that the es-
Dynamics of left-to-right shunt in moderately severe tetralogy of Fallot. The boxed-in area A of figure 1 is reproduced at the top demonstrating the direction of the pressure gradient during ventricular diastole and isovolumic ventricular contraction. Below are shown the time-related individual cine frames demonstrating the left-to-right shunt commencing during early diastole with augmentation during isovolumic ventricular contraction.

Essential hemodynamic factor in tetralogy of Fallot was a shunt from the right ventricle into the aorta. Bing and co-workers documented the occurrence of bidirectional shunting with some arterialization of the right ventricle and indicated that the right-to-left shunt was due to blood coursing through the interventricular septal defect and the overriding aorta directly into the systemic circulation.

The present study has indicated that the direction and timing of shunting across the ventricular defect in tetralogy of Fallot are largely dependent upon asynchronous activity of the two ventricles. A detailed discussion of the complex interrelationships of many factors influencing the asynchronous activity of the ventricles during isovolumic contraction and relaxation is presented in the "Appendix." Flow into the pulmonary artery consistently began 30 to 65 msec before opening of the aortic valve during the period of isovolumic contraction. Interestingly, following injections of contrast media into the left ventricle, during isovolumic contraction the accentuation of the left-to-right shunt could be visualized to occur into the pulmonary artery before opening of the aortic valve. Thus, the period of "isovolumic" or "isovolumetric" ventricular contraction may have to be viewed differently in tetralogy patients than in normals. During this interval, left ventricular volume is decreasing as flow occurs into the right ventricle; the volume of the right ventricle may change as blood enters from the left and as flow occurs into the pulmonary artery. Also, during "isovolumic relaxation," the left ventricle is receiving blood across the defect from the right ventricle. We were unable to ascertain from our cine data whether flow into the pulmonary artery continues during this phase. If so, the right ventricular volume during isovolumic relaxation decreased due to continuing flow into the pulmonary artery and to flow across the defect into the left ventricle. Therefore,
in tetralogy of Fallot, this phase is characterized by a decreasing right and increasing left ventricular volume.

We found no evidence under the control conditions used that the injection of contrast media artificially produced shunting of the blood across the defect at times other than those indicated by the direction of the pressure gradient. Previously, Kjellberg and co-workers suggested that the injection of contrast media might produce flow across the defect. Our studies indicated that if injection of contrast media into the right ventricle in tetralogy of Fallot produced hemodynamic shunt changes, these changes were localized to the period of ventricular ejection with flow of contrast media directly into the aorta (in the absence of induced premature beats). Simultaneously recorded ventricular pressures during cineangiocardiography remained stable at the time of injection, or showed an increase of systolic pressure up to 4 mm Hg (fig. 2A). This is consistent with the findings of Dodge and co-workers. Additionally, following injection of contrast media into the right or left atrium, the pressure gradient across the ventricular defect did not change during the cine run. Although intracardiac injection of contrast media may produce hemodynamic changes, the magnitude of such changes and their effect on shunting mechanisms remain to be clarified.

In the moderate group, in which the right-to-left shunt constituted between 21% and 45% of the systemic flow, the increasing left ventricular gradient during isovolumic contraction resulted in augmentation of left-to-right shunting across the defect. The findings also suggested that opening of the aortic valve was due to pressure transmitted by left ventricular contraction to the subvalvular space, as opposed to pressure generated by the right ventricle (fig. 5). The rise in aortic pressure occurred at a time prior to its intersection by the right ventricular pressure (as recorded near the apex of the right ventricle). A consistent finding in this group was that the right-to-left shunt occurred at two phases of the cardiac cycle and at two sites. During early ventricular ejection, the shunt occurred directly into the aorta from the right ventricle; during isovolumic relaxation, the right-to-left shunt occurred across the ventricular defect into the left ventricle (fig. 5). There was no shunt into the left ventricle during early ventricular ejection despite the fact that the right ventricular pressure exceeded that of the left, when both ventricles were ejecting blood into the aorta. Thus, a consistent pattern in this group of patients was found concerning the relationship of the direction of the pressure gradient and the shunt across the ventricular defect in the various phases of the cardiac cycle. The bidirectional shunt across the ventricular defect occurred largely during the periods of isovolumic ventricular contraction and isovolumic ventricular relaxation and was related to the asynchronous activity of the two ventricles; additionally, a diastolic left-to-right shunt was shown.

The two patients constituting the severe
group of Fallot's complex demonstrated a similar phenomena of asynchronous pressure rise and fall during isovolumic ventricular contraction and relaxation; however, the pattern occurred in a reverse manner when compared to the moderately severe group (fig. 6). The right-to-left gradient and shunt increased during isovolumic ventricular contraction, and during isovolumic relaxation and early diastasis, the right ventricular pressure fell below that of the left resulting in a left-to-right gradient and shunt. These findings warrant further study since they may prove useful in providing evidence of the hemodynamic severity of the condition in patients with tetralogy of Fallot.

The finding of bidirectional shunting across the ventricular defect is consistent with the studies of Gamble and co-workers in which they utilized fiberoptic catheter methods to record ventricular oxygen saturation changes throughout the cardiac cycle in a patient with tetralogy of Fallot. However, direct visualizaton of the shunt locally across the defect may indicate instantaneous events somewhat more reliably without a time lag as probably involved in fiberoptic studies due to catheter tip positioning away from the defect. Their results indicated left-to-right shunting into the right ventricle during ventricular systole. Cine data indicate that, when blood is shunted across the ventricular defect, its movement occurs in such a fashion that time is required for mixing throughout the ventricular chamber. This phenomenon is consistent with the time lag noted in the work of Gamble and associates as compared to the results of the present investigation.

These studies indicated that in patients with moderately severe tetralogy of Fallot the period of diastole is characterized by blood flow from the left atrium entering the left ventricle and spilling over into the right ventricle; whereas, in the two patients with severe tetralogy of Fallot, the period of diastole was characterized by the right atrium contributing flow to the right ventricle which spilled over into the left ventricle during rapid ventricular filling. Since flow may occur easily across a large ventricular defect in tetralogy patients, the ability of either atrium to contribute to the filling of both ventricles may have important implications concerning the volume of both ventricles in such patients.

**Summary**

The present study was conducted to determine the instantaneous pressure-flow relationships across the ventricular septal defect in tetralogy of Fallot. Simultaneous right and left ventricular pressures and the pressure gradient were recorded with matched catheter systems. Biplane cineangiocardiology was used to evaluate the timing of the bidirectional shunts during various phases of the cardiac cycle. The instantaneous pressure differences between the two ventricles and the direction of the pressure gradient correlated well with the timing of the shunt across the defect.

In 27 patients with moderate tetralogy of Fallot's complex...
Fallot, a consistent pattern of bidirectional shunting was shown. The right-to-left shunt occurred at two places and two sites during the cardiac cycle; namely, during early ventricular ejection into the aorta, and during isovolumic ventricular relaxation directly across the ventricular defect into the left ventricle. Left-to-right gradients and shunting across the defect were found to occur during isovolumic ventricular contraction and during diastole. The results of this study suggest that further investigation of various cardiac defects may yield important information concerning shunting mechanisms.

Appendix
First Derivative Studies of Ventricular Pressure Pulse

In collaboration with
Roger C. Barr, B.S., Department of Electrical Engineering, and
Thomas M. Gallie, Ph.D., Department of Mathematics, Duke University.

The complex and intriguing question as to the mechanisms involved in the production of asynchronous rise and fall of the ventricular pressures was approached by digital computer studies of the first derivative of the simultaneously recorded ventricular pressures. The originally recorded tape data were transcribed by an Airborne Instrument Laboratories analog-to-digital converter at a rate of 926 samples per channel per second. The digital tapes were then analyzed by an IBM 7072 digital computer.

The computer calculated the instantaneous values at 1.08-msec intervals for the following: the simultaneously recorded right and left ventricular pressures, the instantaneous pressure difference (pressure gradient), and the first derivative of the two pressures. The instantaneous values of the first derivative for each point were calculated on the basis of the pressure difference over a time interval of 10 msec:

$$\frac{\Delta P}{\Delta T} = \frac{P_2 (\text{pressure 5 msec after}) - P_1 (\text{pressure 5 msec before})}{T_2 (5 \text{ msec after}) - T_1 (5 \text{ msec before})}$$
1,221 to 1,699 mm Hg/second and those of the left from 1,076 to 1,363 mm Hg/second. The values for the left ventricle are consistent with the results of other investigators who have studied the first derivative of the left ventricular pressure pulse. The right ventricular values are much higher than the range we have found in patients without right ventricular hypertension.

The period of isovolumic relaxation showed considerable variation concerning the relationship of the time of onset of the negative derivative of the two ventricles. In one half of the patients, the onset of the negative
derivative of both ventricles occurred simultaneously; in the remainder, there was asynchrony of onset with a decrease in ventricular pressure with either ventricle preceding by as much as 12 msec. However, in all patients the left ventricular negative derivative had a steeper slope and reached a greater maximum negative value than that of the right. Thus, the isovolumic right-to-left shunt across the septal defect was produced by the pressure gradient generated primarily by the more rapid fall in the left ventricular pressure as compared to that in the right.

These preliminary findings suggest a fruitful area for future investigation of the complex interrelationship of factors involved in the production of the asynchronous rise and fall of the ventricular pressures in tetralogy of Fallot. Although the rate of change in pressure is a reflection of the rate of change in myocardial tension, the dimensions, volume, and shape of the chambers, the pattern of electrical excitation, and the anatomy of the ventricles—all of these—influence, in a complex manner, the rate of rise and fall of the ventricular pressures and resultant pressure gradient across the defect.

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References

Ventricular Pressure-Flow Dynamics in Tetralogy of Fallot
AARON R. LEVIN, JOHN P. BOINEAU, MADISON S. SPACH, RAMON V. CANENT, JR., M. PAUL CAPP and PAGE A. W. ANDERSON

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