Comparison of Dilution Technics Using Aortic Injection with Upstream Sampling for Assessment of Aortic Regurgitation

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Warner and Toronto have described a method for detecting and quantitating aortic regurgitation. This method involves simultaneous recording of indicator dilution curves from the left radial and femoral arteries following injections, at specific phases of the cardiac cycle, into the descending aorta at and downstream from the origin of the left subclavian artery. From these measurements they determined the distance down the aorta from the origin of the subclavian artery beyond which no dye would return to this artery during the diastolic phase of the cardiac cycle. This distance multiplied by an estimated average cross-sectional area of this segment of the aorta yields the volume of backflow per stroke in this portion of the arterial bed if nonlaminar flow is assumed. This type of study was applied to experimental animals and to patients with and without aortic regurgitation.

A somewhat analogous but much less refined method has been used by Braunwald and Morrow in patients with and without aortic regurgitation. These workers determined the most distal point in the descending aorta from which injected dye could be detected by an oximeter placed on the right ear. This point is displaced distally in the presence of aortic regurgitation.

The purpose of this study was to apply the method of Warner and Toronto to dogs with graded severity of aortic regurgitation and to correlate the findings with the volume of the aorta determined angiographically and the back-stroke volume computed from the regurgitant fraction \( \frac{LV_{A}}{FA_{A}} \) obtained by injecting indicator at the aortic root and sampling simultaneously from the left ventricle and femoral artery as described previously.

**Methods**

Twelve mongrel dogs, weighing between 16 and 20 kg, were studied. Aortic regurgitation was produced without thoracotomy in 10 of these animals by using a valvulotome introduced via the right carotid artery. These dogs were studied 1 to 8 weeks after operation.

During anesthesia with morphine (IM, 7.5 mg/kg of body weight) supplemented with sodium pentobarbital (IV, about 20 mg/kg), the trachea was intubated and connected to a positive-pressure respirator supplied with 99.5% oxygen. The respiratory rate was set to approximately 50 breaths/min with cyclic pressure variations of 0 to 8 cm of H₂O.

**Instrumentation**

Catheters were positioned under fluoroscopic control without thoracotomy (fig. 1). A 100-cm no. 6 Lehman catheter was advanced from the jugular vein so that its tip was in the pulmonary artery. A 100-cm no. 5 closed-tip catheter with multiple side holes* was introduced through the right femoral artery until it reached the left ventricle. Then, under fluoroscopic control and by monitoring the pressure, this catheter was withdrawn until its tip lay approximately 1 cm downstream from the point at which the transition from a ventricular pressure to an aortic pressure occurred.

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FIGURE 1

Top panels. Roentgenograms used to localize sites of injections of indocyanine green at progressively graded distances downstream from aortic valve. Angiogram shown in panel A was used to estimate the volumes of the aortic segments between either the aortic valve or origin of the left subclavian artery and the various injection sites, designated B, C, D, E, and F. RSC, LSC, A, LV, and RV indicate catheters whose tips are in right and left subclavian arteries, aorta, and left and right ventricles, respectively.

Middle panels. Dilution curves recorded simultaneously from left ventricle and left subclavian and femoral arteries following injections at the sites shown in top panels in a dog with chronic mild aortic regurgitation (dog 4).

Bottom panels. Amount and duration of injection in relation to cardiac cycle, recorded simultaneously by a second camera whose paper speed was 25 mm/sec.

Note that only a trace of immediately appearing indicator was detected in the left ventricle when the distance of injection site from the aortic valve was 3.5 cm (panel C) and a similar amount of immediately appearing indicator was detected in the left subclavian artery following injection 11.5 cm downstream from the valve (panel F). In this dog, origin of the left subclavian artery was approximately 5 cm from the aortic valve.

A 10-cm polyethylene catheter (internal diameter, 0.1 cm) was placed in the left femoral artery. A 40-cm no. 6 Lehman catheter was advanced into the left subclavian artery until its tip was about 3 cm from the junction of this artery and the aortic arch. In four of the dogs, a 100-cm no. 6 Lehman catheter was placed in the right subclavian artery. Finally, an atrial transseptal puncture was performed via the right external jugular vein" and a 50-cm no. 6 Lehman catheter was introduced via the transseptal needle; its tip was positioned in the midcavity of the left ventricle. Pressures from all catheters, as well as from the endotracheal tube, were recorded by strain gauge manometers. In addition, the left ventricular, left subclavian, and left femoral catheters were connected to Waters X100A densitometers through which blood was withdrawn at a constant rate for recording of indicator dilution curves. The dynamic response of these instruments has been described previously.

Indocyanine green dye* was used as an indicator.

*Supplied through the courtesy of Hynson, Westcott and Dunning, Inc., Baltimore, Maryland.

Circulation Research, Vol. XV, October 1964
ASSESSMENT OF AORTIC REGURGITATION

cator and two types of injections were used, designated as manual and mechanical. The manual injections were carried out by the usual technic and were not synchronized with the cardiac cycle. These injections were completed in one to two seconds and, depending on the heart rate, occurred during one to several heartbeats.

The mechanical injections were made by a solenoid-controlled pneumatically activated syringe. These injections were synchronized with the cardiac cycle by means of an electronic circuit activated by the R wave of the electrocardiogram. This assembly was used to make two types of synchronized injections, designated as “diastolic” and as “short-duration.” The diastolic injections were synchronized so as to occupy the complete diastolic phase of one cardiac cycle. The short-duration injections lasted for 40 msec and the delay time from the R wave to onset of the injection could be varied at will from zero up to the duration of a cardiac cycle. Therefore, by proper selection of the delay time, injections of this type could be made in any desired 40-msec interval of the cardiac cycle. The position of the plunger of the mechanical syringe was recorded simultaneously with the pressures and the electrocardiogram at a paper speed of 25 or 150 mm/sec so that the duration and timing of the synchronized injections in relation to the cardiac cycle could be accurately determined.

The 1- to 2.5-mg dose of indicator injected was contained in a volume of 1 ml of distilled water for the manual and diastolic injections. The 0.4- to 1.0-mg dose of indicator injected in the short-duration injections was contained in 0.2 ml of water.

PROCEDURE

A typical experiment was done in the following sequence:

1. Dilution curves were recorded simultaneously from the left ventricle and the left subclavian and femoral arteries following a manual injection into the pulmonary artery and replicate manual injections into the aorta, 1 cm downstream from the valve. These dilution curves were used to determine the animal’s cardiac output by the standard Stewart-Hamilton technic and to determine the amount of immediately appearing indicator in the left ventricle expressed as regurgitant fraction \( \frac{LV_A}{FAA} \), as described previously and defined below under measurements.

2. A series of short-duration injections were then made so that dilution curves were obtained following injections of this type occurring in all or nearly all phases of the cardiac cycle. These curves were used to determine when in the cardiac cycle the maximal retrograde flow of indicator into the left ventricle occurred.

3. The aortic catheter was then withdrawn in successive steps of 2 to 5 cm and the position of the catheter at each step was recorded by a roentgenogram (fig. 1). At each of these positions of the catheter, dilution curves were recorded simultaneously at all three sampling sites following replicate short-duration injections timed so as to occur at the onset of systole, i.e., with zero time delay after the R wave. This process was continued until an aortic injection site was reached at which no immediately appearing dye was detected in the left ventricle.

4. A series of short-duration injections, covering all phases of the cardiac cycle, were then made to determine when in the cardiac cycle there was maximal retrograde flow of indicator from this site in the aorta back to the left ventricle.

5. Using the appropriate delay time for maximal detection of immediately appearing indicator in the left ventricle, the stepwise withdrawals (paragraph 3) were continued until no immediately appearing dye was detected in the left ventricle and then continued further until no immediately appearing dye was detected in the left subclavian artery. At this injection site, several short-duration injections at variable delay times were carried out to be certain that no retrograde flow of dye to the subclavian artery occurred.

6. The aortic catheter was then advanced and repositioned approximately 1 cm downstream from the aortic valve and the first measurements of the sequence (paragraph 1) were repeated.

In five dogs, an additional similar procedure was followed using diastolic injections instead of the short-duration injections to determine the sites in the aorta from which no immediately appearing dye was detected in the left ventricle and the left subclavian artery, respectively, with this type of injection.

MEASUREMENTS

Cardiac output was determined from each of the dilution curves recorded from the femoral artery following injections into the pulmonary artery using the standard Stewart-Hamilton technic. The areas encompassed by the curves recorded simultaneously from the left ventricle and the left subclavian and femoral arteries for each injection were measured by using the total triangle method. The ratio of the areas of the immediately appearing portions of the left ventricular \( LV_A \) and the simultaneously recorded femoral artery \( FAA \) curves, the regurgitant fraction \( \frac{LV_A}{FAA} \), was calculated for each aortic injection; the analogous ratio \( \frac{SA_A}{FAA} \) was calculated for the subclavian artery curves.
Observations following injection of indicator into aorta in a closed-chest, anesthetized dog with a small degree of aortic regurgitation (dog 3).

a. Top panels. Effect of time of injection in cardiac cycle on left ventricular (left panel) and left subclavian (right panel) regurgitant fractions. Duration of systole is represented on the left halves of the abscissae as 100% and duration of diastole, similarly on the right halves. Each of the horizontal bars on the graph represents an injection of indicator; duration of each injection represented by short horizontal bars is 40 msec and the long horizontal bars represent injections which were synchronized with the electrocardiogram so as to extend as closely as possible over the full extent of the diastolic phase of the cardiac cycle during which the injection occurred. The site of each injection expressed as centimeters downstream from the aortic valve is designated by the numeral over each bar. Note that for the short-duration (40 msec) injections the regurgitant fraction (left ventricular sampling) was maximal for injections which occurred toward the end of systole or onset of diastole, with a progressive decrease in this fraction as injections occurred earlier in systole and later in diastole. To avoid overlapping of values, the regurgitation fraction value of zero on the ordinate is represented by stippled area at bottom of each graph.

Circulation Research, Vol. XV, October 1964
The various positions along the aorta of the catheter used for injecting dye were checked by roentgenograms. The position of the animal relative to the x-ray source and to the film cassette was kept constant. From these roentgenograms, the linear distance between the successive positions of the catheter could be measured. Since the tube-film distance was short, a correction had to be made for object magnification on the roentgenogram by using the quotient of the actual external diameter of the aortic catheter and the external diameter of the roentgenographic image of the same catheter.

At the end of the procedure, an angiocardiogram was obtained by injecting 30 ml of contrast medium* into the left ventricle with a pressure syringe; movement of the syringe plunger, intravascular pressures, and the electrocardiogram were recorded simultaneously. A roentgenogram was taken at the end of the injection. The angiocardiogram thus obtained could be measured for computation of the volume of the aorta (fig. 1). This was done by: (1) dividing the length of the vessel into 1-cm segments; (2) measuring the width of each segment on the roentgenogram; and (3) assuming that the cross section of the aorta was a circle, applying the formula for the volume of a cylinder. The sum of the volumes of the segments was taken as the volume of the aorta (fig. 1). This was done by: (1) dividing the length of the vessel into 1-cm segments; (2) measuring the width of each segment on the roentgenogram; and (3) assuming that the cross section of the aorta was a circle, applying the formula for the volume of a cylinder. The sum of the volumes of the segments was taken as the volume of the vessel for any given distance downstream from the valve. A correction was made for x-ray distortion of the silhouette of the vessel.1

Since the mean pressure in the aorta at the moment of recording the angiocardiogram usually was not the same as it was during the catheter withdrawal determinations, a correction was made, using the data of Remington and Hamilton, for variation in the volume of the aortic arch and thoracic aorta with variations in mean pressure.

The distance that the catheter had to be withdrawn until no immediately appearing dye was detected in the left ventricle (disappearance distance from the aortic valve) or until no immediately appearing dye was detected in the left subclavian artery (disappearance distance from the subclavian artery) was determined as described by Warner and Toronto.1 The logarithms of the values of $LV_A/FA_A$ and $SA_A/FA_A$ determined at each step of withdrawal from the aortic valve were plotted against the distance from the aortic valve of the site of each injection. These plots showed approximately linear relationships. The value defined by intercept of this "exponential decay line" with the line, $LV_A/FA_A$ (or $SA_A/FA_A$) = 0.1, was taken as the disappearance distance.1

The disappearance distances from the aortic valve and from the left subclavian artery were used to calculate the disappearance volumes from these sites by multiplying these distance values by the mean cross-sectional area of the aorta over this distance. All values were corrected for distortion on the roentgenograms, as described in preceding paragraphs.

The severity of aortic regurgitation present in each animal was estimated from the regurgitant fraction of indicator detected in the left ventricle following injection just downstream from the valve as previously described, a method that has been verified by independent measurements with an electromagnetic flowmeter.10 The regression equation, determined in the prior study, between

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*Methylglucamine diatrizoate, 60% (Renografin).
Summary of Data on Normal Dogs and on Dogs with Surgically Produced Chronic Aortic Regurgitation

<table>
<thead>
<tr>
<th>Dog</th>
<th>Weight (kg)</th>
<th>Duration of observations (minutes)</th>
<th>Aortic pressure (Start mm Hg, End mm Hg)</th>
<th>Heart rate (Start beats/min, End beats/min)</th>
<th>Regurgitant fraction (LV/A/FA)</th>
<th>Regurgitant flow (ml/beat/10 kg)</th>
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<td>1</td>
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<td>101</td>
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*Dogs 1 and 2 were normal. Dogs 3 to 10 had aortic regurgitation and are listed in order of increasing severity of the lesion as determined by the regurgitant fraction of dye detected in the left ventricle immediately following injection of the indicator just downstream from the aortic valve. Values for dog numbers designated as "a" and "b" are based on indicator injections of short duration and of long duration, respectively. When no letters follow the number, only short-duration injections were done.

†Time from initial injections at aortic valve to final injections after determination of withdrawal distances down aorta.

Portions of the pertinent data obtained from each of the 12 dogs studied are given in table 1. The angiocardiogram was technically unsatisfactory in one instance (dog 11). In two of the 12 (dogs 5 and 6), the study was limited to determination of the disappearance distance from the subclavian artery only. The heart rates and cardiac output values obtained during these studies were within the range of values usually obtained.

Results

 Portions of the pertinent data obtained from each of the 12 dogs studied are given in table 1. The angiocardiogram was technically unsatisfactory in one instance (dog 11). In two of the 12 (dogs 5 and 6), the study was limited to determination of the disappearance distance from the subclavian artery only. The heart rates and cardiac output values obtained during these studies were within the range of values usually obtained.

Circulation Research, Vol. XV, October 1964
in normal dogs under anesthesia of this type. The aortic diastolic pressures of the dogs with severe degrees of aortic regurgitation were abnormally low (table 1).

The relationships of the left ventricular and left subclavian regurgitant fractions to the timing of the injections in the cardiac cycle and to the distance from the aortic valve at which the injections were made are shown in figure 2, for a dog with mild aortic regurgitation (dog 3), and in figure 3, for a dog with severe regurgitation (dog 12).

As reported previously, for short-duration injections carried out just downstream from the aortic valve, the minimal amounts of immediately appearing indicator were detected in the left ventricle when the injections occurred at the onset of systole or end of diastole while the maximal amounts were detected with injections timed to occur toward the end of systole and initial portion of diastole. An essentially similar relationship between the time of injection and the left ventricular regurgitant fraction was obtained when injections were made at more distal sites in the aorta out to a point at which no immediately appearing dye was detected in the left ventricle (fig. 2a, left panel).

When short-duration injections were made at sites downstream from the origin of the left subclavian artery (fig. 2a, right panel), an essentially similar relationship was found: the maximal values for $SA_A/FA_A$ were obtained when the injection occurred just at the end of systole. The subclavian regurgitant fraction for injections upstream from its origin gave a
Observations following injection of indicator into aorta of a closed-chest, anesthetized dog with severe aortic regurgitation (dog 12).

a. Top panels. Effect of time of injection in cardiac cycle on left ventricular and left subclavian regurgitant fractions. Duration of each injection was 40 msec. Duration of systole is represented on the left halves of the abscissa as 100% and duration of diastole, similarly on right halves. Each bar represents a single injection of indicator. The site of each injection expressed as centimeters downstream from the aortic valve is designated by the numeral above each bar. The duration of each 40-msec injection, expressed as a percentage of the particular systolic or diastolic phase of the cycle in which it occurred, is indicated by length of the bar. Note that the regurgitant fraction (both sampling sites) was maximal for injections which occurred toward the end of systole or onset of diastole, with a progressive decrease as injections occurred earlier in systole or later in diastole.

b. Bottom panels. Effect of distance of aortic injection site from aortic valve on left
mean value of approximately 1.0, as would be expected. The considerable variation of these values above and below 1.0 presumably indicates that uniform mixing of the dye in blood had not occurred prior to the time when part of the aortic stream diverged into the subclavian artery.

The regurgitant fractions determined by diastolic injections are represented by the long horizontal lines in figure 2a, which extend over all or nearly all of the diastolic phase of the particular cycle in which each injection occurred. In this dog, the value for the left ventricular regurgitant fraction decreased to zero for this type of injection when the catheter tip was withdrawn to a point approximately 6 cm from the aortic valve and the subclavian value decreased to zero at 10 cm from the aortic valve, a point which was approximately 4 cm downstream from the origin of the left subclavian artery.

Essentially similar relationships between the time of injection and the magnitude of the regurgitant fraction were observed in dogs with severe aortic regurgitation except that the catheter tip could be withdrawn much greater distances down the aorta before these values decreased to zero. This distance was over 32 cm in dog 12 (fig. 3a).

The relationships between the distances from the aortic valve and the regurgitant fractions obtained for variously timed injections for dogs 3 and 12 are shown in figures 2b and 3b. In order to provide an adequate number of points upon which to base these lines, values for short-duration injections occurring at the end of systole and the start of diastole were used to plot a single line, as were the values for the end of diastole and the start of systole. Combining values in this manner is justified by the observation that injections occurring at the end of systole and the onset of diastole uniformly gave closely similar maximal values for the regurgitant fraction, while injections occurring at the end of diastole and the onset of systole gave closely similar minimal values for the regurgitant fraction.

Disappearance volumes from the aortic valve and from the subclavian artery were calculated from the disappearance distances obtained with diastolic injections or short-duration injections occurring at the end of systole or onset of diastole in each of the dogs in which the required data were obtained. The relationship of these disappearance volumes to the independent estimates of regurgitant flow per beat determined by the left ventricular regurgitant-fraction method, using equation (1) shown in section on Measurements, is illustrated in figure 4. The correlation coefficient was 0.88 for volumes measured from the aortic valve and 0.77 for volumes measured from the left subclavian artery. The standard errors of the estimate of the retrograde flow per beat from the regression equations calculated from these data were 2.7 and 2.9 ml per heartbeat for the aortic valve and subclavian artery values, respectively. Since the cardiac output and heart rate, used to calculate the regurgitant flow per beat, and the size of the aorta used in these two sets of values were measured for each dog, the correlations obtained between ventricular and left subclavian regurgitant fractions. The diagonal lines which represent this relationship were drawn as the visual best fit to the values resulting from injections occurring in the initial phase of systole (circles) and values from injections occurring toward end of systole (triangles) and onset of diastole (squares). The latter two sets of values were lumped together and represented by the lines nearest right side of each panel, because injections in these two phases of the cardiac cycle gave closely similar maximal values for the regurgitant fraction (fig. 3a).

Values on the abscissa corresponding to the intersection of diagonal lines and the line, regurgitant fraction = 0.1 (horizontal dashed line), were taken as the respective "disappearance distances," i.e., the maximal distances downstream from the aortic valve or subclavian artery at which a measurable retrograde flow of dye-labelled blood could be detected at the respective sampling sites.
Comparison of severity of aortic regurgitation, determined by the regurgitant fraction of dye detected in the left ventricle immediately following injection of indicator just downstream from the aortic valve (ordinate values), and volume of the aortic segment through which retrograde flow of dyed blood into left ventricle (left panel) or left subclavian artery (right panel) can be detected. The correlation coefficient, r, and the regression equation are included in each panel. Numerals indicate individual animals which are designated as a and b when volume values were based on short- and long-duration injections of indicator, respectively. Numbers with no associated letters indicate that only short-duration injections of indicator were made. Diagonal dashed lines show twice the standard error of estimate on either side of the regression line.

the values are compensated for variations in dog size, heart rate, and cardiac output. Therefore, improvement in these relationships would not be expected by expressing stroke regurgitation in relation to body weight (ml/10 kg); this was found to be the case.

The measurement of the disappearance distance from the subclavian artery, as described by Warner and Toronto, is considerably more easily accomplished than is the conversion of this distance to a volume on the basis of an angiocardiogram and simultaneous measurements of aortic pressure. Therefore the degree of correlation between the disappearance distances and the regurgitant flow per beat determined from the left ventricular regurgitant fraction in these animals was also determined (fig. 5). The correlation coefficients were 0.83 and 0.81 for the aortic valve and subclavian disappearance distances and the standard errors of the estimate of back-stroke volumes from these disappearance values were 3.3 and 3.3 ml/beat, respectively. The closeness of these correlations suggests that a reasonably good estimate of aortic regurgitation can be obtained, under the conditions of these experiments, by measuring the disappearance distance from the subclavian artery and using the regression equation given in figure 5.

Discussion

It is interesting that the relationship between the timing of injection of indicator in the cardiac cycle and detection of the maximal retrograde flow of indicator to the ventricle found for the more distal injection sites in the aorta in the present study is similar to that reported previously for injections restricted to the region immediately downstream from the valve. The probable explanation of these findings on the basis of the phasic variations in velocity of blood flow and the resultant dispersion and mixing of the injected indicator along the aorta has been discussed previously. It is interesting also that similar relationships pertain for retro-
grade flow of indicator to the left subclavian artery. When injections were made upstream from the origin of the subclavian artery, there was considerable variation above and below the value of 1.0 in the ratio of the areas encompassed by dilution curves recorded simultaneously from the subclavian and femoral arteries ($SA_A/FA_A$). This indicates that non-uniform mixing of the dye-blood mixture must occur in this segment of the aorta. These results are in accord with the work of Timm,\textsuperscript{17, 18} in which spiral flow was found by studying a model of the aortic arch and also by cine-angiographic observations in dogs and cats. In these last experiments, it was shown that indicator tends to be carried toward the outer wall of the aortic arch; at the end of systole, the indicator stops temporarily and then resumes a slower forward movement during diastole.

The observation that laminar flow occurs to a variable degree over the major portion of the aorta is of considerable importance when dilution methods are used for measurement of blood flow, particularly with those methods which involve injection of indicator directly into the aorta.\textsuperscript{12, 19, 20} The occurrence of a parabolic flow profile has been cited by Warner and Toronto\textsuperscript{20} as the probable basis for their findings in relation to the effect of heart rate on aortic regurgitation. It is interesting that the disappearance volumes measured from the aortic valve were approximately twice as large as the regurgitant volumes per heartbeat measured by the left ventricular regurgitant-fraction method (fig. 4). Since in true laminar flow the velocity of the axial stream is approximately double that of the mean stream velocity, it would be predicted that retrograde flow of indicator injected into the aorta would be detected in the left ventricle from a distance approximately twice that expected from estimates based on calculations of the mean volume of

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure5.png}
\caption[Comparison of severity of aortic regurgitation, determined by the regurgitant fraction of dye detected in the left ventricle immediately following injection of indicator just downstream from the aortic valve (ordinate values), and length of the aortic segment over which retrograde flow of dyed blood into left ventricle (left panel) or left subclavian artery (right panel) can be detected. The correlation coefficient, $r$, and the regression equation are included in each panel. Numerals indicate individual animals which are designated as a and b when length values were based on short- and long-duration injections of indicator, respectively. Numbers with no associated letters indicate that only short-duration injections of indicator were made.]{Comparison of severity of aortic regurgitation, determined by the regurgitant fraction of dye detected in the left ventricle immediately following injection of indicator just downstream from the aortic valve (ordinate values), and length of the aortic segment over which retrograde flow of dyed blood into left ventricle (left panel) or left subclavian artery (right panel) can be detected. The correlation coefficient, $r$, and the regression equation are included in each panel. Numerals indicate individual animals which are designated as a and b when length values were based on short- and long-duration injections of indicator, respectively. Numbers with no associated letters indicate that only short-duration injections of indicator were made.}
\end{figure}
aortic retrograde flow. This was observed and provides further evidence that flow in the major portion of the aorta is laminar in nature. The sampling of retrograde-flowing dyed blood in the left ventricle following injection into the distal aorta would be expected to be mainly from the more rapidly flowing axial stream while sampling from the left subclavian would be from the more peripheral, slower flowing lamina. It should follow, therefore, that the difference between the measured mean regurgitant flow into the left ventricle per beat and the disappearance volume from the subclavian artery should be less than obtained for the comparison between mean regurgitant flow and the disappearance volume from the aortic valve. This was observed (fig. 4).

Although both are indicator dilution techniques, the measurement of left ventricular regurgitant fraction is independent of measurement of the disappearance distance and volume from the aortic valve or left subclavian artery. The good correlations that were obtained between these values confirm the conclusions of Warner and Toronto \(^1\) that measurement of the disappearance distance from the left subclavian artery can be used as an index of the severity of aortic regurgitation.

The subclavian disappearance-distance method has the advantage that entry into and blood sampling from the left ventricle are not required. It does, however, require recording of dilution curves following multiple injections of indicator at various sites in the aorta and the assumption that a steady state prevailed during the period required for these multiple observations. A reliable estimate of the relative accuracy of determinations of aortic regurgitation by the disappearance-distance and the left ventricular regurgitant-fraction methods cannot be made from data available at this time. It is quite certain, however, that the sensitivity of the regurgitant-fraction method is considerably superior. No overlap has been obtained, in this or a previous study,\(^4\) between values for left ventricular regurgitant fraction from normal dogs and those from animals with aortic regurgitation. In the case of the disappearance distance to the subclavian artery, however, values from the two normal dogs overlapped those from the two dogs with the mildest degrees of aortic regurgitation (table 1). The left ventricular regurgitant-fraction method also has recently been confirmed by comparisons with forward and regurgitant flows in the ascending aorta measured directly by means of an electromagnetic flowmeter.\(^16\)

The possibility of obtaining nonrepresentative values for aortic regurgitation by the regurgitant-fraction method, due to a preferential injection into the ostium of a coronary artery or directly into a defect in the valve, is always present. For these reasons, it has been recommended that replicate injections always be made at the selected injection site (approximately 1 cm downstream from the aortic valve) and also at a site 1 cm further downstream.\(^4\) Since a good correlation exists between the withdrawal distance from the aortic valve and the degree of regurgitation, the reliability of detection and estimation of the severity of aortic regurgitation can be increased considerably if, in conjunction with the regurgitant-fraction measurement, the disappearance distance from the valve is also determined. This requires a moderate extension of the procedure to include recording of dilution curves subsequent to several step withdrawals of the injecting catheter down the aorta.

**Summary**

The distances between the aortic valve and sites in the aorta from which no retrograde flow of injected indicator could be detected in the left ventricle were determined, without thoracotomy, in two normal dogs and in ten dogs with chronic experimental aortic regurgitation. It was found that these distances attained maximal values when the aortic injections were timed to occur just at the end of systole or onset of diastole.

Distances downstream from the origin of the left subclavian artery from which no retrograde flow occurred to this vessel were de-
determined similarly in these same animals and, in confirmation of Warner and Toronto, similar relationships to the timing of the injections were obtained. These distances down the aorta, designated as "disappearance distances," were converted to "disappearance volumes" by measuring the diameters of the silhouette of successive aortic segments from aortograms made after contrast medium was injected into the left ventricle of these animals.

The regurgitant flow through the aortic valve per heartbeat was estimated on the basis of the amount of immediately appearing indicator detected in the left ventricle following injection of indicator approximately 1 cm downstream from the aortic valve. Correlation coefficients of 0.88 and 0.77 were obtained between these stroke-regurgitation values and the disappearance volumes from the aortic valve and subclavian artery, respectively. The standard errors of the estimate of the regurgitant flow per beat from these regression equations were ± 2.7 and ± 2.9 ml/beat, respectively. The correlation coefficients between stroke-regurgitation values and the disappearance distances from the valve and subclavian artery were 0.83 and 0.81, respectively, and the respective standard errors of the estimate of stroke regurgitation from these regression equations were ± 3.2 and ± 3.3 ml/beat.

It is concluded that determination of the maximal distances downstream in the aorta of sites from which retrograde flow of injected indicator can be detected in the left ventricle or subclavian artery is a valid method for estimating the severity of experimental aortic regurgitation in dogs. Since determinations of the disappearance distance from the aortic valve can be carried out readily in conjunction with measurement of the left ventricular regurgitation fraction, it is suggested that advantage be taken of the increase in reliability which accrues from the combined use of these two independent methods for the estimation of the degree of aortic regurgitation.

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