CARDIAC OUTPUT IN MAN BY A DIRECT FICK METHOD

EFFECTS OF POSTURE, VENOUS PRESSURE CHANGE, ATROPINE, AND ADRENALINE

BY

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I. EFFECTS OF POSTURE AND VENOUS PRESSURE CHANGE

In the Fick method of estimating cardiac output (C.O.), where C.O. (litres/min.)=oxygen consumption (c.c./min.) divided by arterio-venous oxygen difference (c.c./litre), the measurement of the numerator can easily be made by spirometric methods. Hitherto the measurement of the arterio-venous oxygen difference in man by respiratory techniques has proved difficult and laborious, and it has not been possible to make frequent serial observations. The difficulties seem to be largely overcome by the method of cardiac catheterization first introduced by Forsmann (1929) and developed by Cournand and Ranges (1941). Over 394 catheterizations can now be recorded without any accidents (Forsmann (1), de Carvolho and Moniz (48), Ameuille *et al.* (60+), Cournand *et al.* (150) and the present authors (135)). The catheter has been left *in situ* as long as 24 hours (Cournand *et al.*), but the present authors have limited the period to one hour in normal subjects. Clotting does not occur on the unwettable surface of the catheter, and a slow drip of 3·8 per cent sodium citrate through the catheter prevents any thrombus formation round the hole at the tip.

METHOD

The observations were made on normal male volunteers about two hours after the midday meal. The subjects were supine, except where otherwise stated. A No. 12 radio-opaque ureteric catheter was introduced through a wide bore needle into the medial antecubital vein of the left arm. The introduction was painless. Usually the catheter passed smoothly into the right auricle where its position was verified by X-ray. In about one subject in seven an obstruction was encountered at the root of the neck, but gentle manipulation may allow passing the catheter to the desired position. Occasionally the catheter took an acute turn up into the left internal jugular vein. The catheter was attached to a citrate manometer which recorded changes in pressure in the right auricle and served to keep the catheter clear of blood; 15 c.c. samples of right auricular blood were withdrawn under oil for estimation of oxygen unsaturation. No accidents or complications have followed this procedure except sometimes an inch or so of thrombosis near the point of insertion in the arm vein.

Oxygen unsaturation of right auricular blood was estimated in a Haldane blood gas apparatus modified to take 6 c.c. samples. The oxygen capacity was estimated by hæmoglobinometry. When the lungs were normal a value of 95 per cent saturation was assumed for arterial blood and the arterio-venous oxygen difference calculated from this assumption. The estimation of oxygen unsaturation was made at room temperature, at which the oxygen consumption was also measured by a Benedict spirometer. This simplifies the calculation considerably. The arterio-venous oxygen differences quoted below are uncorrected for N.T.P.

In the recumbent position the mean right auricular pressure (R.A.P.) is recorded with the posterior surface of the thorax equal to zero level. The pressure averages approximately 14 cm. anterior to this point (Richards *et al.* 1942).

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RESULTS

Normal values.—As will be demonstrated in the second section, heart rate influences resting output, and for this reason we tabulate as " normal " values in which the pulse rate was under 80 per minute.   Numbers are as yet too few to establish a statistical mean and range, and data may conveniently be grouped as follows:—

TABLE I

Arterio-venous oxygen difference (c.c./litre)	Number
30–40	3
40–50	10
50–60	4

Cournand *et al.* (1943) give a mean figure of 45 c.c./litre for the arterio-venous oxygen difference.   Baumann (1930) by heart puncture got an average figure of 51·5 c.c./litre.

. *Posture.*   In 17 subjects the cardiac output was estimated in the erect and supine positions. Samples were taken while subjects were standing quietly immediately after X-ray screening. The actual oxygen consumption in this position was not measured, but previous data (McMichael, 1937; Grollman, 1932; Nylin, 1934) indicate the average value to be 14 per cent over the recumbent oxygen consumption rate.   Results are shown in Table II.   It is seen that cardiac output increases by an average of 33 per cent on lying down.   This agrees with the bulk of previous work (see Hellebrandt and Franseen (1943) for references) and refutes the recent suggestion of Starr and Rawson (1941), based on the ballisto-cardiograph, that there is no change.

TABLE II

POSTURAL CHANGES IN ARTERIO-VENOUS O$_2$ DIFFERENCE

(14 subjects)

Arterio-venous ⎫ Recumbent .. 45 30 34 42 52 42 36 30 42 46 41 44 34 40.   Average: 40
  O$_2$ difference ⎬ Standing   .. 60 66 53 70 65 49 62 43 75 57 61 72 53 65   Average: 61
  (c.c./litre)   Average O$_2$ consumption c.c./min. .. Recumbent: 240.   Standing: 274
                  Cardiac output/min. ..   ..   .. Recumbent: 6 litres.   Standing: 4·5 litres

Change in right auricular pressure.   The venous pressure can be conveniently raised by intravenous infusions of saline (Sharpey-Schafer and Wallace, 1942) and lowered by vene-section (Wallace and Sharpey-Schafer, ·1941) or by cuffs on the thighs at diastolic blood pressure.   Sample data from observations of these types are shown in Fig. 1, 2, and 3, and
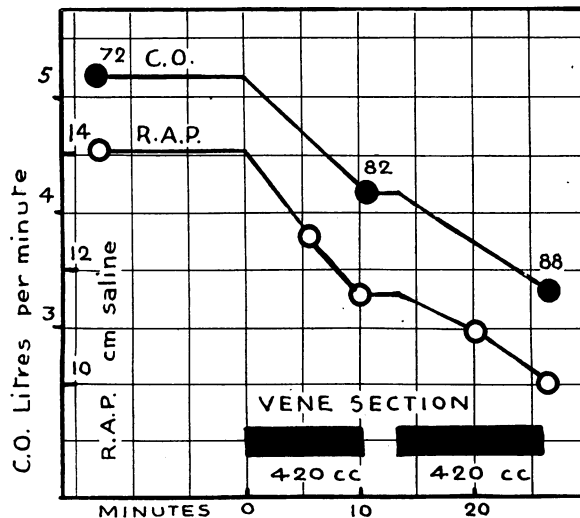

FIG. 1.—Effect of venesection on cardiac output and right auricular pressure.   In Fig. 1, 2, and 3 figures beside cardiac output determinations indicate heart rate.   Right auricular pressure (R.A.P.) and cardiac output (C.O.) fall in parallel.
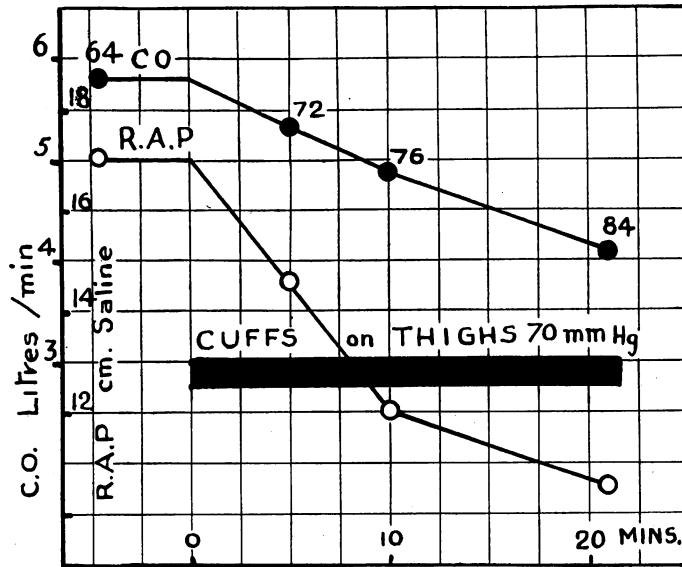
FIG. 2.—Effect of tourniquets on both legs at 70 mm. Hg. Blood is trapped in the leg veins, right auricular pressure (R.A.P.) and cardiac output (C.O.) falling together.
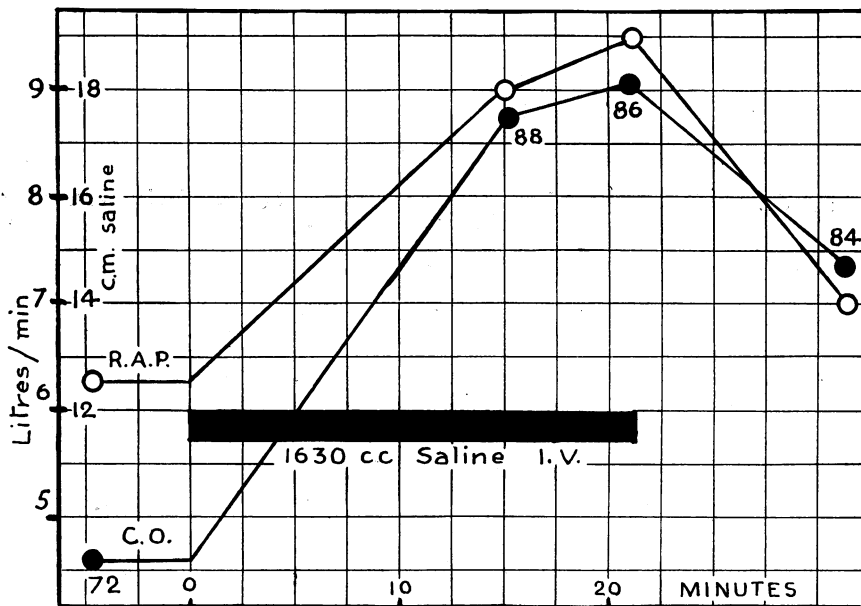

FIG. 3.—Effect of raising right auricular pressure (R.A.P.) by saline infusion. During infusion the cardiac output (C.O.) rises. On stopping the infusion saline is lost from the circulation and right auricular pressure and cardiac output fall together.

the collected data from all observations are shown in Fig. 4. As expected from Starling's law of the heart, a reduction in right auricular pressure leads to a fall in cardiac output, while a rise is accompanied by an increase.

DISCUSSION

Taking all our available data into account, the average normal resting cardiac output in the recumbent position is (240/45) 5·3 litres a minute, while in the standing position it is 25 per cent less, i.e. 4 litres. These are higher than figures previously obtained by the
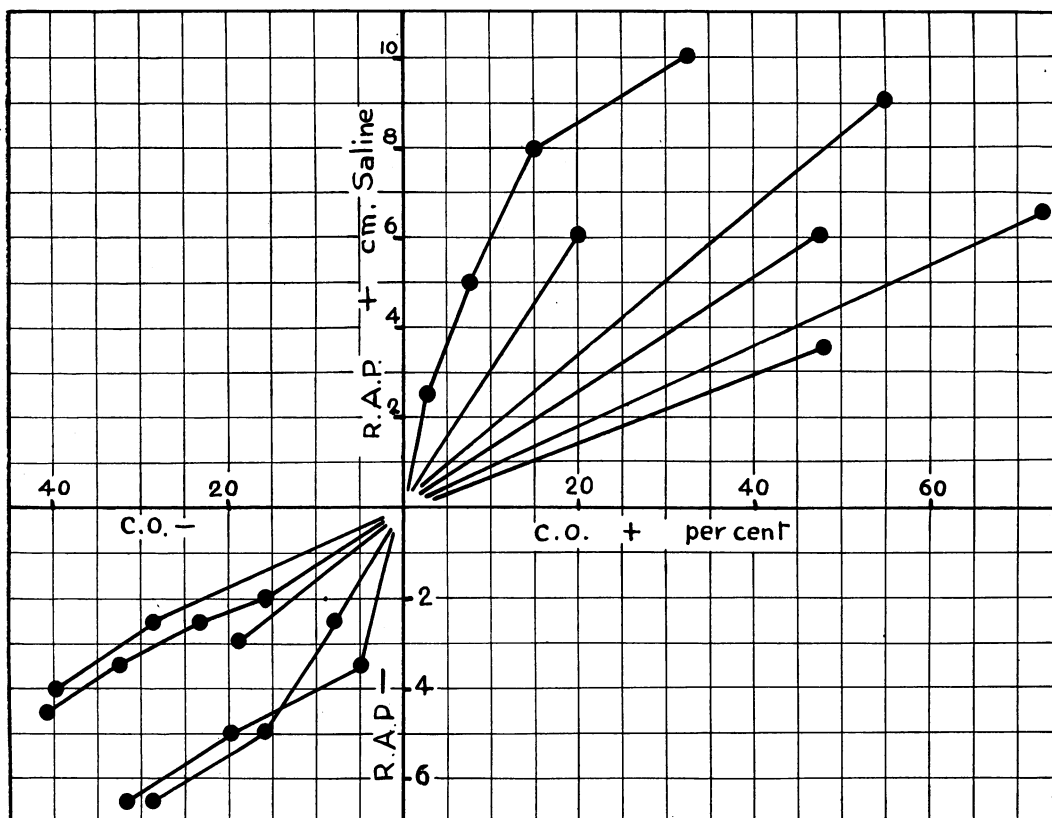
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FIG. 4.—Collected data in 11 subjects showing increasing cardiac output (C.O.) with intravenous infusion and decrease with venesection or cuffs on legs.

acetylene technique, which gave an average cardiac output in the recumbent position of 4 litres a minute (McMichael, 1937): it is of interest, however, that two techniques then used gave an average increase in cardiac output of 32 per cent and 38 per cent in recumbency, which compares well with 33 per cent by the new method. Relative changes seem to have been fairly accurately reflected, but the absolute values were subject to a systematic error.

The assumption of 95 per cent arterial oxygen saturation in these observations may be criticized. Our aim has been to simplify the technique as much as possible for application to clinical problems, and *repeated* arterial punctures do not seem to be justified. For following *changes* in any individual under test the assumption can lead to little significant error. A range of 93–97 per cent oxygen saturation of arterial blood would give a standard error of 2 c.c. per litre in the arterio-venous oxygen differences.

II. Effects of Atropine, Adrenaline, and Heart Rate

The methods and conditions of study were the same as in the first part.

Atropine. Observations were made in 10 subjects. Two main effects were found. Raising the heart rate increased cardiac output in all subjects except two, and there was a fall in right auricular pressure (R.A.P.) in all (Fig. 5). Atropine was given intravenously in doses of 1 mg. and the usual sequence of events was as follows: within 30 seconds the heart rate was increasing, reaching its maximum rate in about 1–2 minutes; at this point the cardiac output was considerably increased; the R.A.P. fall was slower in appearing and only attained a steady level after a few minutes. Fig. 6 shows that this fall in right auricular pressure may be accompanied by a decrease in cardiac output from the high level attained

earlier by atropine.   In two out of ten observations no rise in cardiac output was observed at the time of sampling.   It would appear that a large fall in R.A.P. was sufficient to prevent
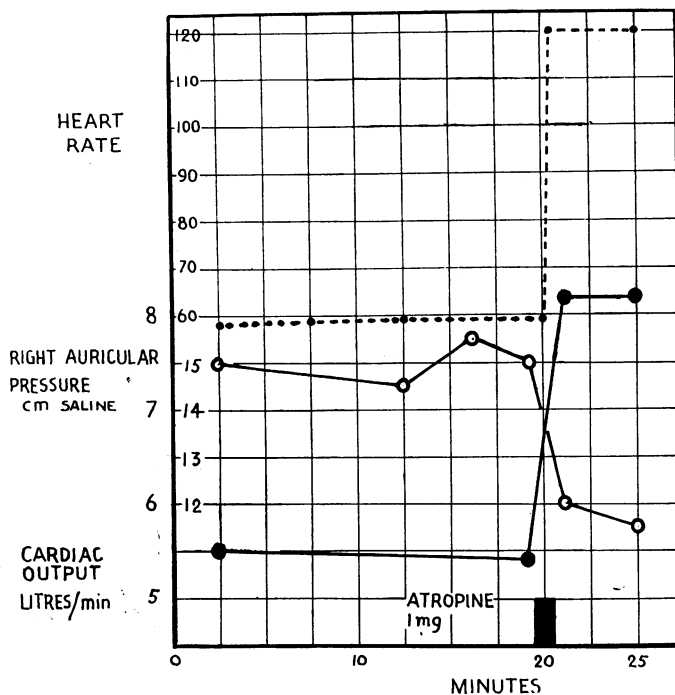

FIG. 5.—Usual immediate response to intravenous atropine.   Heart rate and cardiac output increase, right auricular pressure falls.
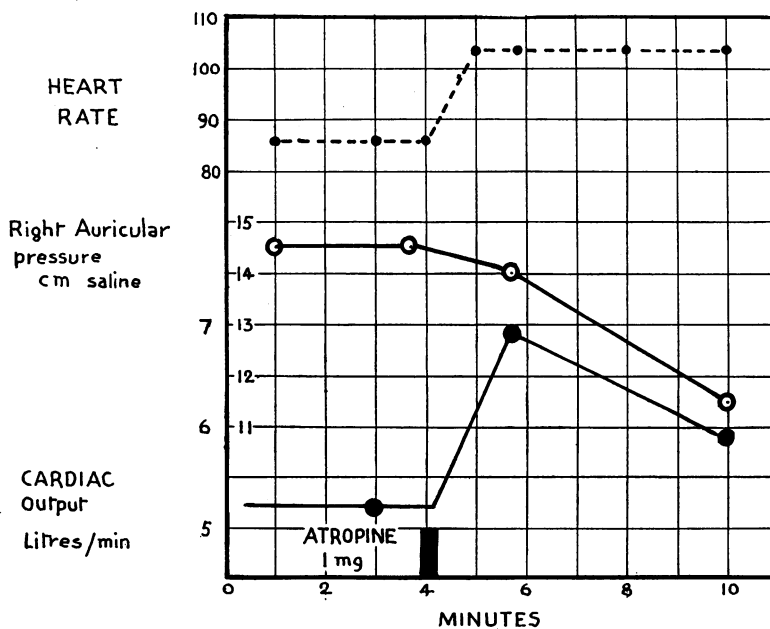

FIG. 6.—Showing initial increase in cardiac output after atropine followed by a fall as right auricular pressure decreases.

the usual rise of cardiac with atropine acceleration (Fig. 7).   These results indicate that the effects of acceleration of the heart rate increasing cardiac output may be modified by venous pressure changes.
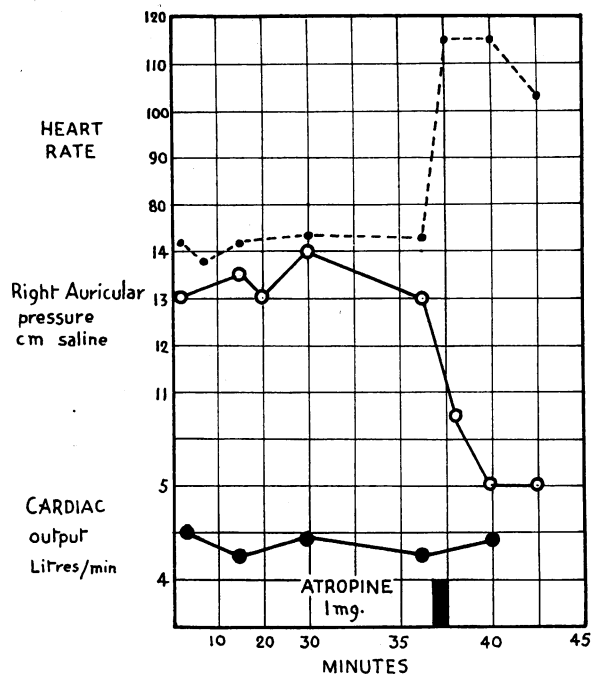
FIG. 7.—Showing no increase in cardiac output after atropine with considerable fall in right auricular pressure.

Adrenaline. We studied the effects of doses that, infused intravenously, did not raise the blood pressure or increase the heart rate. Such doses were under 10μg. a minute, but the suitable dose for each individual may have to be found by trial. Dilatation of muscle vessels is produced by adrenaline administered in this dosage, and in some experiments this
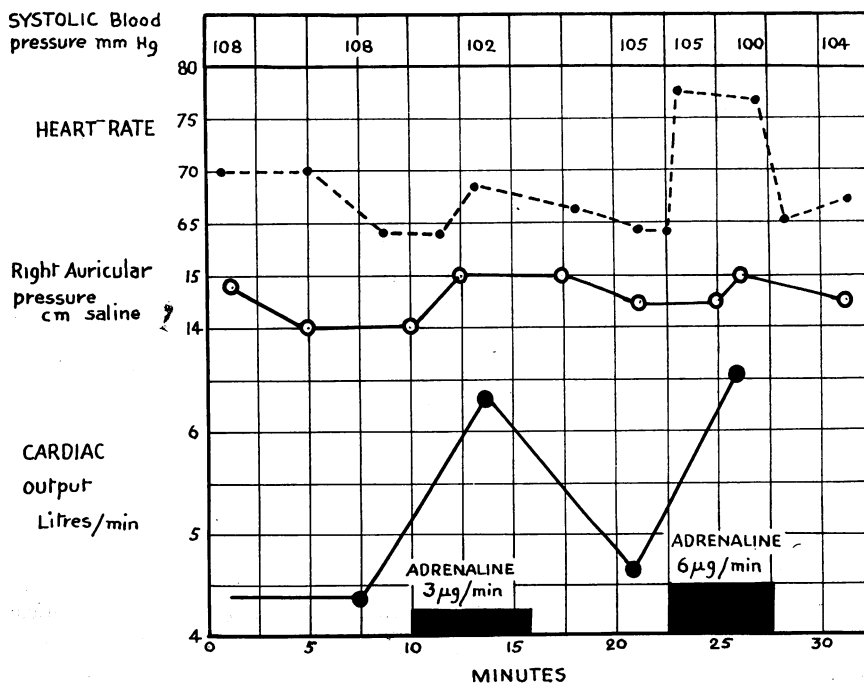

FIG. 8.—Effect of adrenaline infusion at 3μg. a minute. Cardiac output increases without change in heart rate or right auricular pressure or rise in blood pressure. When the dose of adrenaline was doubled, the heart rate increased.

effect was demonstrated by Professor H. Barcroft and Dr. O. G. Edholm, who simultaneously measured forearm flow with a Lewis-Grant plethysmograph. In all of 5 subjects adrenaline increased cardiac output, and a typical observation is shown in Fig. 8. On stopping the infusion, cardiac output returned rapidly to the resting level. Slight pallor of the face was observed during infusion, and some subjects became conscious of the beating of their hearts. Conspicuous flushing of the face appeared when the infusion was stopped. The results show that adrenaline can increase cardiac output without a change in venous pressure or heart rate.

Heart rate. The total data on cardiac output determinations in normal subjects are shown plotted against heart rate in Fig. 9. The majority lie between 4 and 6 litres a minute, while
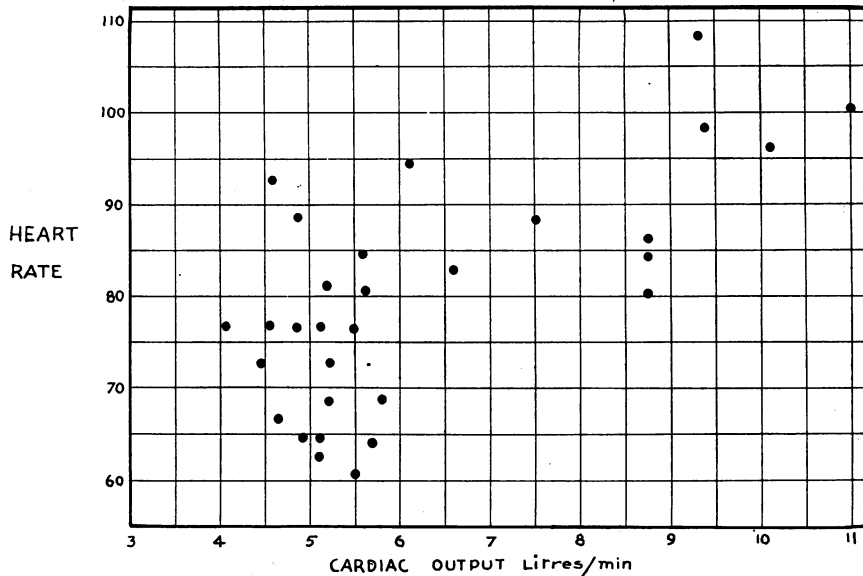

FIG. 9.—Collected data of cardiac output plotted against heart rate in normal resting males in the supine posture. The few with higher outputs show faster heart rates.

a few have higher outputs up to 10 or 11 litres a minute. It will be seen that the latter group tends to have faster heart rates, and this may be one factor in causing increased output. Other possible factors such as secretion of adrenaline or slightly increased venous pressure could not be compared from subject to subject. All those with increased output were in the younger age groups (under 40), when the circulation might be expected to be more labile.

DISCUSSION

There is a mass of physiological evidence that right auricular pressure, determining tension and length of myocardial fibres, is the major factor altering the output of the heart provided the rate remains constant. The first part of this work shows such effects in man, although rate and other factors for obvious reasons could not be controlled.

Wiggers (1938) indicates that within the usual physiological range increased rate leads to increased minute output so long as the venous pressure is kept constant. We have as yet no explanation to offer for the fall in right auricular pressure observed so often after atropine. Its late onset indicates that it may be a physiological adjustment secondary to the initial increase in output.

Independently of rate and right auricular pressure, the adrenaline effects indicate yet another mechanism controlling cardiac output. Adrenalin produces increased systolic ejection at the same mean filling pressure in the right auricle. This is in accordance with the observation of Wiggers (1927) that adrenaline causes a stronger and more rapid ventricular contraction and also a more complete relaxation in diastole.

SUMMARY

Serial estimations of cardiac output and right auricular pressure can be made by means of a ureteric catheter passed along the veins into the right auricle.

Normal resting values for arterio-venous oxygen differences were rather lower than those obtained previously by the acetylene method.

Cardiac output in the supine posture showed a 33 per cent increase over that in the erect.

A fall in right auricular pressure reduced, and a rise in right auricular pressure increased, the cardiac output.

Acceleration of the heart with atropine usually increased cardiac output and caused a fall in right auricular pressure. Occasionally the fall in right auricular pressure may operate against an increase in cardiac output.

Intravenous adrenaline increased cardiac output in doses that did not accelerate the heart or raise the blood pressure.

Normal subjects with high resting outputs had faster heart rates than the others.

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