Determination of Relative Changes in Cardiac Output from Noncalibrated Earpiece Dye-Dilution Curves

By Ivor T. Gabe, M.D., M.R.C.P., John Tuckman, M.D., and John P. Shillingford, M.D., F.R.C.P.

The usual methods for the measurement of changes in cardiac output involve arterial puncture; it would be of value if a technique could be used without involving this procedure.

Coomassie Blue dye and the photoelectric earpiece1-3 make it comparatively simple to obtain successive dye-dilution curves without arterial puncture. If the response of the recording system is linear to blood dye concentration and the vascular content of the ear is constant, it should be possible to measure relative changes in cardiac output without calibrating the curves. The purpose of this paper is to investigate the validity of using noncalibrated earpiece dye-dilution curves for such measurements in man. Arterial cuvette curves were used as the standard of comparison, and simultaneous earpiece curves were recorded during changes in posture, exercise, and intravenous administrations of an antihypertensive agent (guanethidine), sodium amobarbital, and norepinephrine.

Methods

The selenium photoelectric earpiece and cuvette, made by the Cambridge Instrument Company,* were used and were connected to similar chopper amplifiers.* Records were made on a twin-channel 1 ma. direct-writing recorder.*

Linearity of the response of the two systems to concentration of dye in the blood was markedly improved by increasing the input resistance of the amplifiers. Tests with blood showed that both systems were linear up to Coomassie Blue concentrations of 150 mg./L. of plasma.

DYNAMIC ACCURACY OF AMPLIFIER AND DIRECT-WRITING RECORDER

For the purpose of the present investigation, an assessment must be made of the adequacy of the chopper amplifiers and the direct-writing recorders in making graphical records of the signals coming from the earpiece and cuvette photocells. In general, the area beneath any waveform will be changed if there is distortion of its shape. However, changes of shape will be more obvious than the associated changes in area. Nevertheless, distortion should in principle be kept to a minimum, and it may be useful to consider in greater detail the requirements necessary to this end.

The waveform of a dilution curve is that of a nonperiodic pulse and may be analyzed in terms of a continuous frequency spectrum. For the present work, exact estimations of the frequency spectra are not necessary, and a reasonable approximation may be made by regarding a dilution curve as a cosine-squared wave. It can be shown that for such a waveform, of duration t and infinite repetition period, by far the major part of the spectrum involves frequencies less than 2/t; thus, if the main part of a dilution curve has a duration of 10 seconds (a fast curve by human physiological standards), a bandwidth of approximately 0.2 c.p.s. will be required in the amplifier and direct-writing recorder for the curves to be recorded with little distortion. If the dye curve contains sharp deflections (such as occur in right-to-left shunts), the approximation of the curve to a cosine-squared wave will be inadequate, and greater bandwidth will be needed for accurate reproduction of the curve. In figure 1, the measured frequency response characteristics of the chopper amplifier and direct-writing recorder are shown. The relative amplitude varied ± 2 per cent up to a frequency of 0.25 c.p.s., and over this range phase-shift was nearly proportional to frequency. Periodic waveforms consisting solely of frequencies below 0.25 c.p.s. should
Figure 1

Frequency response of the chopper amplifier and direct-writing recorder. A low frequency sine wave oscillator (Solartron Laboratory Instruments Ltd., Chessington, England) was connected to the input of the chopper amplifier and also to a photographic recorder (natural frequency of galvanometer 100 c.p.s.). Simultaneous event signals on other channels of the two recorders enabled measurements of phase to be made. The low paper speed of the direct-writing recorder prevented accurate phase measurement of frequencies above 0.6 c.p.s. $A/A_0$ is the ratio of the amplitude of direct-writing record at a particular frequency to the amplitude at zero frequency.

Therefore, be recorded with minimal distortion, although they will be delayed in time. For an indicator-dilution curve or any other nonperiodic waveform, the available bandwidth will be somewhat greater.

To test the validity of the above conclusions, experiments with an indicator-dilution curve simulator were made. A representative dye curve from a normal patient was selected, replotted in polar form on a circle, and the resulting outline cut out. Rotation of this disc through 5 degrees represented one second in terms of the original dilution curve. One hundred and fifty degrees of the disc were used for the dye curve outline. On the remainder of the circle, three “square waves” were cut for calibration purposes. The disc was mounted on the shaft of a variable-speed kymograph. Immediately below the disc was placed a selenium barrier-layer photocell, of which only a slit 2 mm. wide was exposed. Rotation of the disc affected a parallel beam of light falling on the photocell, and an electric signal corresponding to the original dye curve could in this way be produced. The photocell was connected to a D.C. preamplifier, the output of which was fed to the low frequency galvanometer (natural frequency 100 c.p.s.) of a photographic recorder* and also to the input of the chopper amplifier with its direct-writing recorder. By making records at different disc speeds, the area beneath each “dilution curve” could be varied, and measurement of the curves from the photographic recorder showed that the areas were, as would be expected, inversely proportional to the speed of rotation.

Simultaneous records at various disc speeds were made on the photographic and direct-writing recorders, and measurements were made of the exponential downslopes and of the areas beneath each curve (extrapolated and calculated to infinity). The slowest and fastest photographically recorded downslopes were 0.07 and 0.74 second⁻¹, respectively. The records made on the direct-writing recorder tended to produce downslopes systematically too small by about 10 per cent. The largest area photographically recorded was nine times greater than the smallest and the range of human dilution curves usually found in practice was covered. The direct-writing recorder tended systematically to overestimate the areas by about 5 per cent. Some distortion then takes place when the waveform of a human dilution curve passes through the chopper amplifier and direct-writing recorder. Nevertheless, the distortion is small, and since the downslopes and estimates of areas tend to be in error by constant percentages, comparisons of downslopes and areas may be expected to be accurate.

Description of the Arterial Cuvette System and Its Dynamic Accuracy

Polythene tubing, 1.1 mm. I.D. and approximately 25 cm. in length, was introduced into the patient's artery by the Seldinger technique. Three short metal adaptors connected this tubing to a second polythene tube, 1.5 mm. I.D., and this passed through the arterial photoelectric cuvette. The length of tubing between the adaptors and the centers of the photocells was approximately 15 cm. Blood was manually drawn, as constantly as possible, into a 50- or 100-ml. syringe; the rates of withdrawal were 35 to 110 ml/min. The arterial curves were all of good quality and showed no erratic features of contour.

It was shown in the preceding section that the chopper amplifier direct-writer recording system used in this laboratory is capable of reliably recording changes in the areas and shapes of human dye-dilution curves. On the other hand, any catheter sampling system will distort dye-dilution curves, the distorting influences being diminished if the internal diameter and length of the tubing are decreased and if the flow through the system is increased. The response to a “square front” of indicator is the method usually employed to test the performance of a sampling system, but such information does not immedi-

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*Cambridge Instrument Company.
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ately predict the adequacy of the system for recording indicator-dilution curves. Lacy et al.1 correlated indicator “square front” distortion by a sampling system with distortion of dye-dilution curves in the dog by the same system. To test the adequacy of the cuvette system used in the present investigation, its performance in distorting indicator square fronts of Coomassie Blue in oxygenated human blood was compared with the results reported by these authors. Figure 2 shows the responses to square fronts of dye for different withdrawal rates of blood; they are similar to those obtained by Lacy et al., who produced evidence that distortion of dilution curves began to be significant when the response to a square front of dye was slower than that shown in figure 2 for 36 ml./min. Since the withdrawal rates used in the present study were equal to or exceeded 35 ml./min., it is concluded that the arterial cuvette curves were reliably recorded. This conclusion is strengthened by the fact that the results of Lacy et al. referred to the distortion of very “steep” dilution curves from dogs and, therefore, to curves which demanded more from a cuvette system than the human curves studied here. Also, Milnor and Jose7 have recently reported that distortion of indicator-dilution curves by a sampling system is insignificant when the ratio of volume to flow in that system is 0.5 or less. The ratio of volume to flow in the cuvette sampling system used here closely approached or was smaller than 0.5.

EXPERIMENTAL TECHNIQUE

Forty-eight pairs of simultaneous earpiece and arterial cuvette dye-dilution curves were recorded in eight procedures. The procedures involved tilting, exercise, and the intravenous administration of norepinephrine, guanethidine, or sodium amobarbital. With one exception (patient M.Y., brachial artery), the arterial curves were from the femoral artery. Coomassie Blue was given from a calibrated syringe through a cardiac catheter into the right atrium, and depending on the internal volume of the catheter, 20 to 40 ing. per injection were delivered to the patient. However, in any one procedure, all injections were of equal quantity. The total dosage to any patient did not exceed 4 to 5 mg. per Kg. body weight.

The earpiece and the arterial cuvette dilution curves were plotted on semilogarithmic paper, and the areas were measured by the usual method of numerical summation at one-second intervals until the downslope exponentials and from there calculated to infinity by standard methods of integration.

Since in any one procedure all injections of dye were of equal quantity, each cardiac output is proportional to the reciprocal of the area beneath the arterial dilution curve; a similar relationship is to be expected in the earpiece curves if certain assumptions discussed below are fulfilled.

Results

Results obtained from 48 pairs of simultaneously recorded arterial cuvette and earpiece dye-dilution curves are given in table 1. A set of curves from one patient is shown in figure 3. In the first column of table 1 and in figure 4, cardiac outputs calculated from each series of arterial cuvette or earpiece dilution curves in a procedure are expressed relative to the first determinations in each patient. In the second column, percentage changes in cardiac output were calculated with reference to the average of the control cardiac outputs. In patient T.M. this was not done, and the values for percentage changes are here calculated with reference to the initial cardiac output. This was because of the large variation in cardiac output before sodium amobarbital administration, a variation which was associated with changes in heart rate and emotional attitude. Figure 5 compares the relative cardiac outputs from these columns during those parts of the procedure...
TABLE 1

Values of Relative Cardiac Output and Downslope Derived from Simultaneous Arterial Cuvette and Earpiece Dye-Dilution Curves

<table>
<thead>
<tr>
<th>Patient</th>
<th>Arterial cuvette</th>
<th>Earpiece</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Relative cardiac output</td>
<td>Percentage change in cardiac output</td>
<td>Downslope second</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.W.</td>
<td>1.00</td>
<td>0.53</td>
<td>0.34</td>
</tr>
<tr>
<td>45</td>
<td>0.87</td>
<td>-2</td>
<td>0.55</td>
</tr>
<tr>
<td>Essential hypertension</td>
<td>0.81</td>
<td>-9</td>
<td>0.33</td>
</tr>
<tr>
<td>0.76</td>
<td>-15</td>
<td>0.32</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Intravenous guanethidine and tilting

A.W. 0° (horizontal) 245/145

0° 240/130

0° 240/140

1 minute after 40 mg. I.V. guanethidine

280/170

2 minutes at +30° (head up) 220/140

8 minutes at +30° 200/130

3 minutes at +55° 170/120

7 minutes at +55° 170/110

14 minutes at 0° (horizontal) 245/140

Bicycle exercise (vigorous) by supine patient on daily guanethidine treatment

M.Y. 1.00 | 0.57 | 0.37 | 0.58 | -32 | 0.30 |

23 | 0.95 | -2 | 0.56 | 0.86 | -6 | 0.21 |

Hypertension | 0.96 | -1 | 0.29 | 0.88 | -3 | 0.24 |

Chronic glomerulonephritis | 1.35 | +39 | 0.39 | 1.28 | +41 | 0.27 |

2.57 | +134 | 0.69 | 2.38 | +162 | 0.36 |

nephritis | 1.34 | +38 | 0.37 | 1.27 | +40 | 0.28 |

Intravenous norpinephrine

J.B. 100 | 0.34 | 1.00 | 0.27 |

59 | 1.03 | +1 | 0.36 | 0.96 | 0 | 0.25 |

Essential hypertension | 1.02 | 0 | 0.35 | 0.91 | -5 | 0.26 |

0.89 | -13 | 0.35 | 0.90 | -6 | 0.20 |

1.05 | +3 | 0.32 | 0.94 | -2 | 0.27 |

0.92 | -10 | 0.30 | 0.92 | -4 | 0.25 |

1.07 | +5 | 0.30 | 0.97 | +1 | 0.25 |

Intravenous sodium amobarbital

T.M. | 0.29 | 0.24 |

70 | 0.27 | 0.21 |

Essential hypertension | 1.00 | 3.28 | 1.00 | 0.19 |

1.64 | +64 | 3.25 | 1.60 | +60 | 0.19 |

0.73 | -27 | 0.27 | 0.72 | -28 | 0.17 |

0.85 | -15 | 0.27 | 0.96 | -4 | 0.20 |

0.97 | -3 | 0.22 | 1.02 | +2 | 0.16 |

0.47 | -68 | 0.22 | 0.53 | -47 | 0.17 |

Intravenous sodium amobarbital during 6 minutes

200/110

270/120

265/120

260/115

260/110

180/100

75 mg. I.V. amobarbital during 6 minutes

210/100

220/110

210/105
The purpose of this study has been to investigate a simple technique for measuring relative changes in cardiac output by using earpiece dye-dilution curves. The technique involves simultaneously recording arterial and earpiece dye-dilution curves from patient J.B. in which the stimuli were applied and then removed. Also included are values for the two cardiac output determinations done before sodium amobarbital administration in patient T.M. The correlation between the changes in cardiac output calculated from the arterial cuvette and earpiece dye-dilution curves is high (correlation coefficient 0.98). On the other hand, there is a tendency for the earpiece curves represented in figure 5 to indicate relative cardiac outputs too large by an average of 6 per cent.

![Figure 3](http://circres.ahajournals.org/)

**Simultaneously recorded earpiece and femoral arterial dye-dilution curves from patient J.B.**

<table>
<thead>
<tr>
<th>M.H.†</th>
<th>1.00</th>
<th>39</th>
<th>1.00</th>
<th>1.00</th>
<th>0.19</th>
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<tr>
<td>Mitral stenosis</td>
<td>0.84</td>
<td>-16</td>
<td>0.31</td>
<td>0.80</td>
<td>-18</td>
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<tr>
<td>Stenosis</td>
<td>0.52</td>
<td>-48</td>
<td>0.16</td>
<td>-51</td>
<td>0.04</td>
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<tr>
<td>HR</td>
<td>0.91</td>
<td>-9</td>
<td>0.23</td>
<td>1.01</td>
<td>4.3</td>
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<table>
<thead>
<tr>
<th>Tilting</th>
<th>77 minutes at -12° (head up)</th>
<th>120/75</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>83 minutes at -12°</td>
<td>115/75</td>
</tr>
<tr>
<td></td>
<td>5 minutes at +33°</td>
<td>115/80</td>
</tr>
<tr>
<td></td>
<td>9 minutes at +33° (patient feels faint; see text and figure)</td>
<td>90/60</td>
</tr>
<tr>
<td></td>
<td>5 minutes at -10° (head down)</td>
<td>115/75</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>J.C.;</th>
<th>1.00</th>
<th>0.28</th>
<th>1.00</th>
<th>0.24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchial;</td>
<td>0.39</td>
<td>-2</td>
<td>0.27</td>
<td>1.05</td>
</tr>
<tr>
<td>Tasis</td>
<td>0.62</td>
<td>-37</td>
<td>0.18</td>
<td>0.73</td>
</tr>
<tr>
<td>P= 0.58</td>
<td>-41</td>
<td>0.16</td>
<td>0.84</td>
<td>-18</td>
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<table>
<thead>
<tr>
<th>Tilting</th>
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<th>130/85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0° (horizontal)</td>
<td>130/85</td>
</tr>
<tr>
<td></td>
<td>7 minutes at +30° (head up)</td>
<td>80/60 (see text)</td>
</tr>
<tr>
<td></td>
<td>7 minutes at 0°</td>
<td>130/90</td>
</tr>
<tr>
<td></td>
<td>12 minutes at 0°</td>
<td>130/95</td>
</tr>
<tr>
<td></td>
<td>7 minutes at +30° (head up)</td>
<td>130/85</td>
</tr>
<tr>
<td></td>
<td>14 minutes at +30°</td>
<td>130/95</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>E.L.;</th>
<th>1.00</th>
<th>0.29</th>
<th>1.00</th>
<th>0.23</th>
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<tr>
<td>Paget's disease</td>
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<td>0.26</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>0.75</td>
<td>-25</td>
<td>0.21</td>
<td>0.80</td>
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<td>0° (horizontal)</td>
<td>130/85</td>
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<tr>
<td></td>
<td>7 minutes at +30° (head up)</td>
<td>80/60 (see text)</td>
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<tr>
<td></td>
<td>7 minutes at 0°</td>
<td>130/90</td>
</tr>
<tr>
<td></td>
<td>12 minutes at 0°</td>
<td>130/95</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>J.C.;</th>
<th>1.00</th>
<th>0.34</th>
<th>1.00</th>
<th>0.29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric carcinoma</td>
<td>0.80</td>
<td>-22</td>
<td>0.26</td>
<td>1.01</td>
</tr>
<tr>
<td></td>
<td>0.69</td>
<td>-32</td>
<td>0.19</td>
<td>0.81</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Tilting</th>
<th>0° (horizontal)</th>
<th>130/85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0° (horizontal)</td>
<td>130/85</td>
</tr>
<tr>
<td></td>
<td>10 minutes at +45° (head up)</td>
<td>130/85</td>
</tr>
<tr>
<td></td>
<td>17 minutes at +45°</td>
<td>130/85</td>
</tr>
</tbody>
</table>

*Except for patient T.M., percentage change is with reference to the average of control cardiac outputs. See text.
†Frequent alterations in heart rate and subjective state during procedure. See text.
‡60 mg. promethazine HCl and 50 mg. meperidine HCl before catheterization as premedication.
noncalibrated earpiece dye-dilution curves. The basis of the method is that, in an ideal system, if successive injections of equal quantities of indicator are given, the areas beneath the dilution curves will be inversely proportional to the cardiac outputs.8,9 Earpiece dye-dilution curves can be considered as coming from an ideal system if, during a procedure involving successive dye injections, (1) the response of the recording system to concentration of dye in the blood is linear, (2) the volume of blood within the light path of the earpiece is constant, and (3) any distortion of the shape of the curves produced by the ear sampling system is unaccompanied by change in area. Since the condition of linearity is fulfilled by the present apparatus for most procedures (up to 10 to 12 injections of Coomassie Blue can be given to an adult before nonlinearity becomes likely), attention in this investigation has been directed toward situations which might prevent the second and third assumptions from being satisfied. If there were a change in blood volume of the pinna between successive dye curves, the sensitivity of the earpiece to concentration of Coomassie Blue would be altered, and this would affect the areas beneath the dye curves, although their shapes would be unchanged. Thus, an increase or decrease in pinna blood volume would show falsely large or small areas, and calculations of relative changes in cardiac output by the method considered here would be in error. On the other hand, the effect on area measurement resulting from curve distortion in a sampling system is at present theoretically predictable in only the simplest situations.10,11 It is clear, however,
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Comparison of the relative cardiac outputs calculated from simultaneously recorded noncalibrated arterial cuvette and earpiece dye-dilution curves during those parts of the procedure in which the stimuli (tilting, exercise, drug administration) were applied and then removed.

It is convenient to consider the simultaneously recorded earpiece and arterial cuvette dilution curves in two groups: (1) those from the control period and (2) those from the period in which the cardiovascular changes were induced.

The variations in relative cardiac output calculated from earpiece curves in the control period were not significantly different from those of the arterial cuvette curves. Other studies in this laboratory which have used serial noncalibrated earpiece dilution curves alone in normal subjects also show that variations in cardiac output during resting control periods are within the limits reported for similar circumstances by the direct Fick and arterial indicator-dilution methods. Therefore, it may be concluded that spontaneous variations in ear circulation which may normally be present are diminished or abolished in the present method, presumably by the application of vasodilating ointment and the heat from the earpiece light source. This conclusion is supported by experience in ear oximetry.

Figure 5 shows the results from the 28 pairs of dye curves recorded during those parts of the procedures under changing cardiovascular conditions. It is evident that the correlation between the two methods is very close. The points in the region of small change in cardiac output are as important as those in the region of great change, for circulatory changes causing little change in cardiac output might have drastically altered the local circulation.
in the ear and invalidated the use of noncalibrated earpiece dye curves. However, the earpiece curves represented in figure 5 show relative reductions in cardiac output too small by an average of 6 per cent. Thus, the earpiece curves slightly underestimate decreases in cardiac output; the data are inadequate for determining if they also systematically overestimate increases in cardiac output. Six per cent is an overestimation of this error, but more precise definition in measurements of this nature assumes some complexity. We are concerned not with errors of single absolute estimations but with the errors of relative changes in cardiac output predicted by the earpiece compared with those from the arterial cuvette. Since a given percentage difference between the changes in cardiac output calculated from the two types of curves will become progressively less important when related to increasingly larger changes in cardiac output, a detailed treatment of these errors would involve weighting the values obtained by arterial cuvette curves. However, this error is of no practical significance for measuring changes in cardiac output predicted by the earpiece compared with those from the arterial cuvette. Since a given percentage difference between the changes in cardiac output calculated from the two types of curves will become progressively less important when related to increasingly larger changes in cardiac output, a detailed treatment of these errors would involve weighting the values obtained by arterial cuvette curves. However, this error is of no practical significance for measuring changes in cardiac output, and the variations at any particular level are well within the limits reported for the established direct Fick and usual arterial indicator-dilution methods.

In assessing the limitations of the method presented here, it is necessary to consider distortion of the earpiece dilution curves. Since the earpiece and arterial cuvette curves were recorded from different sites in the vascular system, it is not to be expected that the curves will be identical in shape. To visual inspection, the earpiece curves, with two exceptions, were similar to their arterial cuvette counterparts and only slightly different in shape. Precise measurement of dye-curve distortion presents great difficulty. It will be seen from table 1 that the values of the downslopes of the earpiece curves are systematically less than those of the arterial cuvette curves, although simple estimations of error in the downslope will not of course give a quantitative measure of the distortion. When distortion of the downslope of dilution curves is great, recirculating dye may be included beneath the early part of the curve, and extrapolation to exclude recirculation may be a highly uncertain process; the subsequent measurement of area will then be in error. As already indicated, the distortions of downslope in these procedures were, with the exceptions noted, minimal and thus unlikely to cause error due to dye recirculation. This conclusion was supported by the semilogarithmic reploting of the curves, for the points of recirculation were easily identified. On the other hand, two patients had severe postural hypotension during tilting, and one complained of faintness during the actual recording of the curves. In both instances, the earpiece curves recorded at these times, when compared with those from the arterial cuvette, were grossly distorted to visual inspection, and the downslopes were very flat. The cause of this distortion cannot be stated with certainty, but it is likely to be due to slow flow of blood through the head and ear circulations; similar distortion is seen in in vitro cuvette systems through which flow is exceedingly low.

There are several advantages in determining relative changes in cardiac output by the method investigated here rather than from absolute estimations of cardiac output derived from earpiece dye-dilution curves. In such absolute estimations, calibration of the curves is involved, and this is usually done by equating the measured concentration of dye in an intravenous sample of blood some time after the curve has been recorded to the height of the "tail" at this time. The sample must be drawn well after the injection of dye so that the dye in the arteries and veins is completely mixed. The longer the period of waiting for equilibration, the greater is the likelihood of an error in the estimation of the height of the tail through even slight electrical drift. The use of noncalibrated earpiece dye-dilution curves to determine changes in cardiac output does not require blood samples and demands an absence of significant electrical drift over periods of time, some 20 seconds, well within
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the limits of the apparatus. The price paid
for the increase in accuracy and convenience
is that only relative changes in cardiac output
can be deduced from the curve.

Summary

Many investigations require information on
percentage changes in cardiac output rather
than absolute values. This study investigates
a simple method for measuring such relative
changes, using noncalibrated earpiece dye-
dilution curves. The basic principle involved
is that, in an ideal system, the areas beneath
successive dilution curves produced by equal
injections of indicator are inversely propor-
tional to the cardiac outputs. Applied to the
earpiece dye-dilution curves, the restrictive
assumptions relate mainly to linearity of re-
sponse to blood concentration of dye and to
the constancy of the blood volume of the ear.
The method has been tested by recording
simultaneous earpiece and arterial cuvette dye
curves produced by injections of Coomassie
Blue during changes in posture, exercise, and
intravenous administration of vasoactive
drugs. The relative changes in cardiac output
predicted from the earpiece curves compared
well with those from the arterial cuvette.

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response characteristics for continuous
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Ivor T. Gabe, John Tuckman and John P. Shillingford

Circ Res. 1962;11:405-413
doi: 10.1161/01.RES.11.3.405

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

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/11/3/405

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