Effect of Unilateral Pulmonary Artery Obstruction on Circulatory Dynamics in Dogs with Chronic Atrial Septal Defects


It is generally accepted that the left-to-right shunt across an atrial septal defect is the result of a pressure gradient in this direction between the two atrial chambers during most of the atrial cycle. The maintenance of this pressure gradient and, hence, the direction of the shunt in the left-to-right direction has been attributed to a difference in the volume-elastic properties of the two atria and to a difference in the distensibility of the two ventricles.\textsuperscript{1-3}

In addition, previous investigators have demonstrated by means of indicator-dilution techniques, that both in patients\textsuperscript{4,5} and in dogs\textsuperscript{6} with atrial septal defects located in the region of the fossa ovalis, a higher percentage of blood from the right lung shunts in the left-to-right direction across the defect than from the left lung. This preferential shunting of blood from the right lung has been interpreted as being due primarily to the anatomical proximity of the openings of the right pulmonary veins into the left atrium and the position of the atrial septal defect in the atrial septum.

Fleming\textsuperscript{7} found, on the basis of bronchospirometry of separate lungs with the subject in the supine position, that an abnormally high proportion of oxygen is taken up from the right lung in patients with atrial septal defects of the secundum type. These results suggest that a greater than normal portion of pulmonary blood flow traverses the right lung in these patients, but no completely satisfactory explanation has been offered for these findings.

Thus, it appears that numerous factors may affect the direction and magnitude of the shunts across an atrial septal defect of the secundum type; the relative importance of these various factors has not been completely assessed. In order to investigate some of these factors, circulatory pressures, blood flows, and the magnitude of shunts were determined before and during acute unilateral obstruction of a pulmonary artery in closed-chest dogs with chronic atrial septal defects.

**Methods**

Eleven mongrel dogs averaging 17.1 Kg. (range 14 to 22) in body weight were studied from three weeks to 15 months after the creation of atrial septal defects. Relatively large defects were produced by removing all tissue from the fossa ovalis and the major portion of the muscular septum. Defects averaging 1.5 by 1.0 cm. were obtained.

Intravenously administered sodium pentobarbital (25 mg./Kg.) plus morphine sulphate (5 mg./Kg.) were used for anesthesia in these investigations. The animals were maintained in the supine position and breathed 99.5 per cent oxygen via a cuffed endotracheal tube throughout the procedure. Oxygen uptake and pulmonary ventilation were recorded continuously by closed-circuit spirometry.

Cardiac catheters (no. 6-F Lehman type) were introduced percutaneously via the external jugular veins and manipulated under fluoroscopic vision into the superior vena cava, inferior vena cava, right ventricle, and pulmonary artery. In addition, a single-lumen catheter with a balloon* near its tip was manipulated into the pulmonary artery in order to occlude the branches as desired.

Central aortic pressure was recorded via a 60-
cm. nylon catheter (inner diameter 0.6 mm. and outer diameter 0.9 mm.), which was introduced through a no. 19 thin-walled needle inserted percutaneously into a femoral artery. A no. 19 needle was inserted into the opposite femoral artery for recording dilution curves.

Pressures transmitted through the catheters and needles were recorded by means of specially adapted strain gauge manometers. Intravascular pressures, respiration, and the electrocardiogram were recorded by means of a photokymographic assembly previously described. In each experiment, the zero level for all manometers was set at mid-chest, and calibrations against a standardized aneroid manometer were made over the entire pressure range during and after each experiment.

Measurements of the right atrial pressure pulses included the mean pressure and measurements at four instances in the cardiac cycle, namely, the beginning, peak, and end of the "a" wave and the peak of the "v" wave.

Mean arterial pressure was calculated by adding a third of the pulse pressure to the diastolic pressure. The ratio of pressure to flow, referred to as pulmonary vascular resistance (Rpv) and expressed in relative units, was determined according to the formula:

\[ R_{pv} = \frac{(P_{pa} - P_{la})}{Q_p} \]

in which the terms \( P_{pa} \) and \( P_{la} \) represent the mean pulmonary arterial pressure and mean left atrial pressure, respectively, expressed in millimeters of mercury. In these dogs with large atrial septal defects, the assumption was made that the mean left atrial pressure was equal to the mean right atrial pressure. The systematic errors introduced by these assumptions are believed to be scarcely greater than the random errors in measurement of atrial pressures under these circumstances. \( Q_p \) represents the pulmonary blood flow in liters per minute calculated by the direct Fick method.

In order to calculate the pulmonary vascular resistance of each lung, the ratio of distribution of blood flow to the right and left lungs was assumed to be 58 and 42 per cent, respectively, of the total pulmonary blood flow. These assumptions are well supported by previous investigations that have demonstrated this inequality in the distribution of blood flow to the lungs in dogs.

Samples of blood were drawn through cuvette oximeters for intermittent determinations of oxygen saturation at the femoral artery and at the superior vena cava, inferior vena cava, and pulmonary artery. Also, samples of blood were drawn intermittently for determinations of oxygen content and capacity by manometric techniques. These determinations were carried out by the method of Van Slyke and Neill as modified by Sendroy.

Indicator-dilution curves were recorded simultaneously from the femoral artery and right ventricular outflow tract by means of cuvette oximeters after injections of indocyanine green dye* at various sites in the heart and great vessels. These sites included the venae cavae and the main pulmonary artery and its branches.

*The indocyanine green dye (Cardio-green) was supplied through the courtesy of Hynson, Westcott and Dunning, Inc., Baltimore, Maryland.
Heart and lungs of a dog, arranged to demonstrate relation between openings of pulmonary veins and venae cavae and position of membranous fossa ovalis in atrial septum. Left: Posterodorsal view of heart of normal dog from which posterior walls of atria and ventricles have been removed. Left atrium (LA) is widely opened for demonstration of relation between opening of pulmonary veins into left atrium and position in which an atrial septal defect would be created by removing tissue in fossa ovalis and muscular septal tissue dorsal to fossa. Position that such an atrial septal defect would occupy is indicated by dashed lines drawn between two white pegs. Note that right anterior (RAPV) and right cardiac (RCPV) pulmonary veins open into right cephalad portion of left atrium by means of a common ostium. Right diaphragmatic (RDPV) and right intermediate (RIPV) veins open into left cephalad portion of left atrial chamber, and immediately below is opening of left diaphragmatic (LDPV) pulmonary vein. Not uncommonly, these three pulmonary veins form a T-shaped channel with a single ostium opening into left atrial chamber. Combined opening of left anterior (L Ant.) and left cardiac (LCPV) pulmonary veins is indicated in mid-cephalad portion of left atrium. Note that common ostium draining right anterior and right cardiac pulmonary veins is contiguous with dorsal margin of fossa ovalis and, hence, would be closer to a defect at this site than are any of other venous channels draining other lobes of lungs. Proximity of left atrial ostia of these two pulmonary veins (also evident in photograph at right) results in preferential drainage of blood from these pulmonary lobes into the right atrium. Right: Dorsocephalad portion of the heart of another dog. Bronchial and pulmonary arterial tree and dorsocephalad wall of left atrium have been removed so that large ostia of mitral valve, indicated as LV, is visible in floor of left atrium (LA). Atrial septal defect has been created in usual position by removing entire membranous fossa ovalis and posterior margin of interatrial muscular septum. Large white probe which has been introduced through both venae cavae traverses right atrium and is visible from this left-sided view through atrial septal defect. Note that orifice of inferior vena cava (IVC) into right atrium is contiguous with dorsoocaudal margin of defect in atrial septum and that orifice of superior vena cava (SVC) into right atrium is relatively at a much greater distance from defect in atrial septum. This circumstance is responsible for demonstrated preferential shunting of blood from inferior vena cava right-to-left direction.

The presence and magnitude of venoarterial shunts were determined after injections of indicator into the venae cavae. In order to measure systemic and pulmonary blood flows and to quantitate the magnitude of the left-to-right shunts, the simultaneous arterial and venous sampling dye-dilution method was used. In these animals, a reasonable correlation was obtained between values for flows and shunts, as calculated by the direct Fick method and by indicator-dilution techniques. The results are in agreement with data previously reported, which demonstrated a close correlation between the values obtained by these two independent methods.
UNILATERAL PULMONARY ARTERIAL OBSTRUCTION

Pulmonary veins would drain preferentially into the right atrium. The position of the defect in the atrial septum and the relation between the openings of the venae cavae and pulmonary veins and the location of the defect in the atrial septum are shown in figure 2.

Results

Control determinations of pressures and blood flows with the catheters in situ and with the occluding balloon deflated were made at the beginning of the procedure for each of the 11 animals studied. Additional control values were obtained just prior to and after each subsequent occlusion of a main branch of the pulmonary artery.

These control values showed that pressures, both in the right side of the heart and in the systemic circulation, were within the range for normal animals. Mean right atrial pressure averaged 5.2 mm. Hg (range 3 to 10). Right ventricular systolic pressure averaged 33.9 mm. Hg (range 28 to 40). A small but consistent systolic pressure gradient was present between the right ventricle and the pulmonary artery, averaging 4.7 mm. Hg. Mean pulmonary arterial pressure averaged 16 mm. Hg (range 13 to 20), and mean aortic pressure averaged 126 mm. Hg (range 101 to 132).

The control values for pulmonary blood flow, as determined by the direct Fick method, varied between 1.8 and 9.0 L./min., averaging 4.9. The systemic blood flow was found to be within normal limits, averaging 3.0 L./min. (range 1.5 to 6.0). These values for blood flows when expressed in L./min./10 Kg. body weight showed pulmonary blood flow to average 2.8 (range 1.0 to 4.1), and systemic flow varied between 0.9 and 3.0, averaging 1.6 L./min./10 Kg. body weight.

In these determinations, no apparent correlation could be demonstrated between mean pulmonary arterial pressure and the pulmonary/systemic ratio of blood flow.

In the control situation, indicator was injected into the inferior vena cava in all animals and in five instances also into the superior vena cava. The magnitude of the venoarterial shunt after injection into the inferior vena cava varied between 0 and 35 percent of the systemic blood flow, averaging 9.
Relation of right ventricular systolic pressure to relative magnitude of left-to-right shunt via chronic atrial septal defects in anesthetized, closed-chest dogs during acute unilateral pulmonary artery occlusion. Left-to-right shunts were calculated by dye-dilution methods after injections of indicator into main pulmonary artery, with simultaneous sampling from femoral artery and outflow tract of right ventricle. Control values (open circles) and values from determinations during pulmonary artery obstruction (solid circles) from same animal are connected by arrows. Numerals beside each pair of values designate individual dogs. Note (left panel) that occlusion of left pulmonary artery was associated with an increase in magnitude of left-to-right shunt in every instance, in spite of consistent elevation in right ventricular systolic pressure, and that no systematic effects on left-to-right shunt occurred during occlusion of right pulmonary artery (right panel).

In only two dogs could a venoarterial shunt be detected after injection into the superior vena cava, and in both instances, the magnitude of the shunt from this site was considerably less than that after injection into the inferior vena cava.

Indicator was injected into the main pulmonary artery in all animals in the control situation. The control values for the left-to-right shunt determined by the dye method averaged 30 per cent (range 5 to 70) of the pulmonary blood flow. Additional injections were made into the left pulmonary artery in nine animals. In each instance, a smaller degree of left-to-right shunting of blood was detected, in comparison with the results of injection into the main pulmonary artery; it averaged 17 per cent (range 3 to 50) of the pulmonary flow. Indicator was injected into the right pulmonary artery in only three of the 11 animals; in each instance, the magnitude of the left-to-right shunt was greater than that after injections into the main pulmonary artery. These values averaged 44 per cent (range 20 to 70) of the pulmonary blood flow.

These data support previous observations\(^1\)\(^-\)\(^6\) that in the presence of an atrial septal defect located in the region of the fossa ovalis, (1) there is a larger contribution of blood from the inferior vena cava than from the superior vena cava to shunts in the right-to-left direction, and (2) there is a preferential left-to-right shunting of blood from the right pulmonary veins across the atrial septal defect.

Occlusion of either the right or the left pulmonary artery resulted in immediate and closely similar elevation in right ventricular systolic pressure (fig. 3). After unilateral occlusion of a pulmonary artery, this pressure averaged 40.9 mm. Hg (range 32 to 47), which represented an increase of 7.8 mm. (range 5 to 15) over the average determinations prior to occlusion.

In spite of the elevation in right ventricular systolic pressure to an average level of 40.2 mm. Hg, obstruction of the left branch (fig. 3, left panel) was associated in every instance with an increase in the magnitude of the left-to-right shunt, as calculated by simultaneous right heart-systemic artery indicator-dilution techniques. During the occlusion of the left pulmonary artery, the left-to-right shunting of blood averaged 37.8 per cent of the pulmonary flow, as compared with 26.5 per cent obtained during the control period prior to the obstruction.

During occlusion of the right branch (fig. 3, right panel), no systematic changes were demonstrated in the magnitude of the left-to-right shunting of blood, even though the increase and the average value (41.6 mm. Hg) for right ventricular systolic pressure were closely similar to the values obtained during occlusion of the left pulmonary artery.

An example of the dilution curves obtained prior to and during obstruction of the right and left main branches of the pulmonary artery, as well as of the effects on pulmonary arterial pressures, blood flows, and magnitude...
of the left-to-right shunts in one of the dogs with chronic atrial septal defect, is shown in figure 4.

Obstruction of either the right or the left pulmonary artery was not associated with demonstrable systematic effects on the mean right atrial pressure or on any of the measured points in the right atrial pressure pulse during the cardiac cycle. Similarly, no systematic effects could be demonstrated in the mean aortic pressure.

Oclusion of the left branch of the pulmonary artery was associated in every instance with an elevation in mean pulmonary arterial pressure, which was on the average 3.4 mm Hg more than the control values. Obstruction of the right branch resulted in a similar elevation in the mean pulmonary arterial pressure, averaging 4.1 mm Hg.

No appreciable changes were seen in the magnitude of the venoarterial shunts in association with unilateral occlusion of a pulmonary artery, as determined after injection of indicator into the inferior vena cava. In spite of a slight elevation in right ventricular systolic pressure, the per cent of right-to-left shunt during obstruction of the right and left pulmonary arteries averaged 8.3 per cent of the systemic blood flow, as compared with 8.7 per cent in the control situation.

The values for pulmonary and systemic blood flows and for the left-to-right shunt across the atrial septal defect during unilateral obstruction of a pulmonary artery, as determined by dye-dilution techniques, are shown in figure 5. In nine of 11 experiments, occlusion of the left pulmonary artery was associated with an increase in pulmonary blood flow. Pulmonary blood flow averaged 3.6 L/min. during occlusion of the left pulmonary artery, as compared with 3.2 L/min. prior to the obstruction. However, no systematic effects were demonstrated during obstruction of the right branch; an average value of 3.0 L/min. was obtained during occlusion, as compared with 3.1 L/min. in the control situation.

No systematic effects on systemic blood flow were demonstrated during occlusion of either the right or the left branch of the pulmonary artery (fig. 5, middle panel).

Oclusion of the left pulmonary artery resulted in an increase in the volume of blood shunting across the defect in the left-to-right direction in 10 of the 11 animals studied (fig. 5, right panel). The left-to-right shunt flow via the defect averaged 0.99 L/min. (range 0.2 to 1.8) during the control situation, as compared with 1.44 L/min. (range 0.4 to 3.1) during obstruction of the left pulmonary artery. Occlusion of the right branch was not, however, associated with a significant systematic effect. The average control value for left-pulmonary arterial obstruction. Figure 4

Indicator-dilution curves obtained prior to and during occlusion of right and left main branches of pulmonary artery in a 19-Kg., anesthetized, closed-chest dog (no. 9) with a chronic atrial septal defect. Animal was breathing 99.5 per cent oxygen. Indicator was injected into main pulmonary artery, and sampling was carried out simultaneously from outflow tract of right ventricle and from femoral artery. Obstruction of right and left pulmonary arteries was carried out by means of a balloon placed near tip of a cardiac catheter (fig. 1). Presence of left-to-right shunt is demonstrated by that portion of dye-blood mixture detected in outflow tract of right ventricle in an abnormally short period after injection. Below each set of dilution curves are values for pulmonary and systemic blood flows, left-to-right shunts determined from these curves, and pressures recorded from main pulmonary artery. Arrows indicate instant at which injection of indicator occurred. Note that occlusion of left pulmonary artery (right panel) resulted in an increase in pulmonary artery pressure, and, in spite of acute reduction in available pulmonary vascular bed, an increase in magnitude of pulmonary blood flow and left-to-right shunting of blood occurred. These changes in blood flow, in relation to control situation (left panel), did not occur during obstruction of right pulmonary artery (middle panel).
Figure 5
Effects of acute unilateral pulmonary artery occlusion on pulmonary and systemic blood flow and left-to-right shunt in 11 anesthetized (morphine-pentobarbital), closed-chest dogs with chronic atrial septal defects. Blood flows were calculated from simultaneous systemic artery and right heart indicator-dilution curves. Flow values obtained during obstruction of one pulmonary artery are plotted on abscissa against respective average values obtained in temporally contiguous control determinations on ordinate. Values obtained during obstruction of right pulmonary artery (open circles) and values associated with occlusion of left artery (solid circles) from individual dogs (designated by numerals) are connected by a line. Dashed diagonal lines represent loci of identical values for control and occlusion results. Note that values for pulmonary blood flow (left panel) are, with two exceptions, greater during occlusion of left pulmonary artery than during control situation, while no systematic effects were demonstrated after right pulmonary artery obstruction. Furthermore, in six of eight animals, higher values for pulmonary flow were found in association with occlusion of left pulmonary artery than during obstruction of right artery. No systematic effects on systemic blood flow were demonstrated (middle panel). Magnitude of the left-to-right shunt during occlusion of left pulmonary artery was increased over control determinations in 10 of the 11 animals studied, whereas no systematic effects were demonstrable during obstruction of right artery. Left-to-right shunt during occlusion of left branch consistently exceeded values obtained during occlusion of right branch in some animal.

Discussion
The major hemodynamic alteration in the presence of an uncomplicated atrial septal defect is an arteriovenous shunt, which results to a variable extent in an increase in pulmonary blood flow. However, in spite of a larger volume of flow, the pulmonary arterial pressure has been demonstrated to remain normal or slightly elevated because of low vascular resistance.

The findings reported herein are comparable to those seen in uncomplicated congenital and experimental atrial septal defects associated with high pulmonary blood flow and normal resistance. In addition, in these animals, no apparent correlation could be demonstrated between the time elapsed after creation of the defects and the pressure/flow ratio in the pulmonary circulation.

A fairly uniform increase in pressure was obtained in these animals during the occlusion of either the right or the left pulmonary artery. This elevation in mean pulmonary arterial pressure, although small, was an average of 23 per cent higher than the pressure during the control situation. These results confirm the findings of other investigators that occlusion of the pulmonary artery to one lung is not associated with a pronounced rise in the pulmonary arterial pressure proximal to the obstruction or with a systematic effect on aortic pressure; in addition, the current study indicates that such occlusion is not associated with an elevation in right atrial pressure.

In the experiments reported herein, increasing the resistance to right ventricular outflow than the pressure/flow ratio for the same lung based on the determination of pressure and estimate of blood flow through this lung prior to occlusion (fig. 6). The preocclusion value for pulmonary vascular resistance (indicated by dashed lines in figure 6) was calculated on the basis of a dissimilar ratio of distribution of blood flow across the lungs, assuming that 58 per cent of the total pulmonary blood flow was traversing the vasculature of the right lung when both pulmonary arteries were patent.
of blood resulted in an elevation in right ventricular systolic pressure. Although the elevation in right ventricular systolic pressure was not associated with a demonstrable rise in right atrial pressure, it is likely that a small decrease in the interatrial pressure gradient would occur, and therefore one would expect a decrease in the magnitude of the left-to-right shunting of blood. However, the most striking finding of this study was that when the left or right pulmonary artery was occluded, no systematic decrease in the magnitude of the left-to-right shunts occurred. In fact, when the left pulmonary artery was occluded, systematic increases in the magnitude of the pulmonary blood flow and the left-to-right shunt were demonstrable, as determined by venous indicator-dilution techniques, whereas no systematic effects were seen in association with occlusion of the right pulmonary artery. These alterations were not associated with appreciable changes in systemic blood flow.

In these animals, changes in the magnitude of pulmonary blood flow and left-to-right shunts associated with unilateral occlusion of a pulmonary artery were relatively too small to be detected by the usual direct Fick method, in which differences in oxygen content of the blood are used for determination of blood flow. Barratt-Boyes and Wood have studied the spontaneous variations in oxygen saturation of venous blood and from these estimated the sensitivity of the oxygen-saturation method for the detection of left-to-right shunts. Under these circumstances, a minimal increase of 15 per cent of the pulmonary blood flow must be present in order that a left-to-right shunt be demonstrable by oxygen-saturation determinations. However, indicator-dilution techniques with simultaneous sampling carried out at the femoral artery and outflow tract of the right ventricle or techniques making use of foreign gases have proved distinctly superior to methods utilizing oxygen saturation of blood for detecting left-to-right shunts.

It is believed that the increase in pulmonary flow and in the magnitude of left-to-right shunts during occlusion of the left pulmonary artery are primarily the result of the anatomical relation between the opening of the right pulmonary veins, particularly the veins draining the right anterior and cardiac lobes, and the position of the defects located in the atrial septum.

In the animals under study, the right anterior and cardiac pulmonary veins (fig. 2) were commonly found to drain into the left atrium by means of a small common channel. The floor of this common channel was formed partially by the roof of the right atrium and partially by the dorsal part of the interatrial septum. During the creation of a relatively large defect in the region of the fossa ovalis,
part of the floor of this common channel was removed. This resulted in a preferential drainage of blood from the right pulmonary veins (which average 26 per cent of the total pulmonary mass) into the right atrium rather than into the left atrium.

These findings suggest that dynamic (kinetic energy) factors relating to the manner, site, and direction in which pulmonary venous blood enters the left atrium are of considerable importance in determining left-to-right shunts; therefore, these factors, in addition to the mean levels of pressures in the two atrial chambers, must be considered in this regard.

It was found, as would be expected, that unilateral obstruction of a pulmonary artery caused an increase in the estimated values for pulmonary vascular resistance. However, when this pressure/flow ratio for the unoccluded lung was compared with the estimated value for the same lung prior to occlusion, the resistance values obtained during occlusion of either the right or the left pulmonary artery were found to be less than the preocclusion values. This apparent decline in the vascular resistance of the unoccluded lung was probably due to passive dilation of the pulmonary vessels in that lung, associated with an elevation in intravascular pressure, or the opening of new vascular channels, or a combination of these various factors, the nature of which was not elucidated.

These investigations suggest that in the animals studied, the volume-elastic and flow-resistive properties of the pulmonary vessels in both lungs are closely similar when subjected to the same dynamic (pressure-flow) events. These results do not support the interpretation given by Fleming to his findings of an abnormal ratio of distribution of blood flow through the right and left lungs in patients with atrial septal defects of the secundum type.

Summary

Determinations of pressure, blood flows, and calculated pulmonary vascular resistance were made prior to and during acute individual occlusion of the right and left main branches of the pulmonary artery in random sequence in eight anesthetized, closed-chest dogs with chronic atrial septal defects. Similar observations were made with occlusion of only the left pulmonary artery in three additional dogs.

Obstruction of the pulmonary artery to one lung was immediately followed by a rise in systolic pressure in the right ventricle and pulmonary artery proximal to the obstruction, from an average normal value of 33.1 mm Hg to an average value of 40.9 mm Hg (range 32 to 47). This change was not associated with demonstrable systematic effects on right atrial or systemic arterial pressure or on the systemic blood flow.

As would be expected, the average calculated ratio of pressure to flow (vascular resistance) across the unoccluded lung was elevated during the obstruction. The resistance value during the occlusion, however, was less than the estimated pressure/flow ratio for this same lung, based on the measurements made prior to the occlusion. This apparent effective decrease in vascular resistance of the unoccluded lung is probably related to dilation of the pulmonary vessels as a result of an increase in intravascular pressure caused by the sudden removal of approximately half of the pulmonary vasculature from the circulation.

In spite of the elevation in right ventricular systolic pressure, occlusion of the left pulmonary artery was associated with a slight increase in pulmonary blood flow and a definite increase in the magnitude of the left-to-right shunt across the atrial septal defect, whereas no systematic effects were obtained during obstruction of the right branch in association with the same approximate levels of right ventricular systolic pressure. These data are regarded as further evidence that the preferential shunting of blood from the right lung in the presence of an atrial septal defect of the secundum type is primarily due to the anatomical relation between the opening of these vessels into the left atrium and the position of the defect in the atrial septum. Furthermore, they emphasize the importance of dynamic factors, related to the manner, site, and direction in which the pulmonary venous
blood drains into the left atrium, as important determinants of the left-to-right shunt via such defects.

References


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Circ Res. 1961;9:1316-1326
doi: 10.1161/01.RES.9.6.1316

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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