A Photoelectric Ear Densitometer for Continuously Recording the Arterial Concentration of T-1824 in the Dye-Dilution Method

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To eliminate the collection of serial samples of arterial blood an instrument has been developed which records dye-dilution curves by measuring changes in optical density of a segment of a heat-flushed ear. Comparison with curves from arterial samples shows close similarity in the shape of the curves, and good agreement between the cardiac outputs calculated from them. Other advantages of the technic are the relatively small dose of dye needed, the linear relation between deflection of the recording galvanometer and changes in dye concentration in the blood, and the fact that determinations can be repeated several times at intervals of three or four minutes.

In an effort to simplify the dye-dilution method of Stewart and Hamilton we have designed a "densitometer," using a multiplier phototube, which records dye-dilution curves by measuring the optical density of a segment of a heat-flushed ear at an appropriate wave-length. This instrument makes it unnecessary to puncture an artery, or draw blood through a catheter, and its sensitivity is such that 10.0 mg. of T-1824 is an adequate amount for injection in most patients. The use of the multiplier phototube instead of a selenium barrier-layer photocell makes possible a linear relationship between the deflection of the recording galvanometer and changes in arterial dye concentration.

METHOD

The earpiece of the apparatus contains a light source, glass filter, and multiplier phototube. The light source is a 6 to 8 volt flashligh bulb, supplied by a storage battery through a variable resistor so as to provide any filament voltage from 0 to 8 volts. Before reaching the phototube the light passes through a glass filter (Rubicon Co. #620) which has maximum transmission at a wave length of 620 m which determines the lower limits of the spectral band employed, while the upper limits are restricted by the phototube sensitivity. The result is a band of approximately 40 m half-width, centered at 620 m, corresponding to the region of maximum spectral absorption for T-1824. Ideally, it would be desirable to use a wave length at which the absorption spectra of oxy- and reduced hemoglobin intersect, to eliminate the effects of variations in the ratio of these two substances. Unfortunately the regions of these isobestic points are relatively insensitive for the measurement of T-1824.

After passing through the ear and the glass filter, the light beam falls on the light sensitive cathode of a multiplier phototube (RCA 931-A). The circuit is a modification of that described by Sweet for photographic densitometry, and used by Morgan and Sturm in their quantitative electrokymograph. Its most important characteristic is that the galvanometer deflections bear a linear relationship to changes in optical density and so to changes in concentration of dye in the blood. The linearity of response of the instrument has been tested with known concentrations of T-1824 in whole blood, flowing through a cuvette. In a series of 18 observations, using dye concentrations of 4 to 80 mg. per liter, the mean departure from linearity was 3.99 per cent, with a standard deviation of 6.49 per cent.

We have used the galvanometer of a "direct-writing" Sanborn Model 51 electrocardiograph as our recording instrument, but other standard linear amplifier-oscillograph combinations of similar sensitivity could be used. To give stability the multiplier phototube is operated well below maximum gain, and the power supply for the whole instrument is

* A circuit diagram of the instrument will be furnished on application to the authors.
regulated by a 250 watt constant-voltage transformer (Sola #30807).

In operation, the earpiece is attached to the upper pole of an ear. Because of the low light intensity and high amplification slight movements between ear and earpiece cause wandering of the baseline, which can be minimized by the use of a padded holder over the head and earpiece. Extraneous light must not reach the phototube: the light sensitive area must be completely covered by the ear. The instrument is allowed to "warm up" over a 20-minute period.

Meanwhile the earpiece is applied, the light turned on, and the filament voltage of the lamp gradually increased until the phototube output, indicated by a meter, is within the range of logarithmic operation of the circuit.

During this preliminary period an infrared "heat lamp" is used to warm the whole side of the face and produce vasodilatation. The patient should be kept warm and comfortable during the whole procedure. The recording galvanometer is next turned on, and the gain controls are gradually turned up until pulsations 2 to 3 mm. high are visible. A control baseline of 60 seconds or more is recorded, and without interrupting the recording, the dye is injected. When the curve has been inscribed and a stable new baseline established, which usually takes from two to four minutes after injection, a sample of blood is drawn from another vein for use as a calibrating sample, and the recording can then be stopped.

It is important to keep the injection volume small, and to make the injection as nearly instantaneous as possible, since a slow or discontinuous injection will produce distorted curves. We use 2 to 3 cc. of a 0.5 per cent solution of T-1824* in a 5 cc. oiled syringe, and an 18 or 19 gage needle. The amount of dye injected is measured by weighing the dye-filled syringe and needle before injection and afterward.

The upper tracing of figure 1 shows a dye-dilution curve recorded from the ear in this way. The small regular pulsations are due principally to changes in the volume of blood in the light path with each heartbeat, and correspond in form and timing to the intravascular volume curves for peripheral arteries reported by others. The size of the pulsations varies with the patient as well as with the degree of amplification. Small respiratory variations are also sometimes seen, and are particularly marked in persons with low arterial oxygen saturation. Figure 1 also shows the dye-dilution curve replotted on semilogarithmic paper, with plasma dye concentration on the log scale (ordinate). The downstroke of the curve prior to recirculation is usually a straight line, and its slope is related to the intrathoracic blood volumes.

In order to make quantitative determinations from the ear curve, it is necessary to calibrate the galvanometer deflection in terms of arterial dye concentration. It is not possible to establish a single calibrating factor applicable to all patients, because of the wide individual variations in the factors other than dye which affect the optical density, such as ear thickness, pigmentation, and hematocrit. Each curve can be calibrated individually, however, by drawing a venous blood sample a few minutes after injection of dye, when numerous recirculations of the dye have established equilibrium, with equal concentrations in the arterial and venous systems. By measuring the dye concentration in this sample on a spectrophotometer, and the galvanometer deflection at the corresponding point on the ear curve, a calibrating factor can be calculated, since the relation between the galvanometer deflection and the changes in dye concentration is a linear one. This "one point" method of calibration has given satisfactory results in most cases, but sometimes presents practical difficulties: first, because the instrument must remain stable, or free from "drift," and the

* Kindly supplied by the William R. Warner Company, New York City.
circulation in the ear must remain unchanged, from the time of injection to the time of the venous sample; and second, because the deflection at the time of the calibrating sample is sometimes quite small.

**Comparison with Direct Arterial Curves**

Comparison of curves obtained from the ear with those from simultaneous direct arterial sampling is the only method available for validating this technic. Discrepancies between ear and arterial curves would not necessarily indicate that the ear curve was incorrect, however, since the direct arterial method is also subject to certain errors. Each arterial sample, for instance, represents a two-second collection period, and to that extent is theoretically less accurate than a continuous recording. On comparing ear curves with simultaneous arterial curves, we have found that the form of the curves is very similar. In figure 2, for example, three simultaneous dye-dilution curves are plotted. One was obtained from the ear by the method described, one from direct samples from the femoral artery, and a third from the blood flowing from the femoral artery through a short length of polyethylene tubing, using a modification of the earpiece.* The close similarity in form of the three curves is apparent.

Table 1 gives a quantitative comparison of ear curves so calibrated with simultaneous direct arterial curves from a group of 15 patients. Three measurements were selected for comparison: appearance-to-peak time, slope of the straight-line downstroke, and calculation of cardiac output. The duration of the upstroke from appearance time to peak time, and the slope of the downstroke, both give a rough estimate of the shape of the curve independent of calibrating factors. The slope is measured by extrapolating the straight-line downstroke of the curve, eliminating the portion attributable to recirculation, and expres-

* Although originally designed for the human ear, this apparatus can be easily adapted to suit other experimental situations where the direct photometric measurement of T-1824 is required. The modification referred to here, which is described in detail elsewhere,16 allows blood to flow across the light path through a length of polyethylene tubing.
ing slope in terms of the number of seconds required for a decrement of one decade on the logarithmic ordinate (for example, from 10.0 to 1.0 mg. per liter). The cardiac output is calculated from the area under the curve and therefore gives a measure of accuracy of calibration as well as form of the curve.

The appearance-to-peak times of the arterial and ear curves check closely, as shown in Table 1, especially when we consider that the points on the direct arterial curve cannot be determined more accurately than ±2 seconds. The slopes show much wider variation, and in two cases (6 and 8) are markedly different. In general, there is a tendency for the slope of the ear curves to be steeper than those of the direct arterial curve. Recent experiments suggest that this is due to an error in the direct arterial curves, introduced by the tubing which conducts blood from the femoral artery to the sampling tubes. A similar distortion occurs when curves are recorded on blood withdrawn through a catheter.

The cardiac outputs calculated from ear and from arterial curves show reasonably close agreement. If the difference between the two determinations is expressed as a percentage of the arterial curve determination, the average difference is -3.34 per cent, with a standard deviation of 8.09 per cent.

From these results we feel that in most cases this method gives a close approximation of the curve obtained by direct arterial sampling. The technic offers several advantages: (a) It is a simple and relatively rapid procedure, requiring one venapuncture for the injection of dye and one for the venous calibrating sample, and eliminating arterial puncture altogether. (b) It provides a continuous record of dye concentration in place of a series of measurements on successive one- or two-second samples. (c) The determination can be repeated as soon as the dye has reached equilibrium in the arterial and venous systems. The amount of dye required each time is approximately 10 mg., so that the total amount of dye given in three or four consecutive determinations is not undesirably large. (d) The direct-writing galvanometer makes the curve immediately available for inspection. This is especially useful in the detection of shunts from the form of the curve, and in comparing the form of the curves in consecutive determinations.

**Summary**

1. An instrument is described which records dye-dilution curves in human subjects by measuring changes in optical density of a segment of the heat-flushed ear. Intravenous injection of 10.0 to 15.0 mg. of T-1824 produces satisfactory curves in most subjects. The deflection of the recording galvanometer bears a linear relationship to the changes in arterial dye concentration, other factors being constant.

2. Comparison of curves recorded from the ear by this instrument with those obtained simultaneously by collection of samples of arterial blood from the femoral or brachial artery shows that the form of the curves is essentially the same.

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