Computers in Cardiovascular Investigation

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Few areas of clinical investigation encompass such a variety of basic principles as those used in the measurement of blood pressure and blood flow in man. However, during recent years the progressive evolution of these principles, allied to the rapid development of sophisticated electronic recording methods, has greatly facilitated the clinical application of many of these elegant investigative techniques. But the very facility with which these techniques may now be applied has brought in its wake the increasing problem of the onerous and time-consuming measurement of the circulatory data obtained. This technological complication is now tending to limit the further exploitation of many of these techniques and to restrict severely the design of circulatory investigations.

In no instance is the problem more acute than in the measurement of the cardiac output by the indicator dilution technique. Fortunately the development of computer science has now made readily available a sophisticated method of electronic measurement and calculation of the cardiac output. At present three simple proprietary cardiac output monitors are available. All are primarily designed to work with dye-dilution methods, and all are based on simple integration of the indicator curve area with some standard method of electronic prediction of the exponential decay of the dye curve downslope. A study has therefore been designed to define the precision with which these three analogue computers measure the cardiac output in man and to determine their usefulness in the presence of abnormalities of cardiac rhythm and valvular disease. In addition, a more elaborate technical study was instituted to explore the feasibility of digital computer analysis of cardiovascular measurements of pressure and flow in the central circulation. This report concerns a

comparative analysis of the results produced by these various methods with those produced by the usual manual methods of measurement.

METHODS

The observations were made on patients undergoing routine diagnostic circulatory investigation. As the studies were designed to test the comparative precision of the computer measurements against those made by the manual method, only dye curves produced under as nearly ideal conditions as possible were compared. The observations in the first instance were therefore confined to patients without valvular disorders, abnormalities of rhythm, or cardiac shunts. In each of 10 patients, 10 serial measurements of cardiac output were made at rest at alternate minute intervals and 2 measurements during different levels of supine leg exercise. In all, therefore, 100 resting and 20 exercising values of cardiac output from 10 patients were compared in each computer. Following completion of this study, the influence of dye curve distortion due to cardiac valvular and rhythm abnormalities was assessed in the Sanborn computer by a further comparative study involving 10 patients with chronic rheumatic heart disease, chiefly of the mitral valve, 5 of whom were also suffering from atrial fibrillation. In each patient the plan of the investigation was identical with that described above, so that the comparison again involved a total of 100 resting and 20 exercise observations. In the feasibility trial of the system used for total computer analysis, the reported figures relate to one patient without heart disease studied at rest and during gradually increasing levels of supine leg exercise.

Laboratory Techniques. The indicator method entailed the rapid injection of a small amount of indocyanine-green dye into the pulmonary artery (1 mg. dye in 1 ml. solvent injected in 0.1 sec.). The resulting time-concentration dye curve was sampled from the aorta by high velocity constant speed withdrawal through a nylon catheter 55 cm. long and 0.8 mm. internal diameter introduced percutaneously into the brachial artery. The dye curves were transduced by a Waters X-300 A cuvette-densitometer in series with a modified

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control unit and transcribed for manual measurement by a direct-writing ultraviolet light recording system. In normal dye curves the conventional Hamilton semi-logarithmic replot of the dye curve downslope was required only to determine the last 10 per cent or less of the curve decay due to the relatively undistorted nature of the generated dye curves (Fig. 1). The observer error in measurement of these curves has been assessed at less than 2 per cent. By comparison of consecutive cardiac output determinations at the same heart rate, the reproducibility of the dye method has been determined as less than ± 0.17 l./min. at the 95 per cent level of confidence throughout a cardiac output range of 2–10 l./min., or ± 2.7 per cent at a mean cardiac output of 6.32 l./min. Thus, in practice, differences between duplicate dye outputs in excess of 0.34 l./min. may be expected to be due to factors other than the technique in 95 per cent of instances. This method, together with its validation, an estimate of its errors, and a critical assessment of the theoretical principles upon which it is based, has been described in detail elsewhere (Taylor, 1966; Taylor *et al.*, 1967).

The voltage signals from the dye control unit were so arranged as to allow them to be fed into the ultraviolet light recorder and simultaneously into the computers in parallel. The three cardiac output computer monitors were those manufactured by the Gilford Instrument Laboratories Inc. (Model 104), the Sanborn Division of the Hewlett-Packard Corporation (Model 130), and the Lexington Instrument Corporation. In view of the extreme sensitivity of the Gilford instrument to baseline drift, only dye curves were accepted for comparison in which the Gilford computer count during the dye curve appearance time was between 5 and 20 counts. Whole blood calibration of each instrument was carried out in parallel with that fed into the recorder: the technique of calibration was similar to that described by Taylor *et al.* (1967). To assess the errors introduced into the computer calculations by baseline drift, two methods were used. In the first, acute square-wave changes in an upward and downward direction were induced in the baseline after the dye had been injected and after the integrating mechanism had been activated. The baseline shifts produced were of the order of 10 per cent of the peak height of the curve, i.e. about 1 cm. with a curve height of 10–15 cm. In a second series, the baseline was caused to drift in an upward and downward direction by the use of a ramp wave-form generator, corresponding to a steadily rising or falling baseline. Again the change in baseline was produced after the dye injection had been made and after the integrators had entered the compute mode; it was once more of the order of 10 per cent of the height of the dye curve.

PRINCIPLES OF COMPUTER OPERATION

The basic principle governing the programme of all three analogue computers is that none make any new assumptions regarding the shape of the initial part of the dye curve until the portion of the downslope from which each machine makes its logarithmic extrapolation is reached: from this point on, all three computers assume

that the primary curve will follow a pure and continuous exponential decay.

The Gilford Instrument (Model 104). This computer follows almost exactly the Hamilton method of manual computation of dye curve area. The voltage pattern of the original dye dilution curve is first converted into logarithmic form by a log amplifier. At a predetermined time after the peak of the curve has been passed, the slope of the curve decay is determined by measuring the time required for the downslope to decrease from 75 to 45 per cent of the peak height of the curve: this factor is used to establish the time-constant of an exponential generator, so that the output of this generator has the same decay slope as the original curve over the sampled

FIG. 1.—Illustration of dye curve recorded on ultraviolet paper from a patient without cardiac rhythm or valvular abnormalities. The cardiac output was 5.86 l./min; the vertical time marker is set at intervals of 0.5 sec.

portion. Beginning with the first appearance of dye, the integrator carries out a continuous determination of the area under the primary curve. This continues until such time as the time-constant of the exponential generator has been established, following which the integrator is switched to the exponential generator and the remainder of the dye curve is ignored. The computer reads out in numerals a value that is directly proportional to the total area under the primary curve.

Sanborn Computer (Model 130). The principle of the method used by this computer to determine the exponential decay is based on a simple mathematical function. It is a fundamental exponential property that the value of the integral between two ordinates of known ratio is directly proportional to the integral from the first ordinate to infinity. In this machine the principle is applied by simple triple multiplication of the area under the dye curve downslope between 60 and 40 per cent of its peak height: the remainder of the dye curve downslope is then ignored. This area is then added to that integrated prior to the 60 per cent point to obtain the total area under the primary curve. It is an implicit assumption in this method that the downslope of the dye curve being measured follows an exponential function between 60 and 40 per cent of its peak curve height. The output of the instrument is a three-digit number proportional to the primary time-concentration curve.

Lexington Computer. The design principle of operation of this computer is based on the continuous computation of the total dye curve area at all instances of time during the transcription of the curve. The output signal is a combination of the uncorrected integral of the input signal at any time "t", and a predicted area, the predictor assuming that the curve will continue to decay exponentially at the same slope as is present at the time "t". Thus, the outputs from the actual integrator and the "predictor" will be equal and will balance only when the accretion of area by the integrator occurs as an exponential function, namely when a portion of the dye curve downslope is reached that follows a true exponential decay. At this point the signal outputs from each will balance and a stable read-out value will be obtained and will continue for as long as the downslope continues to follow an exponential function. In the absence of an exponential portion of the downslope, the outputs of the actual integrator and the predictor will differ continuously and a stable output indicating the primary curve area will not be obtained. The output is displayed on a direct read-out meter with inverse scale calibration. Prior calibration of the instrument with a known dye in blood concentration allows cardiac output measurements to be read directly from the meter.

Transducer-computer Link and Digital Computer Programme. The basic outline of the transducer-computer link used in the more comprehensive cardiovascular analysis is illustrated in Fig. 2. The link was developed in conjunction with the systems-engineering division of

Elliot Medical Automation Ltd. The principle of the method involves sampling each of the eight analogue pressure and flow data channels at a prescribed frequency, conversion of the analogue data into three decimal digits corresponding to the instantaneous magnitude of the signal, and storage of this digital data on multi-channel magnetic tape. Each decimal digit is represented as a 5-bit character in the computer code, the code incorporating a "parity" bit used by the computer to check the characters. The further transference, at a slower speed and later time, of the recorded digital data from magnetic to punched paper tape was for the sake of local convenience input to an off-line Elliot 803 digital computer. Since a form of simple pattern recognition was required, it was necessary to sample some of the original data at a speed of 150 samples a second in order to achieve completely adequate discrimination of the signal waveform. This was particularly obligatory with the systemic arterial pressure waveform. The eight times slower playback of digital data from magnetic to punched paper tape was necessary because of the much slower speed of the paper tape punch. The recorded data were then processed in the Elliot 803 digital computer according to a standard but flexible programme in which the following data were printed out.

(1) Patient identification, number of test, and other recognition data. (2) Cardiac output in l./min. and l./min./sq. m. (3) Appearance time for dye curve in sec. (4) Mean transit time in sec. (5) Central blood volume in ml./sq. m. (6) Heart rate per minute. (7) Stroke volume in ml./sq. m. (8) Systolic and diastolic arterial

FIG. 2.—Layout of eight-channel transducer-computer link for intravascular pressure and flow measurements.

pressure in mm. Hg. (9) Mean systolic, mean arterial, and mean diastolic pressures in mm. Hg. (10) First derivative of aortic pressure waveform in mm. Hg/sec. (11) Duration of systole and of diastole in sec. (12) Mean pulmonary arterial pressure in mm. Hg. (13) Mean pulmonary wedge pressure in mm. Hg. (14) Mean right atrial pressure in mm. Hg. (15) Systemic vascular resistance in dyne sec. cm^{-5} sq. m. (16) Pulmonary vascular resistance in dyne sec. cm^{-5} sq. m. (17) Left ventricular minute work in kg. m./min./sq. m. (18) Left ventricular stroke work in g.m./sq. m. (19) Systolic and diastolic tension-time indices in mm. Hg/sec.

In the calculation of the area of the dye curve for the cardiac output determinations the computer was programmed to generate the extrapolation of the downslope by the least squares procedure from points on the dye curve sampled between 60 and 25 per cent of the peak curve height. The dye curve was sampled at a rate of 12 per second so that the number of points from which the semilogarithmic extrapolation was calculated was of the order of 30–50 with a normal resting cardiac output and never less than 20 even during heavy exercise.

MEASUREMENTS AND CALCULATIONS

Cardiac output was calculated from the formula:

$$Q = \frac{I \times 120}{\sum C \times K}$$

where Q = cardiac output in l./min.; $\sum C$ = sum of dye concentration at half-second intervals; I = dye injectate volume ml.; and K = calibration factor.

The downslope was extrapolated through two whole logarithmic cycles by the conventional Hamilton semi-logarithmic plot, trapezoidal approximations being made at half-second intervals. The minimum number of approximations accepted for trial fitting of the extrapolation plot was six, and in all curves used in the present analysis, a straight-line segment was readily discernible. The method used for aortic pressure pulse wave analysis is illustrated in Fig. 3. The manual measurements of compartmental areas of the arterial pressure waveform were made by conventional planimetric techniques.

Statistical analyses were based on orthodox methods. The standard error of the estimate ($S_{E \text{ of } E}$) was calculated from the formula

$$S_{E \text{ of } E} = \sqrt{\left(\frac{n \sum y^2 - (\sum y)^2}{n(n-1)} \right) (1 - r^2)}$$

where r = correlation coefficient.

For any given single computer reading (x) the best measured estimate (y) is given by the equation $y = mx \pm c$. The variance of y is given by Var.

$$y = S_{E \text{ of } E}^2 \left(1 + \frac{1}{n} + \frac{(x - \bar{x})^2}{\sum (x - \bar{x})^2} \right).$$

Then $SD = \text{Var. } y$ and the 95 per cent confidence limits are given by the value $y \pm 1.96 \times SD$. The confidence

FIG. 3.—Illustration of method of systemic arterial pressure pulse-wave measurement and analysis.

limits were calculated at intervals of 1 l./min. throughout the cardiac output range.

RESULTS

The results are presented in three sections. The first section deals with the comparison of the values given by each of the proprietary cardiac output monitors and those obtained by conventional manual measurements. The second section deals with the influence of baseline drift and early recirculation of dye on the values given by these computers. The third section deals with the results of the comparison between the manual method of dye curve and arterial pressure measurements and the results obtained by a systems-engineered transducer-computer link in conjunction with detailed programming of an Elliot 803 digital computer.

I. ACCURACY OF THE SMALL CARDIAC OUTPUT MONITORS

A summary of the statistical analyses of the comparisons between the computer and manual measurements is presented in the accompanying Table. The nearly linear relationship of the confidence limits to the regression line throughout the range of cardiac output values in all three computer comparisons is a reflection of the homogeneous distribution of the variance of the differences throughout the range of values studied.

The Gilford Computer. The results of the com-

TABLE
SUMMARY OF STATISTICAL ANALYSIS OF COMPARATIVE RESULTS

Comparison		No. of observations	Sums	Sums of squares	Correlation coefficient	Standard error of estimate	Slope	Intercept
Gilford	Computer measurements	120	812.54	5894	0.996	0.182	1.115	-0.392
	Manual measurements	120	859.06	6642				
Sanborn 1	Computer measurements	120	667.17	4395	0.993	0.167	0.942	+0.225
	Manual measurements	120	652.42	4189				
Sanborn 2	Computer measurements	120	537.01	2556	0.985	0.233	1.109	-0.301
	Manual measurements	120	559.12	2803				
Lexington	Computer measurements	120	567.28	2952	0.985	0.277	1.048	-0.002
	Manual measurements	120	597.61	3283				

All comparisons relate to measurements in patients without cardiac rhythm or valvular disorders except those in Sanborn 2, which concern studies in patients with mitral valve disease and atrial fibrillation.

parison between the values for cardiac output given by this machine and those measured and calculated by the conventional manual method are illustrated in Fig. 4. The narrow distribution of the comparative observations about the regression line and the linearity of the relation between the computer and measured values is evidenced by the high degree of correlation between these measurements ($r=0.996$; $S=0.182$). The regression equation reveals a small systematic error such that at cardiac outputs greater than 3 l./min. the value given by the Gilford machine is less than that measured by the usual manual methods. In the present series it was necessary in the manual measurements to apply the conventional Hamilton semilogarithmic extrapolation only to the final 10 per cent or less of the downslope; the Gilford computer was extrapolating from much higher level, approximately from 75 to 45 per cent of the peak concentration of the curve. However, the systematic error involved by this underestimate of the computer in the ranges of cardiac output normally under study is small; it amounts to a mean error of 3.3 per cent at a cardiac output of 5 l./min. and 6.8 per cent at a cardiac output of 10 l./min. Furthermore, this small error may be readily and validly corrected because of the complete linearity of the regression line relating the measured and computer values and the nearly homogeneous distribution of their differences.

The cause of this systematic error between the manual and computer measurements is probably due to the design characteristics of the extrapolation

method employed by the machine. The points on the downslope taken for generation of the logarithmic exponential are between 75 and 45 per cent of the peak concentration. In the majority of instances, using the dye dilution technique described, semilogarithmic extrapolation from the primary curve slope between these two points could be expected to give too large an extrapolated area, and, thus, a too small estimate of the cardiac output (Fig. 5). With higher cardiac outputs this error would tend to increase systematically due to the increasing purity of the primary curve as measured manually, while the computer is still bound to use the upper part of the dye curve downslope for its fixed extrapolation points.

The Sanborn Computer. Comparison of the cardiac output values given by the Sanborn computer and those obtained by manual measurement are illustrated in Fig. 6. The close distribution of the comparative measurements about the regression line and the linearity of the regression relation between the values are borne out by the very high degree of correlation between the two methods of measurement ($r=0.993$; $S=0.167$). A very small systematic error is apparent from the regression equation. Above a cardiac output of 3 l./min. the Sanborn computer gives a slightly greater value for cardiac output than the manually measured method. At a cardiac output of 5 l./min. the error is 1.7 per cent and at a cardiac output of 10 l./min. it is still only 3.2 per cent.

FIG. 4.—Comparison of the cardiac output determinations derived from values given by the Gilford computer with those obtained by manual measurements.

FIG. 5.—Comparison of the method of extrapolation of the downslope of the dye curve used by the Gilford computer with that used in manual measurements.

FIG. 6.—Comparison of the cardiac output determinations derived from values given by the Sanborn computer with those obtained by manual measurement.

FIG. 7.—Comparison of the method of extrapolation of the downslope of the dye curve used by the Sanborn computer with that used in manual measurements.

This extremely good agreement between the computer values and those obtained by manual methods of measurement is readily explicable in terms of the compatibility between the dye-curve generating mechanisms and the computer programme. The techniques of dye curve area measurement used by both the manual and computer methods in the present study were nearly identical. The manual trial-fitting procedure to determine the semilogarithmic extrapolation of the primary curve usually utilizes the section of the curve downslope between 60 and 10 per cent of the peak curve height (Fig. 7); the Sanborn computer is programmed to use the upper portion of the same section, namely 60–40 per cent. The Sanborn machine uses a simple mathematical formula to determine the decay

of the primary curve downslope in the presence of recirculation based on the triple multiplication of the area under the curve between 60 and 40 per cent of the peak concentration. It was observed that, with the dye curves obtained by the techniques used in the present study, this portion of the downslope of the primary dye curve was almost invariably incorporated in the upper portion of the part of the curve from which the semilogarithmic extrapolation was made by the conventional method of trial fitting (Fig. 7).

The Lexington Computer. The values for cardiac output, directly read from the machine to one or two decimal places depending on which of the triple scales were used, are compared with the manual

FIG. 8.—Comparison of the cardiac output values given by the Lexington computer with those derived from manual measurements.

measurements in Fig. 8. The imprecision of making the reading at high scale values of cardiac output probably accounts for the slightly greater scatter of comparative values observed ($S=0.277$). The linearity of the relation between the Lexington values and those obtained by manual measurement is still, however, of a high order ($r=0.985$). The regression equation is similar to that calculated for the Gilford comparison and the errors generated are also of a similar order of magnitude. The mean error introduced by the computer is a 4.6 per cent underestimate of the cardiac output as compared with that obtained by manual measurement of the dye curves throughout the range 2–10 l./min. The cause of this small systematic error is not clear. In all instances the computer uniformly yielded a stable read-out value for the corrected integral. This implies that even at high cardiac output values the speed of curve inscription never exceeded the capacity of the computer to integrate, though of course the time available for read-out was correspondingly reduced. Further, the analogue computer is programmed to compute the total area at all instances of time during the transcription of the dye curve, and a stable and acceptable read-out value can only be obtained when the downslope of the curve is following a true exponential decay. In the present study the validity of the comparison was ensured by accepting for analysis only those dye curves in which an extensive portion of the downslope followed an exponential function. The small systematic differences observed are therefore difficult to explain.

II. THE EFFECT OF DYE CURVE DISTORTION ON THE COMPUTER RESULTS

Effect of Changes in Baseline. The limited and unadaptable programme of each of the small cardiac output computers under review does not allow them to deal with any changes in level of the dye curve baseline once the compute mode has been entered and integrating mechanism activated. The effect of upward and downward changes in baseline on the calculation of cardiac output by each of the computers was investigated by causing square wave or drift changes in the baseline of the same predetermined extent. The rapidity with which the changes were produced and values obtained are illustrated in Fig. 9. It will be seen that downward drifts in the baseline, rare in practice, produced, as would be expected, much smaller errors in the calculated dye curve area than the more commonly encountered upward changes. With upward baseline shifts acute changes gave larger "errors" than a slow upward drift in the baseline of the same extent. In each instance, all three computers "erred" equally, emphasizing the strict requirement of absolute base-

line stability for the valid operation of all three machines.

Effect of Cardiac Valvular Abnormalities and Disorders of Rhythm. The influence of dye curve distortion on the computer and manually measured cardiac output values was investigated by repeating the comparison with one of the computers in patients with mitral valve disease, half of whom had atrial fibrillation. The effect of these valvular and rhythm abnormalities is twofold. The low cardiac output usually accompanying these lesions is associated with a spread of the curve due to the appearance of recirculation elements high on the primary curve downslope: severe mitral regurgitation is perhaps the greatest offender in this respect. Secondly, the presence of irregularities of cardiac rhythm not infrequently causes serious and random abnormalities of dye curve shape. This comparison was carried out with the Sanborn computer because of the nearly identical values compared with the manually measured estimates that this machine gave with the normal dye curves. The comparison is illustrated in Fig. 10. Compared to the comparison with the same computer in patients with normal dye curves, illustrated in Fig. 6., the regression line is now depressed below the line of identity (slope of regression line 1.109), though the cross-over point remains at 3 l./min. The reason for this change in the relationship between the measured and computer calculated dye-curve areas is probably the higher appearance of recirculating elements on the downslope, at least as high as 60 per cent of the total peak height. The computer then extrapolates from a portion of the downslope already "impure" while the more abstract trial fitting of the extrapolation plot by eye allows more account to be taken of the pre-recirculatory part of the dye curve downslope. It is of interest that under these circumstances the regression line of comparative values of the Sanborn computer becomes very similar to that of the Gilford computer with normal dye curves. In addition, the wider scatter of values about the regression line ($S=0.233$) is probably a reflection of the random distortion of the curve, due to abnormalities of rhythm, with which the rigidly programmed computer is unable to deal.

III. FEASIBILITY OF THE TRANSDUCER-COMPUTER LINK SYSTEM

The values of systemic arterial pressure and cardiac output obtained from the off-line transducer-computer link system are compared with those obtained from the manual measurement of simultaneously recorded directly-written analogue records in Fig. 11. The cardiac output was calculated by

FIG. 9.—Errors due to baseline changes. Illustration of the effect of square wave and drift changes of the order of 10 per cent of the total curve height on predicted cardiac output values by the three computers.

Measured	Gilford	Sanborn	Lexington
5.74	6.29 (+10%)	6.40 (+11%)	6.30 (+10%)
5.74	6.18 (+8%)	6.27 (+9%)	6.10 (+6%)
6.04	3.80 (-37%)	3.70 (-39%)	3.84 (-36%)
5.95	4.16 (-30%)	4.27 (-28%)	4.30 (-28%)

the digital computer (Elliot 803), assuming a simple exponential decay of the downslope. A least squares procedure was used from points between 60 and 25 per cent of the peak curve height at a curve sampling rate of 12 per second. Although not illustrated, the maximum rate of pressure rise in the aorta derived by the computer from the initial slope of the aortic pressure pulse compared very closely not only with that measured manually but also with the values given by a simple electronic differentiator (George and Taylor, 1967). The agreement between the manually-measured and computer-derived values for all of these primary variables was extremely good. As would be expected, all of the calculated values exhibited a similarly high degree of correlation between the measured and computer derived results.

DISCUSSION

Although computer technology and systems-engineering science are rapidly becoming an accepted

and integral part of investigative practice in human biology, their place in clinical medicine is only now starting to unfold. In the realm of clinical investigation few techniques yield such an abundance of complex biophysical data as those practised in the cardiovascular diagnostic and research laboratory. In fact the very facility and frequency with which these techniques may now be carried out has given rise to methodological advances in which automation and computer facilities are essential if they are to be fully exploited. The development of modern methods of pressure and flow recording now permits the generation of such a large volume of analogue data that its measurement by hand is nearly impossible. Although the ease with which circulatory data can now be safely obtained in man has allowed an increasing freedom in the design of investigation, the tremendous production of data involved is itself now operating to restrict further expansion by the very magnitude of the problem of its measurement and analysis. This problem will become progressively more acute with the increasing

FIG. 10.—Comparison of the cardiac output values given by the Sanborn computer with those derived from manual measurements in patients with mitral valve disease and atrial fibrillation.

trend towards the analysis of systems behaviour in cardiovascular diagnosis and circulatory research. A recent more detailed review of this problem showed that, with current cardiovascular techniques, measurement and analysis of analogue data could add a factor of more than 80 times, i.e. more than 80 hours of data processing were necessary for each hour of investigative procedure (Taylor, 1966). Procedure automation, in association with systems-engineered transducer-computer links and off-line computer analysis, is an obvious method that will allow full exploitation of investigative design offered by these modern cardiovascular methods. In this respect, the results of the feasibility trials with the transducer-computer link system offer convincing evidence of the practicability of such methods. With this technique the personnel time spent in primary data-handling and statistical or other

mathematical analysis can be reduced very considerably if not entirely abolished. In addition, the precision of the investigative methods is considerably enhanced by such automation procedures. The greatly increased attention to experimental design and detailed analysis involved in the development of any computer programme is accompanied by an increasing awareness of the technical errors involved and the inadequacies of the methods used. Such methods of data measurement and analysis are not necessarily confined to the cardiovascular laboratory but have obvious applications in the realm of the acute cardiorespiratory and traumatic resuscitation areas now becoming so popular.

The methods discussed above involve the storage and off-line, or remote, handling of the data produced. Although such techniques are necessary for complete retrospective analysis, for diagnostic

FIG. 11.—Comparison of cardiovascular measurements made with the aid of the transducer-digital computer link with those obtained by manual measurement from simultaneously recorded directly-written records.

purposes it is essential that the operator has some form of immediate computation with visual digital display of such important primary variables as the intravascular pressures and cardiac output. Such "on-line" methods allow the immediate and continuous monitoring of the patient's circulatory state, as for example in the recognition of impending pulmonary oedema, the adequacy of stability of a series of control observations, the precision with which a pharmacologically-induced circulatory change is being brought about, etc. These and many other examples serve to emphasize the essential requirement of digital monitoring of current events both in the circulatory laboratory and in acute cardiorespiratory patient care. While perfectly feasible, immediate digital read-out from such relatively large computers as those used in the foregoing discussion requires not only the proximity of one of these expensive machines but also its immediate availability. In the majority of cardiovascular laboratories such a proposition is at present totally uneconomic on a time-usage basis and,

indeed, with the advent of much simpler and cheaper monitoring devices, unnecessary.

Although the transduction and conversion of the analogue pressure signals into digital form presented some difficulties, the simple calibration techniques usually employed have allowed a relatively inexpensive solution to the problem of intravascular pressure monitoring. However, the immediate computation of cardiac output measurement from indicator-dilution curves has presented considerable difficulties. Chief among these problems are the large variety of methods of dye-curve generation and calibration used by different laboratories, the absolute dependence of the measurement made on certain strict criteria of technique, and the particular solution applied to the theoretical elimination of secondary recirculation of the indicator.

Skinner and Gehmlich in 1959 were perhaps one of the first groups to describe the use of an analogue computer for dye curve measurement. Although they used the theoretically sound principle of generating the exponential decay for each specific

curve from a logarithmic-function generator, their electronic circuit arrangement and their decision to use a function of time and not dye concentration for the portion of the downslope from which to generate the ideal exponential plot were weak points in their technology. Hara and Bellville (1963) have described an analogue computer for dye-curve measurements based on similar principles, but with the important difference that the logarithmic generator was programmed so that the ideal point for generation of the exponential decay was chosen as a function of the peak height of the dye concentration curve and not time. Although these two reports reflected the mounting interest in this field, it was not until the advent of proprietary machines, such as those manufactured by the Gilford, Sanborn, and Lexington companies, that widespread interest was aroused. Unfortunately, the very enthusiasm with which these machines were accepted, a reflection of their urgent need, has tended to cloud critical assessment of their precision in measurement.

Although the present report confirms the general usefulness and high degree of measurement precision of all three machines, a number of hitherto little discussed problems are high-lighted. The first of these is one of the governing laws of computer science, that the precision and quality of the computer answers are a direct reflection of the quality of the input material. With these small rigidly-programmed cardiac output monitors, which have no in-built recognition or correction devices enabling them to deal with abstract changes, such as may occur with baseline drift or with changes in shape of the dye curve with irregular rhythms, etc., the quality of the analogue signals with which they are presented achieves critical importance. It was adequately demonstrated in the present study that changes in baseline level after the computer had entered the compute mode resulted in proportional inaccuracies in the computed answers. Although these changes can be partially offset by manually (Gilford and Lexington) or electronically (Sanborn) delaying the activation of the integrator mechanisms until the final portion of the appearance time is reached, such manoeuvres allow the development of a false appreciation of the accuracy of the computed result. Further, if the dye curves presented to these rigidly programmed monitors are distorted by peripheral dye injections, by hydraulically damped sampling devices, or by other random distorting factors, then the results will again directly reflect the inadequacies of the technique used.

A second point, of equal importance, concerns the compatibility of the dye-curve generating mechanics with that of the associated computer. If the dye-

curve sampling mechanism incorporates a significant amount of hydraulic damping, then the higher the dye curve downslope is sampled by the computer for generation of its extrapolation plot, the more valid is likely to be the result compared with the manual estimate: both results of course will be in error compared to the true flow. In the present study the method of central dye bolus injection with high velocity central arterial sampling produces dye curves with minimum distortion (Taylor *et al.*, 1967). In these circumstances, a computer programmed to extrapolate the curve from the middle or lower ranges of the downslope is more likely to give a better comparison with the manual estimate than a machine programmed to generate its extrapolation plot from higher on the downslope where the curve is more likely to be convex. In this respect, in the present study with dye curves at a normal cardiac output, the Sanborn computer, programmed to extrapolate from points 60 to 40 per cent of the peak dye concentration, gave a better comparison with the manual method than the Gilford machine which was taking somewhat higher points for the generation of its extrapolation.

Thus, the precision of these machines depends critically not only on the quality of the input information but also on their *modus operandi*. In addition, all three computers are programmed on the assumption that the dye concentration will decay as a pure exponential function, an assumption not strictly true in many instances.

A third important point worthy of re-emphasis is that for correct practice of the technique the basic tenets of the indicator dilution principle must always be fulfilled. The computer will not solve errors due to basic inadequacies resulting from the wrongful application of the indicator dilution principle. When the cardiac output is very low, when the curve is distorted by valvular regurgitation, or when the volume between injection and sampling sites is very large, dye curves may be obtained that fail to comply with the basic assumptions of the indicator dilution method. The computer will yield no more precise answer than the practice of the technique allows.

A number of detailed points in the operation of these computers are worthy of mention. All the machines are programmed to deal with curves of a fairly limited size and all are particularly sensitive to dye-concentration height. This is an added safety factor in their operation, in that the curves accepted by the computer must all be of a fairly standard height and curves with unsuitable characteristics, such as low amplitude curves with protracted or abnormally shaped downslopes, are rejected. The Gilford and Lexington machines are

perhaps the most sensitive in this respect. The former registers its extreme sensitivity to positive changes in baseline level by a high read-out count on the digital display. In fact, as demonstrated in Fig. 9, and as would be expected from their design, all machines are equally sensitive to baseline changes, and such shifts will be directly reflected in the calculated cardiac output values. With the Gilford machine, up to 20 counts during the appearance time period can be tolerated for positive baseline shifts; in a normal cardiac output with about 2000 total counts the induced error of 1 per cent due to this slightly raised baseline count is much less than many of the other errors involved.

With regard to calibration methods, the Sanborn machine proved to be particularly easy to calibrate because of the short integrating times necessary with each calibration sample. The direct digital read-out system employed by the Lexington computer was marginally the most useful in practice, though the use of nomograms with the other machines entailed only a small delay in cardiac output calculation. A major disadvantage of direct read-out machines, such as the Lexington, used in conjunction with whole blood cuvette-densitometers, is that to demonstrate their maximum usefulness it is obligatory to calibrate them under completely sterile conditions beforehand. While this is not an insuperable problem, with the normally used "open" stepwise calibration method usually employed, it does impose considerable conditions of sterility and time.

The use of a closed "time-content" dye curve method of calibration similar to the system proposed by Sparling *et al.* (1960), and further developed by Emanuel and Norman (1963), would obviate this difficulty. In this method a junction is interposed between the patient and the cuvette so that blood can be sampled into a sterile container containing a known quantity of dye, the whole sample then being drawn through the cuvette before its re-infusion into the patient. A further difficulty in the use of direct read-out machines such as the Lexington is the transient time the read-out value is held. This becomes particularly important during high cardiac output measurements. A hold device operating only when read-out stability was obtained would be a considerable advantage in future models of this computer.

The information presented here would indicate that these small dye-curve computers give a reliable estimate of cardiac output under ideal circumstances and when particular attention is paid to the compatibility of the computer and the method used to generate the dye curves. However, due to their rigid programme arrangements they are unable to

recognize or rectify unpredicted changes in dye curve transcription, so that simultaneous recording by direct writing or on magnetic tape remains obligatory. In addition, their application, in instances where the basic assumptions necessary for the practical application of the indicator dilution principle are contravened, will yield spurious results which may go unrecognized in the absence of directly written records. They do, however, have a valuable place in cardiovascular investigation as immediate monitors of the cardiac output.

SUMMARY

The practical feasibility of analysing cardiovascular measurements with the aid of a digital computer has been explored with promising results. A systems-engineered transducer-computer link was developed to deal simultaneously with six intravascular pressure channels, an electrocardiographic channel, and a channel for cardiac output determinations by the indicator dilution method. The system offers considerable savings in time, increased precision of data measurement, and greater facility in the mathematical analysis of results.

The accuracy of three small proprietary integrator-computers for determination of the cardiac output by the dye dilution technique has been assessed. Under favourable practical and technological conditions their precision of measurement was comparable with that of manually measured dye curves. Because of their simple rigid programme arrangements, these small computers can be expected to produce precise results only when detailed attention is paid to their operating conditions.

The combination of these small on-line monitors with off-line data storage and analysis by digital computation offers important advantages not only in routine or research cardiovascular investigations, but also in the monitoring of patients acutely ill with circulatory disorders.

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- Determination of Pulmonary Blood Volume by Injection into Pulmonary Artery and Sampling in Left Atrium. By FRED K. NAKHJAVAN, VLADIR MARANHÃO, RODOLFO SAN, and HARRY GOLDBERG
- Electrical Reversion of Cardiac Arrhythmias. By BERNARD LOWN
- Six Cases of Congenital Complete Heart Block Followed for 34–40 Years. By MAURICE CAMPBELL and RICHARD EMANUEL
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