DYE DILUTION CARDIAC OUTPUT: USE OF A DENSITOMETER, SERVO RECORDER, AND COMPUTER IN DOGS WITH AND WITHOUT PENTOBARBITOL ANESTHESIA

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ABSTRACT

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by Roger A. Wolthuis

Modern engineering has developed an ever increasing array of instrumentation to aid and speed the accumulation of data by the research worker. This instrumentation must be verified in its application rpior to its acceptance and general use. The present paper describes the application of a densitometer, servo recorder, and computer in the dye dilution measurement of cardiac output.

The instrumentation was checked for electrical linearity of servo pen deflection vs. servo recorder output, servo pen deflection vs. computer output, and response of the dye-sensing cuvette (and servo recorder) to increasing dye-blood concentrations. These checks showed a high degree of linearity between the systems involved.

Five dogs were chronically implanted with polyethylene catheters. Successive cardiac output determinations were performed on the animals in both the anesthetized and awake states. Cardio-green (indocyanine green) was the dye indicator of choice. Indicator dilution curves produced by the densitometer-servo recorder combination were analyzed according to the Hamilton-Stewart technique. These cardiac output values were compared with those provided by computer analysis of the same dye curve.

The data from Hamilton-Stewart curve analysis show good agreement with that obtained from the computer. Values from the computer ranged from 5% above to 3% below those given by curve analysis. The advantage of using the computer lay in its capacity to give a rapid, semi-automatic measurement of cardiac output, eliminating the need for a time-consuming analysis of the actual dye curve. The effect of anesthesia on cardiac output is inconclusive because of the small series of observations. However, when all measurements were averaged, heart output was only 1% higher in anesthetized animals. On a similar basis computer determined cardiac output averaged 1% higher than that derived from curve analysis. These percentages were based on an average minute volume heart output of about two liters.

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Roger A. Wolthuis

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INTRODUCTION

Modern methodology brings with it a new responsibility often overlooked by the uninitiated research worker or the eager clinician. Numerous accounts testify to a problem which centers around the use of instrumentation, devised in theory by the engineer and applied in practice by the scientist. All too often the scientist is willing to use the engineers' tool to attack a certain problem without, however, verifying the reliability of that tool with respect to its application. The report to follow represents such a verification. It will describe the method by which a cardiac output computer and associated instrumentation has been tested, and point the way to its use as a tool of the research biologist and medical scientist.

The present paper is a report on experience with a hitherto unpublished system for estimating cardiac output. The system consisted of a densitometer and servo recorder which jointly produced a continuous curve for each indicator injection. In addition, this report compares results from the foregoing system against the application of a digital readout computer for estimating cardiac output. Cardiac output data from these two estimating systems are compared using dogs with and without pentobarbital anesthesia.

REVIEW OF LITERATURE

Indicator Dilution Measurement of Cardiac Output

In 1829 Hering reported on a technique for the measurement of blood circulation time. He injected potassium ferricyanide into one jugular vein of an animal and measured the elapsed time before this indicator could first be detected in the other jugular vein. The principle was developed further by Stewart in 1897, and he is credited for the first application of an indicator dilution technique in the determination of cardiac output.

The early work of Stewart (1897) involved continuous infusion of an indicator until an arterial plateau of indicator was reached, sampling of the arterial and venous blood for concentration of the indicator, and application of the data to the Fick equation:

$$\text{cardiac output (liters/min.)} = \frac{\text{rate of indicator infusion (mg./liter/min.)}}{\text{artero-venous difference of the indicator (mg.)}}$$

The indicator favored by Stewart (1897) was hypertonic saline, and its concentration in the blood was determined by a conductivity cell.

Stewart (1897), unfortunately, labored under the illusion that his indicator arrived at the sampling site as a "square front". This idea did not adversely affect his technique as long as he utilized the continuous indicator dilution infusion method. However, a later paper by Stewart (1921) noted that he had tried the single injection technique, but the details

were not described. His efforts in this direction were no doubt hampered then by lack of information on blood rheology (i.e., laminar nature of flow) or the significance of blood flow properties. The first application of a single injection indicator dilution technique has been generally attributed to Henriques (1913) who derived its formula, described a method, and pointed out the problem of indicator recirculation.

While Stewart generally has been given credit for first using indicator dilution to measure cardiac output, Hamilton (1928b, 1929, 1929b, 1932, 1945a, 1947a, and 1948) and his colleagues gave the greatest impetus to application and verification of this method. Their primary interest was with the single injection procedure. Through intensive study of model circulatory systems, Hamilton (1929, 1932) was able to show that the downslope of the plot of an indicator time-concentration curve was a straight line when plotted on a semi-logarithmic scale. Extrapolation of the downslope, necessary to determine the complete area under the curve, could be made correctly in spite of the appearance of recirculated indicator in blood. Flow calculations were made using the following equation:

$$\text{cardiac output (liters/min.)} = \frac{60\ I}{\bar{c}\ t}$$

I is the amount of indicator used (Hamilton used Evans Blue Dye), $\bar{c}$ is the average concentration of dye under the curve (summation of concentration values at one-second intervals divided by the duration of the curve in seconds), and t is the duration of the curve in seconds. Hamilton (1929, 1932)

also pointed out the necessity for an adequate indicator, that is, one which mixed evenly with blood, did not leave the circulation between the points of injection and sampling, and could be measured accurately in blood samples. Hamilton (1948) further applied his findings to show a correlation between his indicator dilution technique and the then accepted direct Fick procedure.

/Fick (1870) proposed that the cardiac output could be calculated from the following formula:

$$\text{cardiac output (liters/min.)} = \frac{\text{oxygen uptake (ml./min.)}}{\text{difference of oxygen content of arterial and mixed venous blood (ml./liter)}}$$

It was assumed that the lungs themselves neither extracted oxygen from nor passed carbon dioxide into the blood as it flowed through the lesser circulation. The assumption was recently confirmed by Mitchell and Cournand (1955). It was further assumed that samples of mixed venous blood could be obtained from a cardiac catheter located in the right heart./

Early methods for obtaining serial samples of arterial blood at fixed intervals, following injection of the indicator, consisted of a moving row of test tubes above which hung a catheter carrying the arterial blood. The tubes were moved in sequence beneath the flowing blood stream until sufficient time had elapsed for recirculating indicator to appear at the sampling site. The blood in each tube was centrifuged; the serum was separated and analyzed for indicator concentration.

The effect of varying the sampling site has been inves-

tigated. In one such report, Lange, Smith, and Hecht (1960) described local constriction in peripheral arteries as the biggest handicap to adequate blood sampling. Estimates of cardiac output seemed to be only slightly effected. The preferred withdrawal site in animals and man is either the femoral artery or the thoracic aorta via catheterization of the femoral artery.

While early workers injected their indicator into an accessible peripheral vein, the acceptance of cardiac catheterization as a safe procedure was slow in coming. Zuntz and Hagermann (1898) cannulated the heart of a horse and determined cardiac output during rest and exercise by the Fick method. However, Andre Cournand and colleagues in New York (Cournand and Ranges, 1941), are credited with the introduction of the cardiac catheter for physiological investigation in man. Ebert, Borden, Wells, and Wilson (1949) were the first to inject an indicator into the right heart of man through a catheter, and they claimed that the effect of recirculation was thus more clearly separated from the primary indicator curve. Since Hamilton (1929) had shown a necessity for absolute mixing of indicator and blood, the technique by Ebert, et al. (1949) was one more step in the direction of better methodology.

The effect of indicator injection site on the shape of the indicator dilution curve has been studied extensively by Pearce, et al. (1953). In Figure 1 the sampling site was the carotid artery. The aortic injection and resulting sharp peak were explained by a lack of cardiac mixing combined with

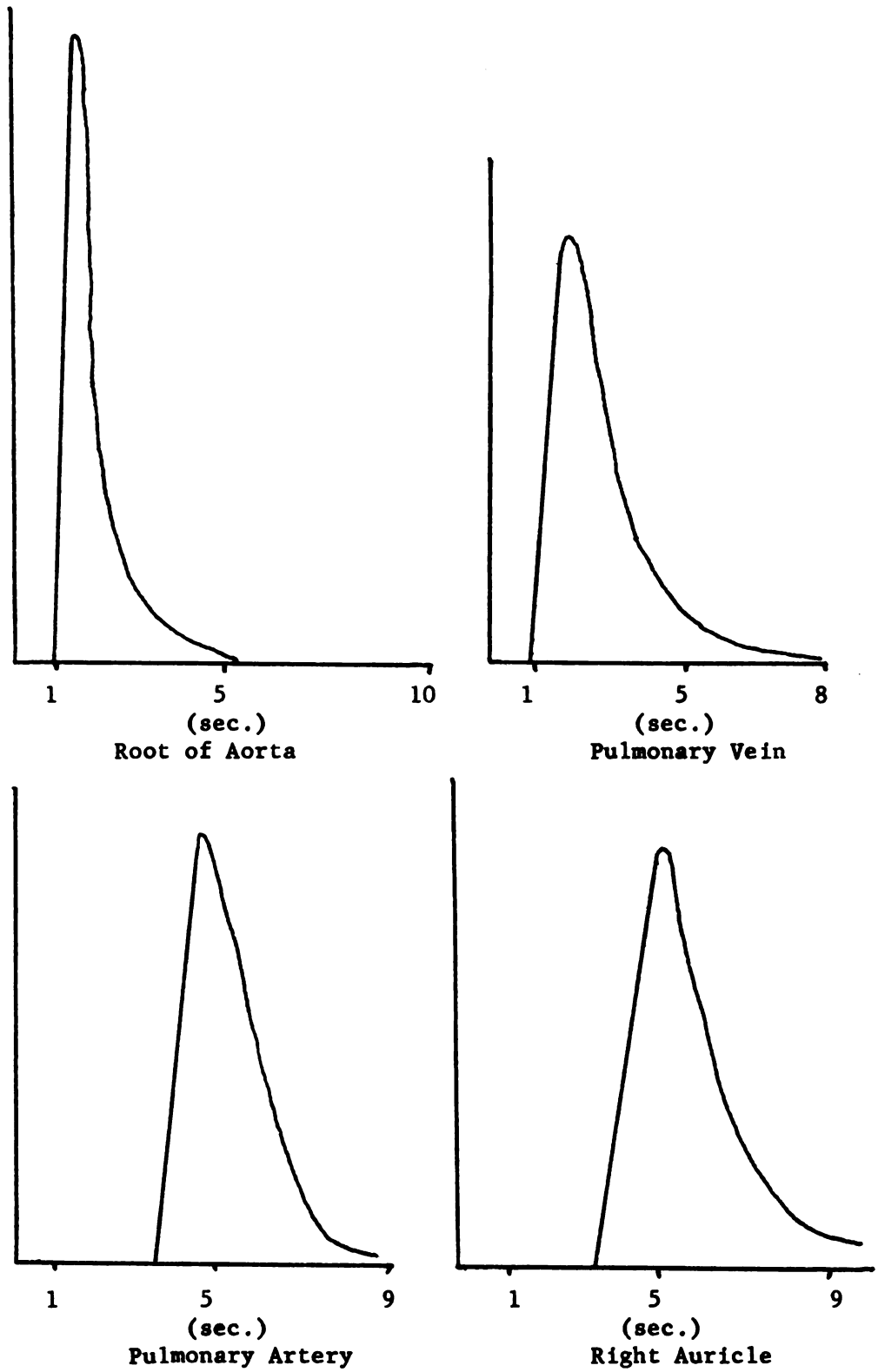

Fig. 1 Densitometer Records from a Carotid Cuvette Showing Examples of Curves from Various Injection Sites (from Pearce et al., 1953)

peripheral laminar flow. The other three injection sites produced a more "normal" curve configuration. (Unfortunately, it is impossible to assess the difference between injection sites and estimated cardiac output all within the same cycle. After a single injection only one set of dye concentration values can be obtained at a time.) Pearce (1953) reported a rather high consistency in cardiac output data from a dog, despite variation in injection sites. Table 1, from Pearce, et al. (1953), gives the mean cardiac output for four different injection sites.

TABLE 1

Dog No.	Weight	Mean Cardiac Output	S.D.
24	13.2 kg.	1.80 liters/min.	± .16
25	14.0 kg.	4.16 liters/min.	± .13
27	16.3 kg.	2.29 liters/min.	± .13
28	11.8 kg.	1.70 liters/min.	± .15
32	18.2 kg.	1.72 liters/min.	± .11

The low standard deviation is noteworthy when the variability in dogs' minute volume rate of output under normal physiological conditions is considered.

An impressive array of indicators has been used to modify, in a quantifiable way, some property of passing blood. These include chemical, electrical, optical, thermal, and radioactive properties. As mentioned earlier, Hering (1829) used potassuim ferrocyanide (detected by the Prussian Blue reaction) and Stewart (1897) used hypertonic saline. With

the advent of a visual colorimeter in 1926, dyes came into greater use. Hamilton (1929) first used tetraiodophenolphthalein and then switched to Brilliant Vital Red in an effort to rule out indicator penetration of vessel walls. More recently (Lawson, et al. 1952), T-1824 was shown to perform adequately as an indicator by comparing its cardiac output values with those obtained from a radioisotope indicator, Na^{24}. Unfortunately, this dye was optimally detected at a wave length of 640 mu--the same as for reduced hemoglobin. Since the detector could not discriminate between the dye and reduced hemoglobin, oxygen saturation of the blood was a critical factor, especially in cardiac output determination for congenital heart disease. Fox, et al. (1957), reported on the use of photographic sensitizing indicators called tricarbocyanine dyes. One example, indocyanine green (cardio-green, Hynson, Westcott, and Dunning, Inc., Baltimore, Maryland) has a spectral absorption at 800 mu, and is easily protein-bound in the blood. Its characteristics have now eliminated the hemoglobin interference problem. While this green dye is the best all-around dye indicator to date, its instability in dilute aqueous solution after a period of several hours can present a problem in prolonged dye detection studies (Wood, et al., 1960).

As already mentioned, early indicator dilution cardiac output methods utilized a serial blood sampling technique. The sampling difficulties in this procedure led toward several attempts to develop very rapid or continuous detectors for

indicator concentration changes in the blood. Matthes and Kramer (1935) applied a Lange barrier cell to the quantitative photometry of flowing blood in unopened arteries, and Millikan (1942) improved on their technique with the use of an ear oximeter. The earliest publication of a continuous photorecorder is that of Friedlich, Heimbecker, and Bing (1950). They injected T-1824 centrally and drew arterial blood through their photometer by a constant flow mercury system. Using high efficiency interference filters, they were able to isolate a narrow spectral band centered at 628 mu for the detection of their dye. The photometer signal was fed into a recorder which produced a continuous dye curve. This early work, however, consistently and significantly underestimated cardiac output when compared to simultaneous direct Fick determinations. Several laboratories then modified a basic circuit published earlier by Sweet (1947). The result was an extremely stable instrument (which could be called a densitometer) whose sensitivity did not change over a wide range of light intensities. Because of its linear response to the indicator, only one dye-blood mixture (standard) was necessary for calibration. With this instrument, and the Hamilton method for extrapolating the curve downslope, it was now possible to do a series of successive indicator-dilution studies with ease and consistency. Time-consuming colorimetry on plasma samples was no longer essential.

It is of interest to note the relationship between indicator dilution cardiac output and cardiac output measured by

the accepted direct Fick technique. Many investigators used one technique while experimentally modifying the other as a test for its validity. In recent work, Theye, et al. (1963) performed simultaneous indicator dilution and direct Fick cardiac output on eight anesthetized dogs. Their results from twenty-four dual observations showed close correspondence between the two methods. This supported earlier theoretical and experimental evidence. The significance of this, and other similar studies comparing these two methods, remains questionable because both methods are indirect measurements of an actual physical process (i.e., blood flow).

Malooly, et al. (1953) have done some stroke-volume output comparisons in the dog using the indicator dilution technique and a more direct method which employed an indwelling aortic blood flow probe. Their results unfortunately are complicated by experimental aortic regurgitation. The regurgitation study was the problem of primary interest. Confirmation of the indicator dilution or the direct Fick technique in the intact animal may have to await the application of a third process, such as further blood flow metering in the ascending aorta, before theory can be satisfied by the evidence.

Given the continuous recording cuvette densitometer and resulting completed indicator curve, one factor remained; namely, analysis of the curve to determine cardiac output. Benchimol, et al. (1963) applied the "forward triangle method" to analysis of their indicator dilution curves. Their equation was as follows:

$$\text{cardiac output (liters/min.)} = \frac{60\ I}{BT \times \frac{1}{2}\ PC} \times K$$

I is indicator injected (in mg.), BT the time in seconds from first detection of indicator until peak of indicator curve is reached, and PC the maximum value (in mg.) for indicator appearing at the sampling site. The proportionality constant K was established at 0.34 for peripheral injection of indicator, and 0.37 where the injection was made at the heart or into the pulmonary circulation. While the method was devised to eliminate time-consuming replotting of the indicator curve downslope, the Hamilton method of curve analysis is still necessary where careful experimentation is desired and tolerances are minimal.

Note: During the preparation of this paper a report (Benchimol, et al.) has been published on a study similar to that which follows.

MATERIALS AND METHODS

Five mongrel dogs (10-14 kg. in weight) were anesthetized with sodium pentobarbital (Halatal, Jensen-Salsbery Laboratory, Kansas City, Missouri) ½ cc./kg., and fitted with a thermistor-modified endotracheal tube as a means of recording respiration. The thermistor (Western Electric 20-B) was connected via a simple balancing bridge to a G.M.E. (Gilson Medical Electronics, Middleton, Wisconsin) model CH/CBPP chopper amplifier and the gain was set to produce a two to three centimeter deflection. No attempt was made to quantify respiration depth. The throat area was clipped, washed with soap, and rinsed with 70% alcohol. A five centimeter incision was made just medial to the jugular vein with subsequent exposure of both the jugular vein and the carotid artery. The jugular vein was tied off rostrally and a Luer end polyethylene catheter (Intramedic PE-90, I.D. .034", O.D. .050") inserted toward the heart. The catheter was located by means of a venous recording pressure transducer (Statham, model P23BB). An effort was made to place the catheter tip in the right atrium or, when possible, in the right ventricle. The catheter was tied to the vessel and the Luer end was fed subcutaneously to the nape of the neck where it was brought out and sutured in place. The carotid artery was likewise tied off rostrally, and a Luer end polyethylene catheter (Intramedic PE-190, I.D. .047", O.D. .067") fed caudally toward the aorta, coming to rest in the descending thoracic aorta approximately six to eight centimeters from

the arch proper. The catheter was tied to the vessel and the Luer end brought subcutaneously to the back of the neck, next to the jugular catheter. A stainless steel Luer plug was inserted into each catheter and taped to the polyethylene. The neck wound was wetted with streptomycin and closed with silk suture. Each animal was given 900,000 units penicillin, I.M., daily for several days after the operation. The indwelling catheters were infused daily with weakly heparinized saline solution.

Cardiac output estimations were made with the animal resting in a burlap hammock, feet down, and EKG electrodes attached to each leg. The catheters were fitted with stopcocks, and the jugular catheter filled with the indicator, cardio-green. Registered tuberculin syringes were filled to a pre-determined level with the dye, and weighed on an analytical balance to four decimal places. The carotid catheter was attached by way of rubber tubing to a G.M.E. dye tracer cuvette, operating at the isobestic point (800 mu) of oxygenated and reduced hemoglobin. The blood was drawn through the cuvette into a 50 ml. plastic syringe which was operated by a modified Harvard withdrawal pump (model 600) at the rate of 40 ml./min. Approximately 15-25 ml. of blood were drawn through the cuvette, from the animal, for each dye curve. The blood was returned to the animal upon completion of each curve. The cuvette was attached to a control unit, G.M.E. model DTL, which included a power supply and linearizing circuit to provide a linear output within 1% up to 16 mg. dye/liter. The signal was

then led to a G.M.E. model SE-21 servo amplifier with a maximum pen deflection of 20 cm. Attached to the shaft of the servo motor was a 5K, three-turn potentiometer connected across a 1.4 volt Mallory (ZM9) battery. The output produced at the top end of the servo chart was 1.2 volts. The servo variable signal was fed, finally, to a Sanborn Cardiac Output Computer (Sanborn Co., Waltham, Mass.), model 130 (Figure 2).

The computer unit operates as a digital readout voltmeter which takes from 60 to 40 per cent of the dye curve downslope (a segment which is linear on a logarithmic scale) and extrapolates it to the baseline. The digital readout is a figure which can be used to compute quickly the cardiac output value (see next section). In effect the computer integrates the dye curve and corrects for dye recirculation.

Electronic component linearity was checked in this study as follows. First, servo pen deflection in mm. was compared with servo amplifier voltage. Servo output was linear within $\pm$ 0.5% (Figure 3). The computer unit was then attached to the servo amplifier output, and measurements were made of servo pen deflection against computer output voltage. Excellent linearity was again observed (Figure 3). Finally, known blood-dye mixtures of 2, 4, 6, 8, and 10 mg./liter were drawn through the cuvette at a constant rate, and the servo pen responded in a linear manner (Figure 3). It made no appreciable difference whether or not the cuvette was flushed between consecutive blood-dye samples in this test. This shows that the cuvette chamber did not become stained

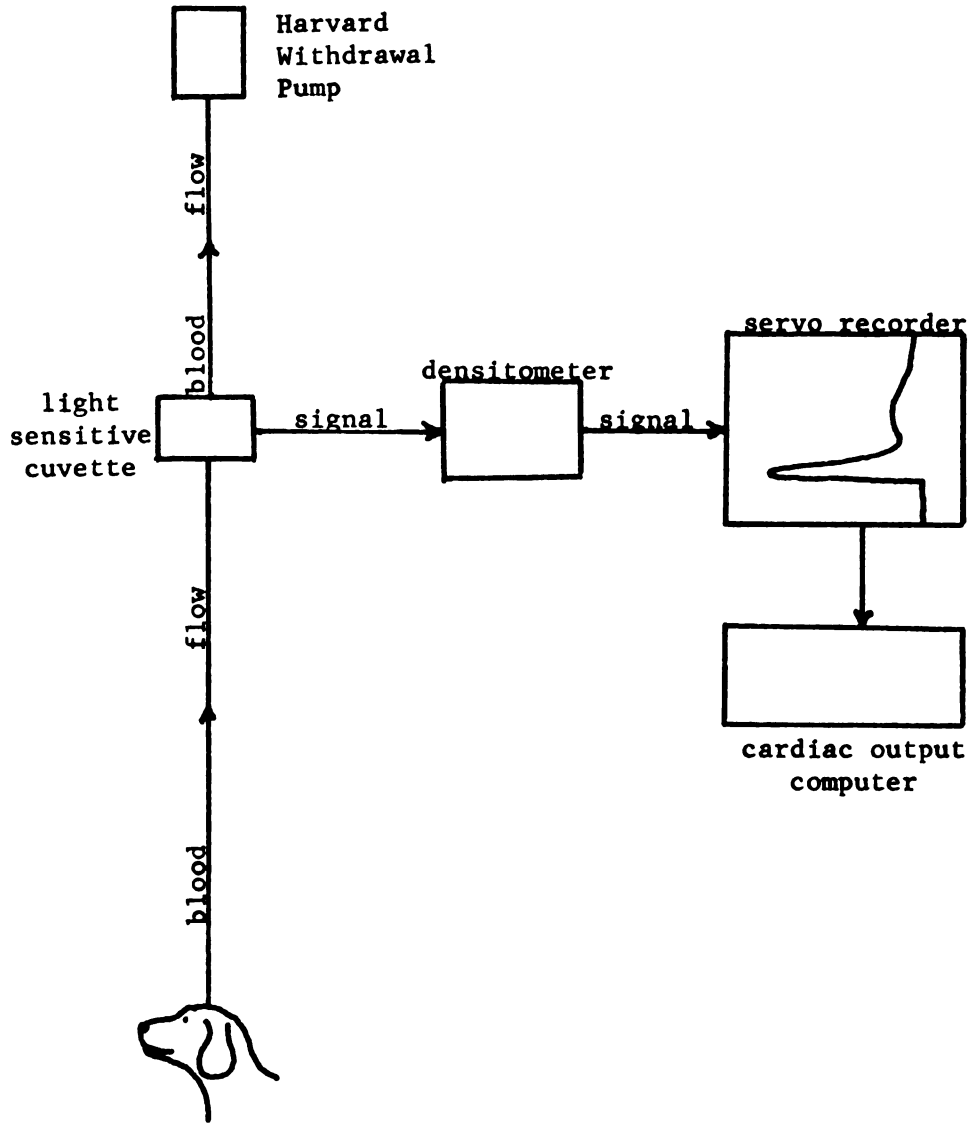

Fig. 2 System for Recording Cardiac Output

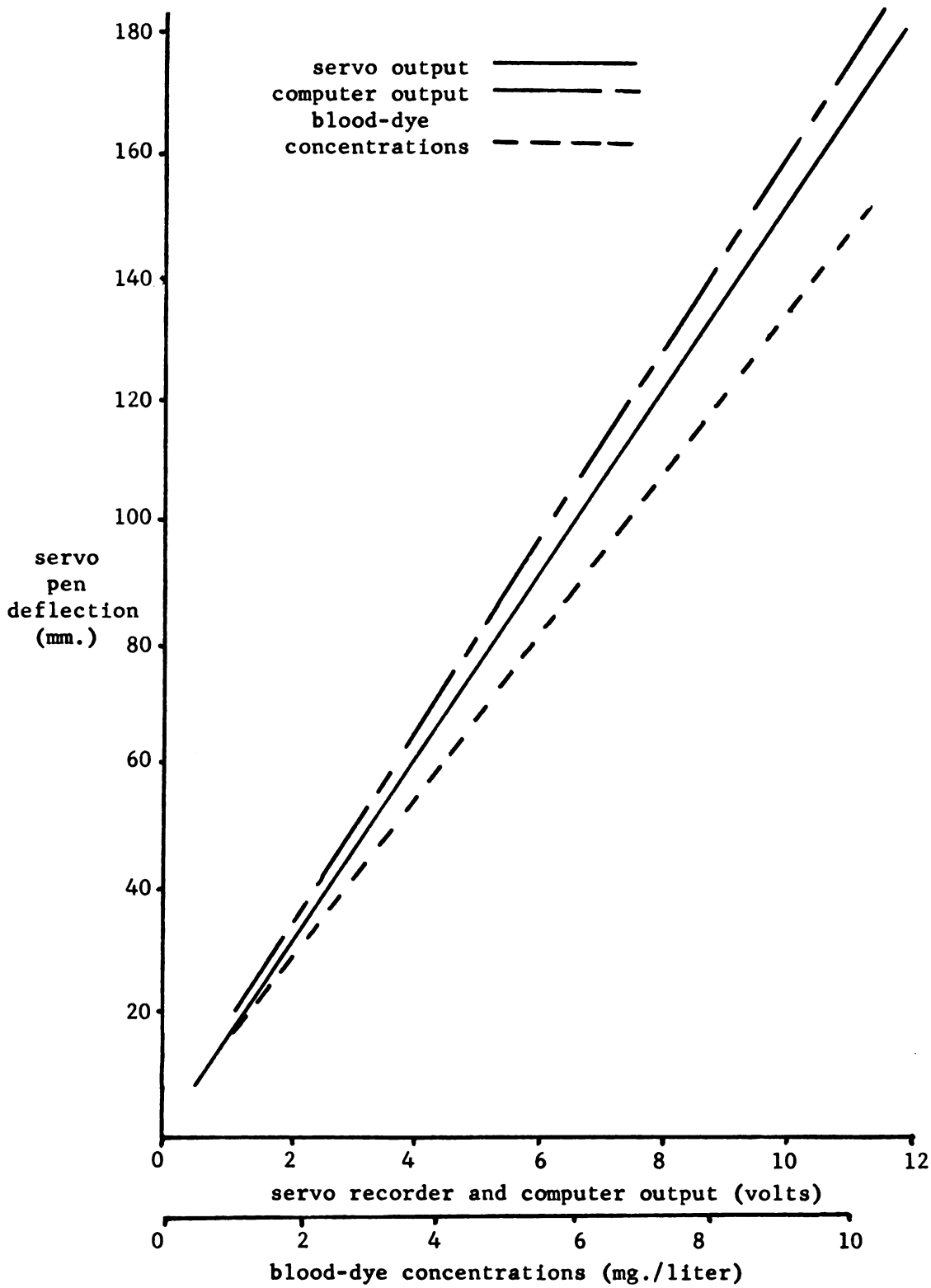

Fig. 3 Graph of Servo Pen Deflection vs. Servo Output Voltage, Computer Output Voltage, and Varying Blood-Dye Concentrations

by the dye.

Calibration for an actual determination consisted of drawing blood into a heparin-containing syringe, and adding the blood to a volumetric flask containing a given amount of dye. Eight mg./liter was the standard concentration for calibration: .08 ml. of dye (2.5 mg./ml.) to a 25 ml. flask of blood. The sequence of events then involved the following: first, normal blood (5 to 20 ml.) was drawn from the animal through the cuvette and the densitometer unit balanced against this blood to maintain the zero input baseline of the recorder; secondly, the blood-dye standard was drawn through the cuvette and a corresponding pen deflection noted. In the above two sequences, a readout was obtained from the computer. The symbol "Nb" designated the number obtained for normal undyed blood, and "Nd" the readout number for the standard.

The actual indicator dilution curves were made at two different times for each dog. Initial determinations were made immediately post-operatively while the animal was still under surgical anesthesia. Following the calibration procedures outlined in the previous paragraph, weighed dye was injected at ten-minute intervals to obtain a series of three cardiac output estimates. A readout number on the computer was obtained for each curve. The syringes were then weighed empty, and the amount of dye injected was determined. On subsequent days the dogs were exercised, and, with the exception of dog no. 5 (distemper?), appeared to remain in good health.

Prior to the second series of output determinations an

attempt was made to train the dogs to lie quietly in the hammock while awake. This was later discontinued when it was found that merely taping together the two front legs and two rear legs would produce a quiet animal. The second series of cardiac output measurements were made from three to seven days after catheter installation and the initial determinations under anesthesia. Calibration, injection of the dye, and recording procedures were identical to the initial series. All five dogs were sacrificed after the second series of indicator curves had been completed, and an autopsy performed to confirm location of the catheter tips. (Table 2).

TABLE 2. Catheter Placement

Dog No.	Average Cardiac Output with Anesthesia	Tip Location of Catheter	
		Venous	Arterial
4	2.20 liters/min.	vena cava	descending aorta
5	2.39 "	right ventricle	" "
6	2.45 "	right atrium (?)	" "
7	1.04 "	right atrium (?)	" "
8	2.17 "	right atrium	" "

CALCULATIONS, DATA, AND RESULTS

The cardiac output was calculated from computer data in two steps. First, a "calibration factor" was obtained:

$$\text{calibration factor} = \frac{Nd - Nb}{c}$$

Nd was the computer readout obtained for the blood-dye standard, Nb the computer readout for blood only, and c the concentration of dye in the blood-dye standard (8 mg./liter). A typical calculation was as follows (using data from dog no. 4, first run):

$$Nb = 42; \quad Nd = 148; \quad c = 8 \text{ mg./liter}$$

$$\text{calibration factor} = \frac{Nd - Nb}{c} = \frac{148 - 42}{8} = \frac{106}{8} = \underline{\underline{13.25}}$$

The second step was likewise simple and straight-forward:

$$\text{cardiac output (liters/min.)} = \frac{\text{calibration factor} \times 60 \times \text{dye injected (mg.)}}{\text{computer readout for dye curve}}$$

Using the data, again from dog no. 4, first run, cardiac output was computed as follows:

computer readout for dye curve = 776; dye injected = 2.114 mg.

$$\text{cardiac output} = \frac{\text{calibration factor} \times 60 \times \text{dye injected (mg.)}}{\text{computer readout for dye curve}}$$

$$= \frac{13.25 \times 60 \times 2.114}{776} = \underline{\underline{2.17 \text{ liters/min.}}}$$

These formulae were suggested by the manufacturer of the computer.

Analysis of the indicator time-concentration curve from

the servo recorder was carried out by the Hamilton (1929, 1932) method. Dye concentrations were read from the curve at one-second intervals. Two to four readings were taken from the downslope before recirculation occurred. These were plotted on two-cycle semi-logarithmic graph paper, and a straight line drawn through the points. Dye concentrations were then read off this extrapolated line and replotted on linear scales to extend the original curve. This step amounts to correcting the original curve for recirculation of dye and produces a linear plot as though only one circulation of dye had occurred. Figure 4 is a typical example of a continuous dye-curve from the servo recorder. Figure 5 shows a semi-logarithmic replot and extrapolation of the falling dye concentration after the peak. The primary circulation time is indicated where the extrapolated curve meets the baseline (zero concentration). The dye concentrations at one-second intervals were then added, and divided by the total time in seconds under the curve to find the average dye concentration. Finally, the results were applied to the Hamilton equation (see METHODS) given as:

$$\text{cardiac output (liters/min.)} = \frac{60 \times I}{\bar{c} \times T}$$

Table 3 gives the results on observations from five dogs. With one exception (dog no. 4, awake), three successive dye injections were averaged. With regard to these average values, the differences between the two systems ranged from zero to 120 ml. The computer was higher than curve analysis by an

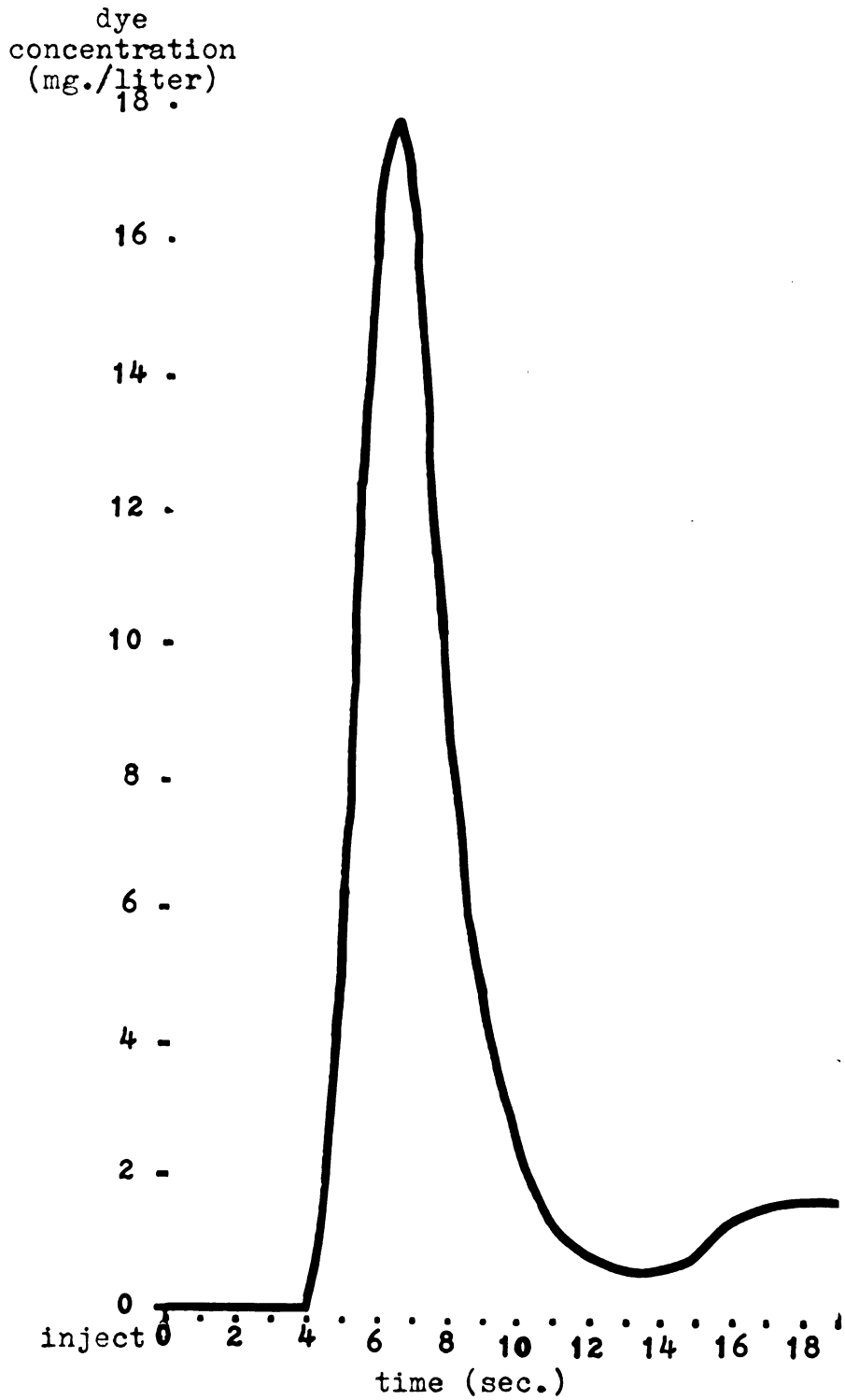

Fig. 4 Copy of Original Dye Curve Produced by Servo Recorder from the First Injection, Dog no. 4

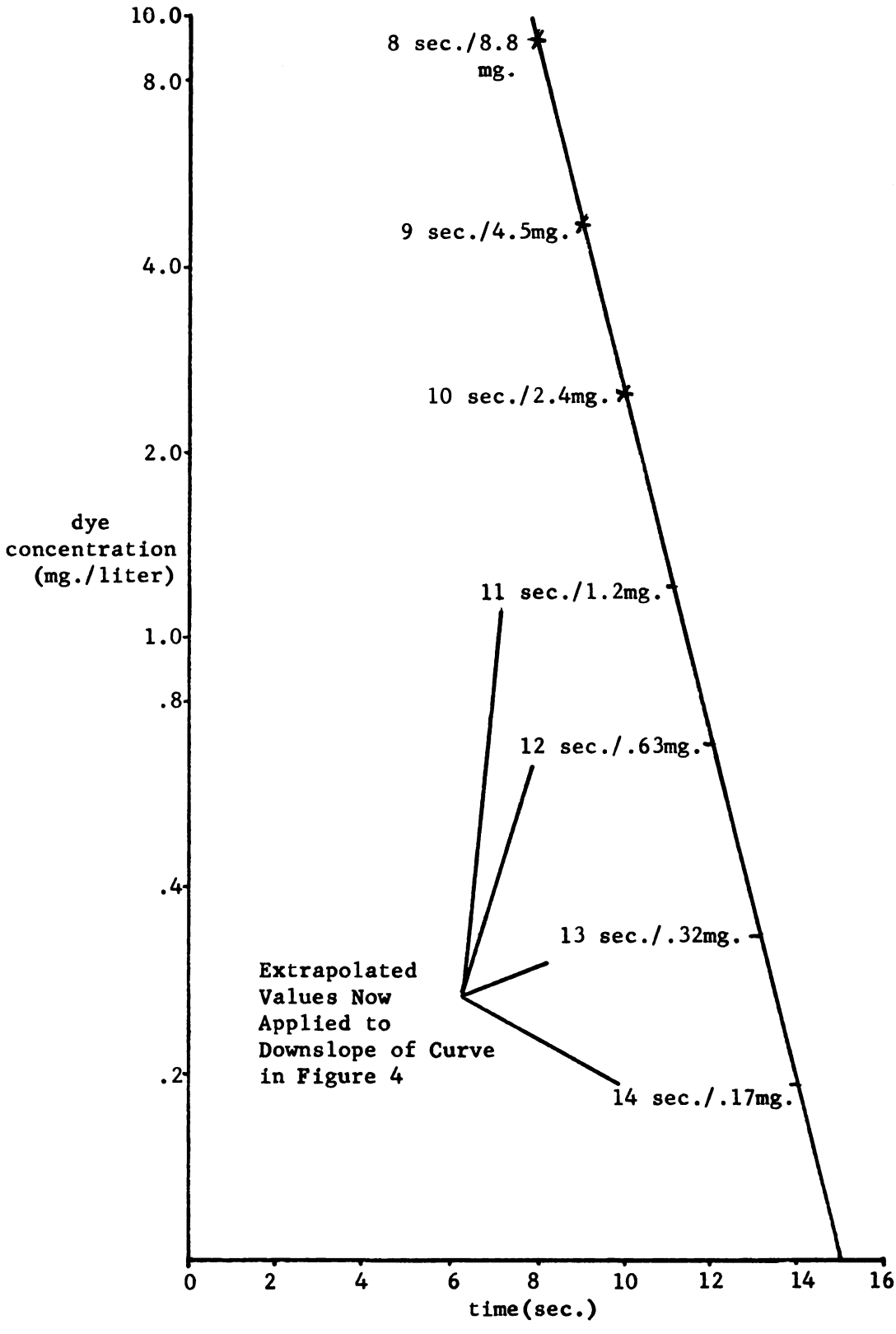

Fig. 5 Semi-logarithmic Plot of the Downslope from Curve Shown in Figure 4

TABLE 3. Cardiac Output Values from Computer and Curve Analysis on Five Dogs Anesthetized and Awake

Dog	Weight (kg.)	Condition	Computer (L/min.)	Difference (L/min.)	Curve Analysis (L/min.)
4	10.5	anesthetized	2.17	.06	2.23
			2.37	.04	2.41
			2.07	.05	2.12
		average:	2.20	.05	2.25
		awake	2.10	.03	2.13
			2.20	.--	2.20
		average:	2.15	.02	2.17
5	12.0	anesthetized	2.31	.12	2.19
			2.35	.17	2.18
			2.51	.08	2.43
		average:	2.39	.12	2.27
		awake	1.65	.05	1.60
			1.70	.01	1.71
			1.93	.08	1.85
		average:	1.76	.04	1.72
6	13.0	anesthetized	2.36	.04	2.32
			2.43	.11	2.32
			2.57	.06	2.51
		average:	2.45	.07	2.38
		awake	1.75	.03	1.72
			1.72	.01	1.71
			1.93	.13	2.06
		average:	1.80	.03	1.83
7	11.0	anesthetized	1.09	.02	1.07
			1.07	.02	1.05
			.96	.01	.97
		average:	1.04	.01	1.03
		awake	1.48	.13	1.35
			1.51	.--	1.51
			1.31	.13	1.44
		average:	1.43	.--	1.43
8	14.0	anesthetized	2.20	.--	2.20
			2.08	.06	2.14
			2.24	.09	2.33
		average:	2.17	.05	2.22
		awake	3.07	.15	2.92
			2.75	.13	2.88
			3.15	.28	2.87
		average:	2.99	.10	2.89

average of 68 ml. in five instances; the two systems were identical in another instance; in four cases the computer was lower than curve analysis by an average of 37 ml. In Table 4 this variation is indicated. The data show that this variation occurred within a given dog (as in nos. 6 and 8) as well as between individuals, i.e., nos. 4 and 5. The number of animals used in this study is considered too small to support statistical analysis.

Table 5 compares the recorder pen deflection, produced by the blood-dye standard, in two separate runs made with each dog. The standard was prepared in the same manner for each run. Dogs no. 5 and no. 7 gave nearly identical values on both of their runs, dogs no. 4 and no. 8 showed a slight difference, and dog no. 6 recorded the greatest difference between its first and second run.

Finally, an additional animal (dog no. 9) was prepared in the usual manner. Dye dilution was carried out while the animal was still under surgical anesthesia, and the instrumentation order was varied as follows:

PLAN 1: DENSITOMETER ⟶ SERVO RECORDER ⟶ CARDIAC OUTPUT

PLAN 2: DENSITOMETER ⟶ COMPUTER ⟶ CARDIAC OUTPUT

From plan 1 the cardiac output value obtained was 1.83 liters/min.; from plan 2 the estimate was 1.79 liters/min. The difference between these two methods was two per cent.

TABLE 4. A Comparison of Average Values from Table No. 3

Dog No.		Computer (liters/min.)	Curve Analysis (liters/min.)	Difference Between Computer and Curve Analysis (liters/min.) High	Low
4	a*	2.20	2.25		-.05
	b*	2.15	2.17		-.02
5	a	2.39	2.27	+.12	
	b	1.76	1.72	+.04	
6	a	2.45	2.38	+.07	
	b	1.80	1.83		-.03
7	a	1.04	1.03	+.01	
	b	1.43	1.43	--	--
8	a	2.17	2.22		-.05
	b	2.99	2.89	+.10	
averages:					
	a	2.05	2.03	+.068	-.037
	b	2.03	2.01		

TABLE 5. Response of the Servo Recorder to the Blood-Dye Standard

Dog No. (and run)		Standard	Pen Deflection (mm.)
4	a	8 mg./liter	76
	b	" "	51
5	a	" "	69
	b	" "	70
6	a	" "	66
	b	" "	106
7	a	" "	70
	b	" "	69
8	a	" "	95
	b	" "	64

*a: anesthetized state
*b: awake state

DISCUSSION

The sampling of arterial blood from the descending aorta presented no problems once the optimal catheter size had been selected. A small catheter prevented adequate withdrawal rate. A larger catheter allowed the arterial pressure pulse to produce pulsations in the sampling cuvette, causing irregularities in the dye curve tracing.

The initial arterial cannulations in dogs no. 7 and no. 8 were performed so that the catheter tip came to rest in either the carotid or brachiocephalic artery. Clotting in these two cases was a frequent problem and the blood withdrawal rate (40 ml./min.) could not be achieved. Catheters in these dogs were subsequently re-installed so that withdrawal was from the thoracic aorta.

The work of Pearce, et al. (see REVIEW OF LITERATURE, Table 1) demonstrated that cardiac output values obtained from injections at the right heart, pulmonary circulation, and root of the aorta produced a variation of between 110 and 160 ml./min. for these three sites. In the present study, the injection site was either the vena cava, the right auricle, or the right ventricle. It is felt that the relatively consistent placement of injection catheters in this study helped to minimize the effect of injection technique on cardiac output estimations in the five dogs presented.

There is no immediate explanation for variability of data presented in Table 5. The dogs were not fasted prior to their

cardiac output estimations. The differences observed in dogs no. 4, no. 6, and no. 8 between the first and second runs for blood-dye standards, with regard to servo pen deflection, may be due to some variations in the blood for the two runs. There was no obvious difference in plasma turbidity but no measurements of it were made. In addition, dog no. 6, which showed the greatest difference, was re-catheterized twice between runs. The animal lost an unknown amount of blood, and the effect of hemorrhage may have some bearing in this case.

Dobkin and Wyant (1957) found cardiac output unchanged even after the injection of large doses of barbiturates (thiopentol). The incidental effect of anesthesia in the present series of cardiac output estimations was inconclusive. Dogs no. 4, no. 5, and no. 6 showed an average of 17% decrease in cardiac output in the awake state versus the estimation while under anesthesia. Dogs no. 7 and no. 8 showed a 38% increase. On the other hand, the average cardiac output estimates for all dogs differed by only 20 ml. between asleep and awake states with either estimating system (Table 4). The value of data on anesthesia in this study is questionable because the two runs (asleep and awake) were made from three to seven days apart.

While the data showed a very favorable correspondence between dye curve analysis and computer operation, it was deemed necessary to compare the two systems separately. The computer was used alone for one determination, and then a

second output measurement was made with the dye curve recorder. The data on dog no. 9 show agreement between the two systems suggesting that one or the other may be used independently. However, by using the computer in connection with a servo recorder, one is able to follow the dye curve shape. This is useful in assessing the quality of the dye curve itself. Irregular curves may be produced by faulty dye injection, irregular catheter placement, and pulsations in the dye cuvette. Such irregular curves presented to the computer for analysis will produce an error in cardiac output estimation.

The work of Theye, et al., (1963) showed a 10% difference between indicator dilution and direct Fick cardiac output determinations. Their indicator dilution average was lower than the direct Fick average. In the present study, the computer results varied both above and below those obtained by Hamilton curve analysis (Table 4). However, the average computer value was above that obtained from curve analysis.

Values for cardiac output found in the literature vary widely for dogs of the same body weight. Pearce, et al. (1953) reported on five dogs ranging in weight from 11.8 to 18.2 kilograms. Cardiac output values varied from 1.70 to 4.16 liters/min. Schmid (1954) had five dogs ranging from 11.0 to 14.0 kilograms and cardiac output values varied from 1.5 to 4.3 liters/min. In the present study, cardiac output ranged from 1.03 to 2.99 liters/min. These values agree with those established in the literature for dogs of this general weight class.

The computer provided a rapid, semi-automatic measurement of cardiac output when used as an analyzer of the dye dilution curve. Its advantage is to provide a cardiac output figure within minutes after the dye injection has been completed. It further provided a sampling of dye concentrations along the entire curve whereas the replotting method samples dye concentrations every second, or at best, every one-half second. Given proper calibration, rapid dye injection, and acceptable curve shape, the computer is a means of rapid repeated cardiac output determinations.

SUMMARY

A dye dilution method using indocyanine green as the indicator and a system composed of a densitometer, servo recorder and computer is described for the measurement of cardiac output in dogs. The densitometer functions well in providing continuous accurate sampling of arterial dye concentration. The servo recorder provides a large, direct record of the dye curve which could then be analyzed by the Hamilton technique. The computer, as an alternate method, integrated the dye curve obtained from either the densitometer or servo recorder and gave a rapid, semi-automatic measurement of cardiac output. The data comparing curve analysis from the servo recorder with computer estimations agreed within five per cent.

Chronic catheter implantation is described as a method for obtaining repeated cardiac output estimations from the unanesthetized dog. The awake animal offers little resistance to the procedure when suspended upright in a burlap hammock. The effects of anesthesia in this study are inconclusive.

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