Estimation of the Residual Volume of the Ventricle of the Dog’s Heart by Two Indicator Dilution Technics

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A dye dilution and an electric conductivity method for measuring end-diastolic volume and stroke volume of the left ventricle are described, and equations for the calculation of stroke volume are given. When dye is injected “instantaneously” into the left ventricle during diastole, the aortic dye concentration-time curve obtained is a step-like curve and not a smooth curve. The ventricle empties itself in a “fractional” manner, approximately 46 per cent of its end-diastolic volume being ejected with each stroke and 54 per cent remaining in the ventricle at the end of systole.

In order to understand the functioning of the mammalian heart as a pump, it is necessary to know the volume of blood within each ventricle at the end of diastole (EDV), at the end of systole (ESV), as well as the stroke volume, heart rate, and the pressures distending the ventricles. Methods for measuring heart rate, stroke volume, and pressure are well established. Up to the present time, no adequate method has been available for measuring the EDV and ESV of the individual ventricles. In roentgenologic methods the measurements include the musculature of the heart, as well as the volume of blood within the chambers of the heart. From these determinations some investigators have estimated the volume of blood within both ventricles and both auricles. By injecting radio-opaque materials into the circulation and making high-speed motion pictures of the fluoroscopic image of the cardiac chambers Rushmer has measured the area of the individual ventricular chambers in one plane. Also, by means of implanting suitable measuring devices within the ventricular chamber, Rushmer has obtained data on the length and width of the ventricle during different parts of the cardiac cycle. Dye dilution technics have been used in attempts to measure the volume of blood within the ventricle by Bing, Heimbecker and Falholt, and by Lewis and Shadle. Lewis has estimated the ventricular plasma volume by means of theoretic and mathematic analysis of the dye dilution cardiac output curve, and Newman and associates, have developed theoretic equations for the calculation of residual volume from dye dilution curves.

In the studies by Bing and his associates, the dye, T-1824, was injected into the right ventricle and its concentration in the pulmonary artery blood was recorded continuously. The dyed blood withdrawn from the pulmonary artery mixed with the blood in the long-bleeding catheter as the blood passed through the catheter, and this changed the down-slope of the dye concentration-time curve. As a result, it was not known whether the estimated volumes represented the EDV, the ESV or some value between these two.

The technic with which the present paper is concerned is a modification of that described by Bing and associates, in which these difficulties have been overcome.

METHODS AND CALCULATIONS

Dye Dilution Technic. In the anesthetized dog (morphine, dial-urethane, phenobarbital) an ureteral catheter is passed by way of the carotid artery through the arch of the aorta and the aortic valves...
Fig. 1. Aortic blood T-1824 concentration-time curve obtained after the “instantaneous” injection of T-1824 into the left ventricle. See text for discussion.

into the left ventricle, either with or without the aid of the fluoroscope. The presence of the catheter tip in the ventricle is proven by recording a ventricular pressure curve from the catheter, as well as at autopsy. Two to 4 mg. of the dye, T-1824, in 1 or 2 ml. of saline is injected as quickly as possible (approximately 1 second) into the ventricle using a 5 ml. syringe. It is desirable, but not absolutely necessary, that the injection be made during diastole. Another short polyethylene catheter having a volume of 0.6 ml. is passed through the carotid artery into the ascending aorta very near the aortic valves. Blood is drawn through this catheter continuously for about six seconds, beginning at the instant of dye injection into the left ventricle. In order that the volume of the bleeding catheter may assume a relatively unimportant role, and that the mixing of the dyed aortic blood with the blood in the catheter may become a minor factor, the end of the bleeding catheter is inserted into a negative pressure chamber, which is evacuated to a pressure of 500 mm. Hg below atmospheric. In this way, the rate of flow through the bleeding catheter is greatly increased, and equals approximately 6 ml. per second; thus the bleeding catheter volume, 0.6 ml., is washed out once every 1/60 second. The blood is collected in small test tubes (4 mm. diameter), placed on the circumference of a revolving kymograph drum which is located inside the evacuated chamber. In this way samples are collected every 1/60 second for a period of 6 seconds after the “instantaneous” injection of dye. The collected blood is then centrifuged, and the plasma dye concentration determined on a 0.3 ml. sample of diluted plasma with a Beckman DU spectrophotometer and micro-cuvettes. Because of the high velocity of flow of blood into the collecting tubes there is frequently considerable hemolysis; in order to minimize this error a high concentration of the dye, T-1824, is injected, and the plasma samples are diluted with 5 parts of saline before reading in the spectrophotometer. A correction for hemolysis is made by reading each sample at a wave length of 540 millimicrons, and calculating the correction as described by Gibson and Evans. The hemocrit is determined by the method of Wintrobe and it is assumed that the packed red blood cells contain 5 per cent trapped plasma. Femoral arterial pressure is measured with a Statham Strain Gauge and recorded on a Brush Ink-writing Electromagnetic Oscillograph. Heart rate is calculated from the arterial pressure record. The aortic blood dye concentration-time curve is plotted; the results of a typical experiment are shown in figure 1.

The genesis of the dye concentration-time curve is interpreted as follows: It is assumed that the dye injected into the ventricle during diastole mixes with the blood in the ventricle, and that each ventricular ejection replaces the blood in the ascending aorta with the blood that was in the ventricle just prior to ejection. With the first ventricular ejection after the dye is injected, the dye concentration in the ascending aorta abruptly rises to a high level where it remains constant until the next ejection. It has been shown that there is little forward flow of blood through the ascending aorta or the pulmonary artery near the pulmonary valves during diastole. Thus the concentration of dye in the blood of the ascending aorta during diastole is the concentration that existed in the left ventricle at the end of the previous diastole. During the diastole following the first ejection of dye undyed blood passes into the left ventricle from the left auricle and dilutes and mixes with the dye which remained in the left ventricle. With the next ventricular ejection the dyed blood in the ascending aorta is replaced by ventricular blood that has been diluted with the undyed blood from the left auricle. Thus the concentration of dye in the aortic blood abruptly decreases to a lower concentration in a step-like fashion, where it remains until the next ventricular ejection lowers it another step. This continues with each ventricular ejection until the ventricle empties itself of the dye.

Since the amount of dye injected, (Q) and the concentration (C1) in the ascending aorta after the first ventricular ejection of dye are known, and since C1 is the concentration of dye that existed in the ventricle just prior to ventricular ejection, the volume of blood in the ventricle at the end of diastole can be calculated from the equation

$$EDV = \frac{Q}{C_1} - \frac{Q}{C_2}$$

If each beat of the ventricle emptied one half of its volume, the concentration of dye in the ascending aorta following the second ejection of dye would be one half the concentration following the first ejection, and each subsequent ventricular ejection would give rise to a concentration one half that which existed in the ascending aorta following the prior ventricular ejection. If each beat of the ventricle ejected some fraction of its EDV other than one half, then, of course, the step-like decrease in
aortic concentration would differ accordingly. Thus, in each experiment, the ratio of \( \frac{C_2}{C_1} \), \( \frac{C_3}{C_2} \), \ldots, \( \frac{C_n}{C_{n-1}} \), can be determined from records such as shown in figure 1 and the average of \( \frac{C_n}{C_{n-1}} \) ascertained. Then, if it is assumed that the stroke volume, EDV and ESV remain constant for the few seconds of the determination, another calculation of EDV is made as follows:

Let \( C_{n-1} \) (EDV) = mg. dye in ventricle at end of diastole, \( C_{n-1} \) (ESV) = mg. dye in ventricle at end of corresponding systole, and \( C_n \) (EDV) = mg. dye in ventricle at end of next diastole

Then
\[
C_n(EDV) = C_{n-1}(ESV)
\]

\[
\frac{C_n}{C_{n-1}} = \frac{(ESV)}{(EDV)}
\]

by Definition:
\[
EDV - ESV = Stroke
\]

dividing by EDV:
\[
EDV = \frac{Stroke}{1 - ESV/EDV}
\]

therefore:
\[
EDV = \frac{Stroke}{1 - \frac{C_n}{C_{n-1}}}
\]

Cardiac output is determined by integrating the area under the dye concentration-time curve with a planimeter, calculating the average dye concentration, and dividing this into the quantity of dye injected.12

Since the above experiment was tedious, and made more than a few determinations in one animal impractical, another indicator dilution technic was developed, using a concentrated salt solution (NaCl) instead of the dye, T-1824. In this method, the concentration of the salt solution in the ascending aorta was determined by means of a small electrical conductivity cell placed in the ascending aorta, and end-diastolic volume was calculated according to the foregoing equation.

**Electric Conductivity Technic:** The electric conductivity cell and technic for measuring conductivity are similar, in some respects, to that described by White,13 but differ considerably in detail from White's method.

The first electric conductivity cells that we used were made as follows: Within a catheter having a length of 50 cm. and an inside diameter of 1.5 mm., a thin-walled tube of platinum, approximately 5 mm. long, and with an outside diameter of 1.5 mm., is so placed that the end of the platinum tube is approximately 2 mm. from the end of the catheter. A similar piece of platinum tubing is placed within the lumen of the polyethylene tubing, separated by about 0.5 mm. from the end of the other piece of platinum tubing. The end of this piece of platinum is connected to a small polyethylene tube located inside the larger polyethylene tube. A no. 34 insulated copper wire is connected to each of the platinum tubes. These wires occupy the space between the two pieces of polyethylene tubing. Other types of conductivity cells, in which one platinum tube is placed inside a larger platinum tube but insulated from the larger tube, have been constructed and used; but most of our studies have been with a double-lumen catheter (fig. 2) for the left ventricle manufactured* to our specifications.

When separate catheters are used the electrical conductivity catheter is passed into the ascending aorta via a common carotid artery and another catheter into the ventricle through the aortic valve. When, as in most of our experiments, a double-lumen catheter (fig. 2) is employed it is similarly introduced so that the tip of the injection catheter is approximately in the center of the left ventricle and the tip of the electrical conductivity cell catheter lies in the ascending aorta very close to the aortic valves. A small flow of heparinized saline continuously flushes the catheters preventing blood from running into the catheters. When one wishes to measure the conductivity of the blood in the ascending aorta, blood is drawn through the electrical conductivity catheter by connecting its distal end to a chamber which is evacuated to minus 300 mm. Hg pressure; in this way, blood in the ascending aorta passes over the electric conductivity cell. The rate of flow of blood over the cell is approximately 1 ml. per second, and is such that the cell is bathed with blood which was in the

* The U. S. Catheter & Instrument Corporation has kindly cooperated by fabricating these catheters, as well as double-lumen catheters for the right ventricle and single-lumen catheters.
ascending aorta a small fraction of a second before it reaches the cell. The wires leading from the conductivity cell are connected to two arms of a Wheatstone Bridge (fig. 3) which connects to a Brush Universal Amplifier. The Brush Amplifier sends a 2,000-cycle alternating current through the Wheatstone Bridge and the conductivity cell. The electric resistance of the conductivity cell is a function of the electrolyte concentration of the blood bathing the cell. A variable resistance in one arm of the Wheatstone Bridge is adjusted to balance the resistance in the electrical conductivity cell; a rough balance is obtained by noting when the hum in a set of earphones diminishes to zero. A Brush BL-202 Electromagnetic Ink-writing Oscillograph is connected to the amplifier and records the resistance change of the electrical conductivity cell. The deflection of the electromagnetic oscillograph is linear with a change in resistance of the conductivity cell.

In an experiment, 1 to 1.5 ml of 4 per cent NaCl solution is injected "instantaneously" into the left ventricle and the electric conductivity of the blood in the ascending aorta is measured for a few seconds before, during, and after the injection period. The conductivity catheter is then immediately flushed with heparinized saline, and the slow perfusion of heparinized saline through it is started in order to prevent clotting within the cell. The results of a typical determination are shown in figure 4. A calibration curve is made at the end of each experiment by placing a known quantity of the dog's blood in a beaker held at a constant temperature of 40°C., adding to this a known volume of 4 per cent salt solution and determining the electrical conductivity.

The electrical conductivity cell is sensitive to temperature changes and to changes in the rate of flow of blood through the conductivity cell, and therefore it is important to carry out the calibration in a constant temperature bath and to keep a constant rate of blood flow through the conductivity cell. With each arterial pulse there is a sudden decrease in electrical conductivity, which causes an artifact, as shown in figure 4. We have been unable, to date, to eliminate this artifact, and the exact nature of its cause is not known. However, since the electrical conductivity remains constant during diastole, this is taken as the base line, and it is felt that the artifact introduces no great error in the method, although it is desirable that it be eliminated. In an occasional experiment, there is some drift of the base line, the cause of which is unknown. Since a determination requires only from 5 to 10 seconds, it is seldom that this drift introduces any appreciable error. Since the electric conductivity of blood varies with the hematocrit, it is important that the hematocrit of the calibrating blood be the same as the hematocrit of the blood during the determination of electrical conductivity in the animal.

With this technic, it is possible to measure the change in the sodium chloride concentration in the blood in the ascending aorta nearly instantaneously, and thus any error introduced into the residual volume determination by virtue of aortic blood mixing with blood in the catheter is eliminated.

Cardiac Output Determination. In our earlier studies we determined the average concentration of the injected sodium chloride solution from records such as that shown in figure 4 in the conventional way. The area under the curve measured with a planimeter was divided by the length of the base line from the beginning of the ejection of the sodium chloride solution from the ventricle until the deflection returned to the base line. It soon became apparent that this was inaccurate if the heart rate was irregular or the fractional emptying of the ventricle varied from beat to beat. Also, since the ventricle may not completely empty itself of the injected sodium chloride solution during the few seconds of the determination, the record may not return completely to the base line before re-circulation occurs. In an attempt to correct this, the data were plotted on semi-log paper in the manner described by Kinman, Moore, and Hamilton. Since the sodium chloride concentration decreased in a step-like fashion, no smooth down slope of the semi-log plot could be obtained. The best that could be obtained by this method was to draw a line through the middle of the steps of the down slope. This method of calculation is theoretically accurate provided the heart rate remains constant and the fractional emptying of the ventricle is constant for each beat during the determination. However, in a large percentage of the cases, either the heart rate does not remain constant or the fractional emptying of the ventricle varies from beat to beat during the determination, and in these cases the conventional method of calculating cardiac output is inaccurate. Therefore another method was developed.

![Fig. 3. Wheatstone Bridge Circuit for recording with platinum electrical conductivity cell. Contacts numbered 1, 2, 3, and 4, are connected to similarly numbered contacts on a Brush Universal Amplifier (Model No. BL-320), which in turn is connected to a Brush Ink-writing Oscillograph (Type BL-202) for recording.](http://circres.ahajournals.org/DownloadedFrom)
The ventricle pumps blood intermittently, by a series of ejections, and the flow of blood in the ascending aorta is a discontinuous flow. The calculation of the flow from a pump, which ejects intermittently, resolves itself into the calculation of the volume ejected during each beat. If Q amount of indicator is placed in the ventricle during diastole, the amount of indicator ejected from the ventricle with each stroke is equal to the average concentration, \(\bar{C}\), of the indicator in the blood ejected times the stroke, \(S\), that is, \(Q = SC\).

If the ventricle completely empties itself of the indicator during the determination, then:

\[
Q = S_1C_1 + S_2C_2 + S_3C_3 + \ldots + S_nC_n
\]  

\[
Q = \text{ml. of concentrated NaCl solution injected into the ventricle}
\]

\(S_1 = \text{1st stroke in ml.}\)

\(S_2 = \text{2nd stroke in ml.}\)

\(S_n = \text{nth stroke in ml.}\)

\(C_1 = \text{Average concentration of injected NaCl solution in aortic blood in 1st stroke}\)

\(C_2 = \text{Average concentration of injected NaCl solution in aortic blood in 2nd stroke}\)

\(C_n = \text{Average concentration of injected NaCl solution in aortic blood in nth stroke}\)

If it is assumed that the stroke is constant during the determination, then:

\[
Q = S(C_1 + C_2 + C_3 + \ldots + C_n)
\]

Therefore:

\[
S = \frac{Q}{(C_1 + C_2 + C_3 + \ldots + C_n)}
\]  

If, at the end of the nth beat the concentration has not returned to zero, then the above equation may be corrected for the amount of indicator that remains in the ventricle as follows:

\[
S = \frac{Q(C_1 - C_{n-1})}{C_1 + C_2 + \ldots + C_{n-1}}
\]

In some cases the record does not return completely to the base line before re-circulation occurs but returns nearly to the base line. In these cases \(C_n\) is taken as the concentration nearest to 25 per cent of \(C_1\) but less than 25 per cent of \(C_1\). The stroke volume is calculated using equation (3).

Since the stroke volume is known, the cardiac output per minute can be calculated by multiplying by the heart rate per minute.

Results

**Dye Dilution Technic.** The results of a typical experiment are shown in figure 1 and data of six determinations on 4 dogs are given in table 1.

### Table 1—Normal Values of End-Diastolic Volume (EDV), End-Systolic Volume (ESV), and Stroke Volume, Obtained with the Dye-Dilution Method

<table>
<thead>
<tr>
<th>Dog Weight (Kg.)</th>
<th>EDV (ml.)</th>
<th>ESV (ml.)</th>
<th>Stroke (ml.)</th>
<th>Heart Rate (beats/min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.9</td>
<td>106</td>
<td>60</td>
<td>46</td>
<td>66</td>
</tr>
<tr>
<td>13.1</td>
<td>77</td>
<td>56</td>
<td>31</td>
<td>78</td>
</tr>
<tr>
<td>23.6</td>
<td>90</td>
<td>43</td>
<td>47</td>
<td>72</td>
</tr>
<tr>
<td>16.0</td>
<td>96</td>
<td>54</td>
<td>41</td>
<td>66</td>
</tr>
<tr>
<td>23.3</td>
<td>123</td>
<td>76</td>
<td>47</td>
<td>102</td>
</tr>
<tr>
<td>Av. 19.5</td>
<td>100</td>
<td>57</td>
<td>43</td>
<td>77</td>
</tr>
</tbody>
</table>

**Fig. 4.** In the lower curve is shown the aortic blood electrical conductivity-time record obtained after the “instantaneous” injection of 0.5 ml. of 4 per cent NaCl solution into the left ventricle. The calibration of this curve is in ml. of 4 per cent NaCl solution per 100 ml. of blood. Note the artifact with each pulse.

The upper curve is a simultaneous record of femoral arterial pressure, calibrated in mm. of mercury pressure.

In all these experiments the ventricle emptied itself in a “fractional” manner, and the dye concentration-time curve decreased in a step-like fashion with each ventricular ejection. A large volume of blood always remained in the ventricle at the end of systole. This residual volume was, on the average, 57 per cent of the EDV, while the stroke volume was only 43 per cent of the EDV.

**Electric Conductivity Method.** The results of a typical experiment are shown in figure 4 and data of 8 experiments on 8 dogs are given in table 2. In the dogs having an average heart rate of 79 beats per minute the residual volume was, on the average, 54 per cent of the EDV and the stroke volume was 46 per cent of the
TABLE 2.—Normal Values of End-Diastolic Volume (EDV), End-Systolic Volume (ESV) and Stroke Volume Obtained with the Electric Conductivity Method

<table>
<thead>
<tr>
<th>Body Weight (Kg.)</th>
<th>EDV (ml.)</th>
<th>ESV (ml.)</th>
<th>Stroke (ml.)</th>
<th>Heart Rate (beats/min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow Heart Rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21.3</td>
<td>82</td>
<td>40</td>
<td>42</td>
<td>60</td>
</tr>
<tr>
<td>15.5</td>
<td>68</td>
<td>39</td>
<td>29</td>
<td>100</td>
</tr>
<tr>
<td>22.2</td>
<td>57</td>
<td>50</td>
<td>37</td>
<td>75</td>
</tr>
<tr>
<td>20.0</td>
<td>44</td>
<td>22</td>
<td>22</td>
<td>80</td>
</tr>
<tr>
<td>Av. 19.8</td>
<td>70</td>
<td>38</td>
<td>32</td>
<td>79</td>
</tr>
<tr>
<td>Fast Heart Rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.9</td>
<td>94</td>
<td>77</td>
<td>17</td>
<td>158</td>
</tr>
<tr>
<td>19.8</td>
<td>94</td>
<td>31</td>
<td>18</td>
<td>170</td>
</tr>
<tr>
<td>27.1</td>
<td>63</td>
<td>45</td>
<td>18</td>
<td>182</td>
</tr>
<tr>
<td>19.9</td>
<td>63</td>
<td>47</td>
<td>16</td>
<td>140</td>
</tr>
<tr>
<td>Av. 20.9</td>
<td>67</td>
<td>50</td>
<td>17</td>
<td>153</td>
</tr>
</tbody>
</table>

Fig. 5. Thirty-two control determinations of end-diastolic volume in seven dogs. The mean EDV was 62 ml. The standard deviation was determined for each dog; the average of the standard deviations for the seven dogs was ±9 ml.

The results of 32 control determinations of EDV in 7 dogs with the electrical conductivity method are shown in figure 5. In some of these experiments a second control determination was made 20 minutes later. However, in most of the cases a first control determination was made and then an experimental procedure, such as breathing air under positive or negative pressure was carried out; this was followed in about 20 minutes by a second control determination. These results show a reasonably good agreement between the two control determinations. The average of the standard deviations from the mean for each dog was ±9 ml. with a mean EDV for all dogs of 62 ml.

In order to test the accuracy of the electrical conductivity method, the cardiac output was calculated simultaneously using it and a dye dilution (T-1824) method in 8 experiments on 4 dogs. In the dye dilution method samples of blood were collected from the ascending aorta each 3/2 second. The T-1824 was mixed with the 4 per cent sodium chloride solution which was injected into the left ventricle. A typical experiment is shown in figure 6. Additional results are given in table 3. Since the dye-dilution curve obtained in this experiment (with a relatively slow rate of sampling from the ascending aorta) gave a smooth curve with no steps, it was necessary to calculate the output by determining the area under the dye-dilution curve. The cardiac output simultaneously obtained by use of the electric conductivity method was calculated both according to equation (2) and by measuring the area under the curve with a planimeter.

As shown in table 3, in all but two determinations the electric conductivity method gave a lower cardiac output than that obtained with the dye dilution method. One reason for this is that the concentrated salt solution injected interferes with the dye dilution technic. Each sample of blood collected in a test tube for the dye dilution determination contains a certain amount of 4 per cent sodium chloride solution. These samples must be centrifuged, in order to obtain the plasma, and this requires about one-half hour or more. During this time, the hypertonic salt solution extracts water from the red blood cells by osmosis and therefore in-
Fig. 6. Simultaneous aortic electric conductivity and T-1824 concentration-time curves for the determination of cardiac output. Electrical conductivity record is shown above and T-1824 record below. T-1824 mixed with 4 per cent NaCl was injected into the left ventricle "instantaneously" at arrow. See text for discussion.

Increases the volume of plasma and decreases the volume of the red blood cells within the test tube. Thus the concentration of T-1824 within the plasma is decreased. A decrease in the T-1824 concentration in the plasma gives an increase in the plasma cardiac output calculated by the dye method. Since the determination of cardiac output by the dye dilution technic measures the plasma cardiac output, and this is converted to whole blood cardiac output by dividing by the plasma hematocrit, an increase in the plasma hematocrit will give a decrease in the calculated cardiac output. It appears, on the basis of preliminary studies, that the concentrated salt solution causes a greater decrease in the plasma T-1824 concentration than it causes increase in the plasma hematocrit, as determined by the Wintrobe technic. This may be caused by the fact that the crenated red blood cells do not pack as well as the uncrenated red cells. These effects result in the calculated T-1824 cardiac output being too high.

In the electric conductivity technic, concentrated salt solution is in contact with ventricular blood for only 5 or 6 seconds, and thus there is only a short time to withdraw fluid from the red blood cells by osmosis. In the calibration of the blood in the electric conductivity technic, it takes about 11 seconds to make a determination from the time the 4 per cent salt solution is added to the blood. Therefore, in the calibration, the concentrated salt solution has a somewhat longer time to withdraw water from the red blood cells. This error would tend to make the cardiac output determined by the electrical conductivity method smaller than the true value.

Thus, on the basis of the above, the cardiac output determined by the T-1824 method tends to be too large and that determined by the electrical conductivity method tends to be too small when the determinations are made simultaneously.

**COMMENTS**

If the indicator is injected into the ventricle during systole as well as during diastole, stroke...
volume is estimated in the manner described by equation (2), except that calculation of EDV is modified in that the calculation of the ratios of $C_{n-1}$ is begun with the concentration following the end of the injection instead of with $C_1$. Such calculation of stroke volume should be just as accurate, as when the indicator is injected into the ventricle during diastole, provided the injected indicator mixes with the blood during systole to the same degree that it mixes during diastole. Very probably, the mixing is not as adequate during systole, and therefore some error is introduced.

Although the assumption that the injected indicator completely mixes with the blood in the ventricle before each ventricular ejection is no doubt somewhat in error, the fact that control determinations show considerable agreement with each other (fig. 5) indicates that the assumption is satisfied to a reasonable degree.

It is assumed in the determination of EDV that all of the injected indicator leaves the ventricle by way of the ascending aorta and that none regurgitates into the left auricle. That this assumption is correct is shown by the fact that in 23 determinations on 5 dogs, in which T-1824 was injected into the left ventricle and samples simultaneously taken from the left ventricle and the left auricle, the concentration of dye in the left atrium was on the average only 2 per cent of the concentration in the left ventricle. This slight regurgitation may have been caused by the fact that one catheter passed from the left ventricle through the mitral valve into the left auricle and may have tended to hold the valve open, and that two catheters passed from the arch of the aorta through the aortic valves into the left ventricle.

The calibration carried out at the end of each experiment presents some difficulties. Since a variation in the red cell concentration of the blood changes the electric conductivity, it is important that the blood be thoroughly mixed in the beakers during the course of the calibration. This is accomplished by stirring continuously during the course of the calibration curve. Also, we have found it important to determine the base line electric conductivity of the blood in a particular beaker and then as quickly as possible add the concentrated salt solution to the blood remaining in the beaker, mix thoroughly, and then determine the electric conductivity. This is done by placing a known quantity of blood in a beaker, withdrawing blood at a constant rate for 15 seconds through the electric conductivity cell and thus determining the base line. A known amount of 4 per cent sodium chloride solution is immediately added to the blood remaining in the beaker, mixed, and the electrical conductivity determined. This procedure generally requires 11 seconds from the time the sodium chloride solution is added until the calibration is complete. If a control sample of blood is placed in one beaker and quantities of the same blood are placed in other beakers to which are added different quantities of concentrated sodium chloride solution, the calibration is likely to be inaccurate and unsatisfactory. The reason for this appears to be the fact that small temperature differences cause a change in the electrical conductivity of the blood, and in the water baths that we have used, the temperature varies slightly from beaker to beaker.

Since no other independent method for measuring EDV or ESV is available, it has not been possible to check the accuracy of the data presented here. Preliminary studies with a model suggest that the electric conductivity method measures the EDV and ESV with a reasonable degree of accuracy. On the basis of the data presented, as well as preliminary results of model studies, it is felt that the electric conductivity method gives an accurate measure of cardiac output and stroke volume, especially since the electric conductivity method is not subject to error when the heart rate is irregular or the "fractional" emptying of the ventricle varies as is the case with the conventional dilution methods.

**Summary**

Two methods, a dye dilution method and an electric conductivity method, for measuring the volume of blood within the left ventricle at the end of diastole (EDV) and the stroke volume are described. From these determinations, the volume of blood within the ventricle at the end of systole is calculated. The left
ventricle empties itself in a “fractional” manner and, on the average, ejects approximately 46 per cent of its EDV with each stroke and retains approximately 54 per cent of its EDV at the end of systole. The aortic blood dye concentration-time curve obtained when dye is injected into the left ventricle is a step-like, not a smooth curve. Equations for the calculation of stroke volume are described.

ACKNOWLEDGMENT

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SUMMARIO IN INTERLINGUA

Es describite duo methodos pro mesurar le volumine de sanguine intra le ventriculo sinistre al fin del diastole e le volumine cardiac per pulso. Le prime es un methodo a dilution de colorante, le secunde un methodo a conductivitate electric. Ab iste determinationes es calculate le volumine de sanguine residue in le ventriculo al fin del systole. Le ventriculo sinistre se vacua “fractionalmente.” Illo ejice con omne pulso un quantitate median de circa 46 pro cento de su contento al fin del diastole e retine al fin del systole circa 54 pro cento de ille quantitate. Le curva de concentration de colorante in tempore pro sanguine aortic, obtenite post le injection de colorante in le ventriculo sinistre, es un curva terrassate e non lisie. Es describite equationes pro le calculation del volumine per pulso.

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Estimation of the Residual Volume of the Ventricle of the Dog's Heart by Two Indicator Dilution Technics

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