Relative Effects of Heart Chambers, Lungs, and Mitral Insufficiency on the Shape of Indicator Dilution Curves


With the assistance of William H. Goodson and William G. Wheeler

The shape of dilution curves obtained by sampling from different sites was studied in dogs following superior vena caval injections of dye. Synchronous sampling from paired sites enabled observations to be made on the separate effects of the right heart, left ventricle and aorta on the dye dilution curves, with and without mitral insufficiency.

The results show that the left ventricle and aorta have little effect on the final slope of a dilution curve across the lungs in dogs with normal hearts. In the presence of mitral incompetence the final slope across both lungs and heart was slower than in the normal, but these changes were related to cardiac output and increase in lung mixing volume rather than primarily to the incompetence of the valve.

Knowledge of the factors which primarily determine the downslope of an indicator dilution curve across a multiple compartment-in-series system such as the heart chambers, lung, and aorta is of considerable importance in the application of such curves to determination of volumes and flows. As shown previously, the relative size of the mixing compartments in the heart and lungs is one of the prime determining factors of the downslope.\(^1\) It has recently been suggested that incompetence of valves might be measured by analysis of the slopes of dilution curves.\(^2\) The present experiments were designed to assess the effect of the various compartments in the heart-lung system on the exponential portion of the downslope of dye curves, and to determine under what circumstances mitral valvular insufficiency might influence this downslope.

After injection of dye into the superior vena cava or right ventricle, curves, obtained synchronously from paired sampling sites, were compared in 244 dye dilution curves obtained in 33 dogs. Sampling from paired sites in the left side of the heart and arterial tree allowed detection of any changes in the shape of the curve caused by the compartment between the proximal and distal sampling site. In this way, the effect of one or more compartments on the shape of the curve could be assessed.

Method

Mongrel dogs were prepared so that a sampling catheter could be accurately introduced into the left atrium (L.A.) without opening the chest at the time of each experiment. At thoracotomy, 4 to 8 days before any observations were made, one end of a polyethylene guide tube (internal diameter 3.76 mm.) was sutured to the left atrial wall, and the other end of this tube was brought out through the chest wall and buried just beneath the skin where it was sutured and readily accessible. The left atrial sampling catheter of polyethylene tubing (internal diameter 1.67 mm.) with the shaft of a thin-walled no. 18 needle at the tip was introduced via the guide tube, and the L.A. was easily punctured. This method of left atrial puncture was simple, provided excellent sampling, and could be repeated many times in the same dog.

Other sampling catheters were introduced into the following sites as required: (a) via carotid artery to aortic root just distal to the aortic valve, (b) the aortic bifurcation via the femoral artery, (c) the femoral artery itself. The position of catheters was checked prior to the experiment by fluoroscopy, and pressure readings and frequently their positions were confirmed at necropsy.
TABLE 1.—Comparison of the Shape of Dilution Curves from Various Sites

<table>
<thead>
<tr>
<th>Injection site</th>
<th>Sampling sites</th>
<th>No. of obs.</th>
<th>Mean percentage difference between slopes</th>
<th>S.D. of mean percentage difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.V.C. L.A. and aortic root</td>
<td>32</td>
<td>-1.13</td>
<td>2.78</td>
<td></td>
</tr>
<tr>
<td>S.V.C. L.A. and aortic bifurcation</td>
<td>10</td>
<td>-2.78</td>
<td>3.34</td>
<td></td>
</tr>
<tr>
<td>S.V.C. L.A. and femoral artery</td>
<td>13</td>
<td>-20.75</td>
<td>13.36</td>
<td></td>
</tr>
<tr>
<td>S.V.C. Aortic root and aortic bifurcation</td>
<td>14</td>
<td>-1.53</td>
<td>1.9</td>
<td></td>
</tr>
</tbody>
</table>

*Data obtained from 20 dogs.

The dogs were anesthetized with pentobarbital, 25 mg./Kg. Their respirations were controlled by a “Penophore” demand respirator with 100 per cent oxygen in order to minimize fluctuations in optical density of blood due to variable arterial oxygen saturation. Dye injections (indigo carmine) were made through a no. 8 cardiac catheter that had been previously positioned in the right heart under fluoroscopic control.

Sampling and recording were carried out by methods previously described from this laboratory and were such as to prevent significant distortion of the curves.

Cardiac output (C.O.) is calculated from the dilution curves according to Hamilton and his co-workers. The slope (washout slope) is calculated from the semi-logarithmic replot of the original dilution curve as

\[ \text{Slope} = \frac{\ln C_1 - \ln C_2}{\text{seconds}} \]

The term “slope volume” indicates the largest mixing volume. It is derived from \( S = F/V \) where

\[ S = \text{washout slope}, F = \text{flow}, \text{and } V = \text{slope volume}. \]

RESULTS

Effect of the Left Ventricle, Aorta, and Femoral Artery on the Downslope of the Dilution Curve. After a single injection of dye into the superior vena cava (S.V.C.), dilution curves were obtained synchronously from paired sites: (a) L.A. and aortic root, (b) L.A. and aortic bifurcation, (c) L.A. and a peripheral site in the femoral artery, (d) aortic root and aortic bifurcation.

The effect of including the left ventricle, the left ventricle plus aorta, or the aorta alone was expressed as the percentage difference between the slopes obtained from the distal site and the slope recorded at the proximal site (table 1).

From these results it is concluded that neither the left ventricle nor the aorta changed the dilution curve appreciably and that the terminal slope of a dilution curve following injection into the S.V.C. was determined before the dye reached the L.A. Dye curves obtained from the femoral artery, on the other hand, were unreliable, as the mean percentage difference between these slopes when compared with those obtained synchronously from the L.A. varied by an average of 20.75 per cent (range -2.8 to -46.7 per cent).

Twenty-six of these curves were analyzed for cardiac output, “central volume” and needle-to-needle volume (table 2).

The inclusion of either the left ventricle or the left ventricle and aorta between injection and sampling sites did not substantially alter values obtained for cardiac output, slope, and “slope volume.” The absolute value for “slope volume” calculated from these dilution curves (52 separate observations) was 65 ml. This represents the average “slope volumes” for this particular group of mongrel dogs.

Effect of Mitral Incompetence on the Dilution Curve. Mitral incompetence (M.I.) was created surgically in a group of 5 dogs in which observations had previously been made.

\[ S = \text{washout slope}, F = \text{flow}, \text{and } V = \text{slope volume}. \]
MITRAL INSUFFICIENCY AND INDICATOR DILUTION CURVES

TABLE 2.—The Effect of Including the L.V. and L.V. Plus Aorta between the Injection and Sampling Site on Mean Percentage Difference. Dye Was Injected into S.V.C. and Curves Were Obtained by Synchronous Sampling from Paired Sites*

<table>
<thead>
<tr>
<th>Injection site</th>
<th>Sampling sites</th>
<th>No. of obs.</th>
<th>Between C.O.</th>
<th>Between slopes</th>
<th>Between &quot;slope&quot; volumes</th>
<th>Between N-N volumes</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.V.C.</td>
<td>L. A. and aortic root</td>
<td>14</td>
<td>-1.15 (SD 4.42)</td>
<td>-2.25 (SD 1.75)</td>
<td>+2.68 (SD 5.66)</td>
<td>+28.58 (SD 10.24)</td>
</tr>
<tr>
<td>S.V.C.</td>
<td>L. A. and aortic bifurcation</td>
<td>12</td>
<td>-3.10 (SD 4.55)</td>
<td>-2.78 (SD 4.05)</td>
<td>+6.16 (SD 2.52)</td>
<td>+46.14 (SD 8.99)</td>
</tr>
</tbody>
</table>

*Data obtained from 10 dogs.

Due to the poor long-term survival rate in such preparations, the second group of observations was made as soon as possible after the chest was closed following the operation for M.I. In all, we analyzed 30 dilution curves from the above 5 dogs, all of whom had had mitral incompetence created surgically. The following points were common to all 5 dogs:

1. Cut chordae tendinae were demonstrated at necropsy.
2. All had a loud systolic murmur on auscultation. (In two cases a soft systolic murmur was present before surgery but increased markedly after mitral incompetence had been produced.)
3. At necropsy, after clamping of the aorta and injection of fluid into the L.V., there was a free flow of fluid from the L.A.

Dye was then injected into the S.V.C., and dilution curves were obtained synchronously from L.A. and aortic root. The findings were similar to those in the original experiments with a competent mitral valve, in that there was no significant difference in the downslopes of "slope volumes" of the curves obtained from the left auricle and aortic root (table 3).

Further analysis of curves from normal and mitral insufficient dogs shows that the slopes are slower in the presence of mitral insufficiency (table 4). This can be explained in part by the lower cardiac outputs with M.I.; but since the slopes diminish out of proportion to the outputs, one finds that the "slope volume" has increased.

To determine whether this alteration in slope in acute mitral incompetency was caused by changes in the dilution curves from the lungs or the left heart, a further series of left heart dilution curves was obtained. Dye

TABLE 3.—The Effect of Mitral Incompetence on Mean Percentage Differences Calculated from Dilution Curves Obtained by Synchronous Sampling after Injection of Dye*

<table>
<thead>
<tr>
<th>Valve state</th>
<th>Injection site</th>
<th>Sampling sites</th>
<th>No. of obs.</th>
<th>Between C.O.</th>
<th>Between slopes</th>
<th>Between &quot;slope&quot; volumes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>S.V.C.</td>
<td>L. A. and aortic root</td>
<td>12</td>
<td>-1.7 (SD 3.70)</td>
<td>-2.21 (SD 2.21)</td>
<td>+4.13 (SD 4.66)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.I.</td>
<td>S.V.C.</td>
<td>L. A. and aortic root</td>
<td>12</td>
<td>+1.36 (SD 3.92)</td>
<td>+0.23 (SD 1.60)</td>
<td>-2.16 (SD 4.98)</td>
</tr>
</tbody>
</table>

*Data obtained from 5 normal dogs and 5 dogs with M.I.
was injected into the L.A., and the dilution curves were obtained by sampling from the aortic root (table 5). Results show that the left heart curves are modified by M.I., but their slopes (0.345 to 0.764) were in all cases steeper than the slopes of curves obtained from similar preparations when the lungs were included between injection and sampling sites (0.161 to 0.315). This confirms that in acute M.I. following S.V.C. injection, the terminal exponential slope of the aortic curve is governed by the compartment of the lungs before the dye reaches the L.A.

**DISCUSSION**

An analysis of the factors governing a time-concentration curve of an indicator after passage through serial compartments has been set forth by Newman et al. These considerations, though they were carried out on continuous flow, constant volume systems, show this basic fact: In a series of compartments, each imposing an exponential downslope, the compartment imposing the slowest slope will determine the slope of the terminal exponential portion of the curve. This is true, whether the slope of each compartment is determined by a simple flow-to-volume ratio \( S = \frac{F}{V} \) as in a fixed volume, or by a more complicated dilution volume \( S = R \ln \left( \frac{V_R}{V_R + V_E} \right) \) as with contractile chambers. In normal circumstances in dogs the data here show that the lungs act as the largest mixing compartment and determine the final slope, since passage through the left heart leaves the slope unaltered. For either left or right heart with normally functioning valves to change the slope imposed by the lungs, one of the chambers must have a \( \frac{V_R}{V_R + V_E} \) ratio of sufficient magnitude to impose a slower slope than that imposed by the lung.

Further studies, not reported here in detail, showed that the slopes across the right heart alone, obtained by injecting into the S.V.C. and sampling from the pulmonary artery, correspond with those reported here for the left side. There is no reason, therefore, to suppose that the right heart normally has any more influence on the final slope than does the left. This presupposes that the investigator has not imposed a slow curve on the system, either by a slow injection or by a slow recording and sampling system, since these can alter the final slope.

When incompetence of a valve is present, the same conditions hold regarding the determination of the final downslope across the entire system. The slope imposed across the two compartments connected by an incompetent valve must be less than that imposed by the lungs for this to govern the final slope. In acute insufficiency as examined here, the slope of the curves across both heart and lungs was slower than normal for these cardiac outputs. However, the slopes of curves across the left heart alone were always steeper than they were when the lungs were included and therefore could not account for the changes. This means that in the presence of insufficiency the lungs still impose the dominating slope, and this "slope volume" of the lungs is larger.
TABLE 5.—The Effect of Mitral Incompetence on the Slope of Left Heart Dilution Curves after Injection of Dye and Sampling from Aortic Root

<table>
<thead>
<tr>
<th>Valve state</th>
<th>Injection site</th>
<th>Sampling site</th>
<th>No. of obs.</th>
<th>Mean slope of slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>L.A. Aortic root</td>
<td>14</td>
<td>1.12</td>
<td>(0.390 – 1.73)</td>
</tr>
<tr>
<td>M.I.</td>
<td>L.A. Aortic root</td>
<td>18</td>
<td>0.50</td>
<td>(0.354 – 0.764)</td>
</tr>
</tbody>
</table>

*Data obtained from 5 normal dogs and 5 dogs with M.I.

than it is in absence of incompetence. With small residual volumes, extremely large unphysiological regurgitation would have to occur to impose a slope as slow as that from the lungs. That the left heart will become the determining compartment is quite likely in cases of long-standing insufficiency where increased residual volumes are present.

For any given dilution curve across both heart and lungs the downslope may be governed by one of several parameters: the lungs, a very large residual volume of a heart chamber, or valvular incompetence plus increased residual volume. It would seem that quantitation of valvular incompetence from the slopes of curves across the entire system would be in error unless some methods of measuring both lung and residual volumes were employed. Accurate representative sampling is important for the analysis of the shape of dilution curves. The wide and variable differences of slope when obtained from the aortic root and femoral artery show that the latter is unsatisfactory as a sampling site in the dog.

In the presence of acute mitral incompetence, the final slope is slower than can be accounted for by changes in cardiac output or changes in the dilution curve across the left heart. The final slope is determined by the lungs compartment which has a slightly larger "slope volume" than it does in the absence of incompetence.

In the dog, the femoral artery is unsatisfactory as a sampling site for accurate reproduction of dilution curves.

**Acknowledgment**

We are indebted to Dr. Michael Weidner, Jr. for his help and operative skill, which enabled us to use the method of L.A. puncture described, and to carry out studies on mitral incompetence. We also wish to acknowledge the help of Dr. John H. Brewer, Director of Biological Research, Hynson, Westcott and Dunning, Baltimore, Md., for further supplies of indigo carmine.

**SUMMARIO IN INTERLINGUA**

Le effecto producite in le curva del dilution de colorante per includer le ventriculo, le aorta, e le corde dextere inter le sito del injection e le sito del obtention del specimen es demonstrate per le obtention synchrone de specimenes al sitos apperante. In normal canes anesthesiate, le declino final de un curva dilutional a transverso corde e pulmon es determinate per le processu dilutional in le pulmon.

In le presentia de acute incompetencia mitral, le declino final es plus lente que lo que pote esser explicate per alterationes del rendimento cardiac o per alterationes in le curva dilutional a transverso le corde sinistre. Le declino final es determinate per le compartimento pulmonar que ha un levemente plus grande "volumine de declino" in le presentia que in le absentia de incompetencia.

In le can, le arteria femoral non es satisfacto como sito de obtention de specimens si un accurate reproduction del curvas de dilution es desirate.
REFERENCES


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