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STUDIES OF THE PULMONARY CIRCULATION. II. THE CIRCULATION TIME FROM THE PULMONARY ARTERY TO THE FEMORAL ARTERY AND THE QUANTITY OF BLOOD IN THE LUNGS IN PATIENTS WITH MITRAL STENOSIS AND IN PATIENTS WITH LEFT VENTRICULAR FAILURE

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The pathogenesis of dyspnea in left ventricular failure and in mitral stenosis is not entirely understood but it is generally conceded that pulmonary vascular congestion is involved (1). Preceding the congestion there is probably an elevation in the left auricular and pulmonary venous pressures but to date it has not been possible to measure such pressures in the human being. Accurate quantitation of the pulmonary vascular congestion itself is difficult and the use of the vital capacity for this purpose is far from satisfactory. Much more promising in this connection is a method, described in a previous paper (2), which measures the volume of blood in the lungs, left heart, aorta, and certain systemic arteries. The method is based on the measurement of the mean circulation time from the pulmonary artery to the femoral artery, and the simultaneous determination of the cardiac output. An increased volume of blood in the pulmonary vessels should result in a corresponding increase in the total volume of blood (Q) measured by the technique. The results of studies based on this premise are presented in the following account.

MATERIAL AND METHODS

A group of 10 men with rheumatic heart disease and mitral stenosis were studied. All these patients had dyspnea on exertion and some degree of pulmonary hypertension. As examples of left ventricular failure, 18

men with disease of the aortic valve or hypertensive heart disease were chosen. All had dyspnea on exertion and had suffered from several episodes of paroxysmal dyspnea in the past, but none were severely orthopneic at the time the study was performed. Two of the patients with rheumatic heart disease and two with left ventricular failure previously had evidence of right ventricular failure manifested by hepatomegaly, peripheral edema and an elevated systemic venous pressure.

A catheter was introduced into the pulmonary artery by the method of Cournand and co-workers (3). The mean circulation time from the pulmonary artery to the femoral artery was measured and the cardiac output was determined as previously described (2). The volume of blood in the pulmonary vessels, left heart, aorta, and iliac arteries, together with all the blood contained within the other branches of the aorta to points where dye arrives no later than it does at the femoral artery (Q) was determined from Stewart's formula (4). The pressures in the pulmonary artery, right ventricle, and right auricle were measured with a Hamilton manometer. The level of the right auricle was determined by the method of Lyons, Kennedy, and Burwell (5). The pulmonary arterial diastolic pressure was measured immediately before auricular systole to avoid artifacts which occur in the pulmonary arterial tracing during auricular systole. The systolic pressure was determined from the right ventricular tracing, since artifacts due to motion of the catheter interfered with this measurement in the pulmonary arterial tracings.

Heart volumes were determined from the teleroentgenogram by the method of Keys et al. (6). The predicted normal frontal area of the heart for the individual was estimated from the nomogram of Ungerleider and Gubner (7). The predicted heart volume was obtained by the use of the tables of Keys et al. (6).

The vital capacity was measured in the sitting position with a spirometer. The predicted normal figure for the individual was obtained by applying the formula of Baldwin, Cournand, and Richards (8). Four and four-tenths per cent were added to the value obtained by this formula to correct for the difference between the supine and sitting position (9).

Dye Concentration Mg./100cc

Mean c.t. = 12.6 sec.

Time in Seconds

(a)

Dye Concentration Mg / 100cc

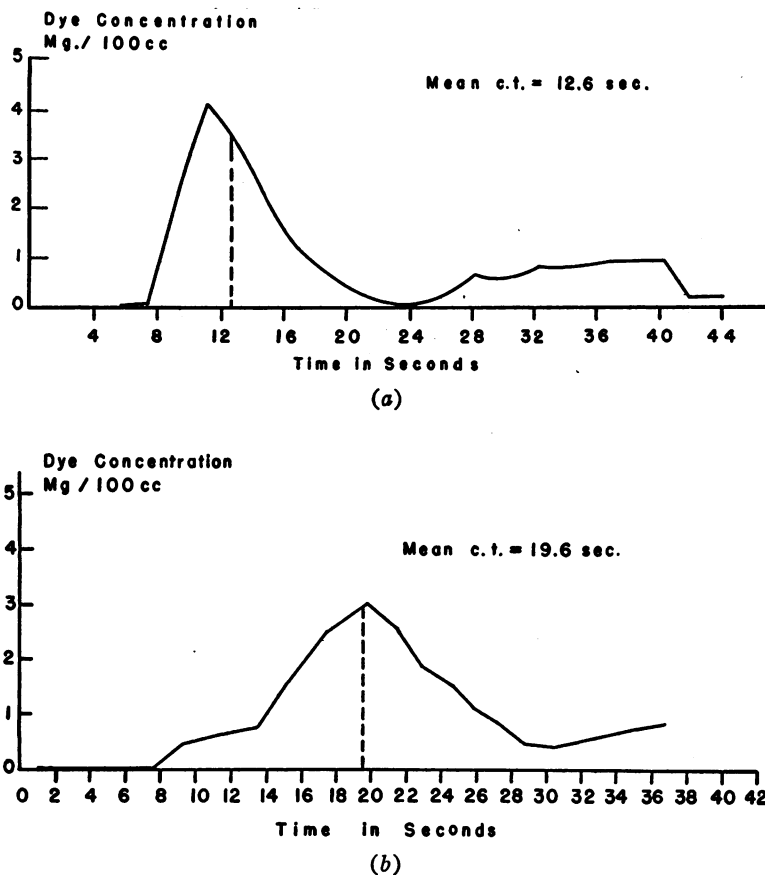Mean c.t. = 19.6 sec.

Time in Seconds

(b)

FIG. 1. DYE CONCENTRATION CURVES IN PATIENTS WITH HEART DISEASE

(a) The chart above is the dye concentration curve in a patient with mitral stenosis (Subject R. C.), and (b) the chart below is the dye concentration curve in a patient with left ventricular failure (Subject J. K.).

TABLE I

Cardiac output, mean circulation time and Q in a group of patients with rheumatic heart disease and mitral stenosis

Subject	Surface area	Oxygen consumed	Arterio-venous oxygen diff.	Cardiac output	Cardiac index	Mean circu-lation time	Duration of curve	Q	Total blood volume	Vital capacity	Pulm. arter. press. systolic	Pulm. arter. press. diastolic	Right ventric. press. diastolic
	sq. m.	*cc./min.*	*vol. per cent*	*L./min.*	*L./min./ sq. m.*	*sec.*	*sec.*	*cc.*	*cc.*	*per cent normal*	*mm. Hg.*	*mm. Hg.*	*mm. Hg.*
J. K.	1.58	220	3.36	6.55	4.15	9.2	14.2	1000	5340	95.5	31.9	15.6	1.7
H. H.	1.69	245	8.43	2.91	1.72	24.1	26.0	1170	7726	57.2	83.5	38.5	5.9
M. O.	1.70	253	8.75	2.89	1.70	33.4	45 2	1610	—	60.4	83.5	36.2	13.8
V. S.	1.74	206	4.13	4.99	2.87	13.6	17.4	1130	5060	102.8	33.6	16.5	6.9
M. M.	1.77	284	8.98	3.16	1.79	21.7	32.7	1140	—	47.8	78.1	46.0	1.4
E. M.	1.77	286	5.79	4.94	2.79	15.7	22.0	1290	7710	86.8	43.0	20.3	6.1
F. M.	1.77	272	5.92	4.59	2.59	19.6	26.1	1500	5000	50.4	113.5	61.7	8.6
L. N.	1.79	242	5.30	4.57	2.55	14.0	13.2	1070	7200	52.9	64.0	43.0	7.3
R. C.	1.84	249	4.72	5.28	2.87	12.6	17.8	1110	6510	79.3	68.0	31.0	1.0
G. W.	1.93	270	4.82	5.60	2.90	13.5	20.0	1260	6930	89.3	40.4	22.3	2.8
Mean	1.76	253	6.02	4.55	2.59	17.7	23.5	1230	—	71.2	64.0	33.1	5.6
Standard deviation	±0.10	±26	±2.01	±1.22	±0.74	±7.1	±9.7	±190	—	±19.0	±27.6	±14.9	±3.9

TABLE II

Cardiac output, mean circulation time and Q in a group of patients with left ventricular failure

Subject	Diagnosis*	Surface area	Oxygen consumed	Arterio-venous oxygen diff.	Cardiac output	Cardiac index	Mean circulation time	Duration of curve	Q	Heart volume	Total blood volume	Vital capacity	Pulm. arter. press. systolic	Pulm. arter. press. diastolic	Right ventric. press. diastolic
		sq. m.	cc./min.	vol. per cent	L./min.	L./min./sq. m.	sec.	sec.	cc.	cc.	cc.	per cent of normal	mm. Hg.	mm. Hg.	mm. Hg.
A. D.	R.H.D.—A.I.	1.58	218	5.39	4.04	2.56	32.6	19.3	2200	1440	5500	91.8	32.0	12.9	1.4
J. K.	H.H.D.	1.62	235	6.01	3.91	2.41	19.6	22.4	1280	1023	4730	59.8	39.0	12.9	1.4
R. D.	H.H.D.	1.68	246	7.20	3.42	2.04	27.0	40.1	1540	1491	7810	70.4	62.3	24.6	7.7
B. D.	H.H.D.	1.68	277	6.22	4.45	2.65	18.4	28.4	1360	1202	5200	68.3	56.5	30.7	1.4
H. H.	R.H.D.—A.I.	1.71	295	10.21	2.89	1.70	26.4	41.3	1270	1298	6580	85.0	73.0	34.0	10.8
E. O.	R.H.D.—A.S.	1.71	308	7.16	4.30	2.51	21.0	28.6	1510	1679	6700	73.1	31.3	19.4	2.2
M. S.	R.H.D.—A.S.	1.80	307	4.37	7.03	3.91	14.6	14.6	1710	845	4450	—	30.6	18.9	6.6
E. S.	S.H.D.—A.I.	1.80	264	5.69	4.64	2.58	23.2	24.6	1790	1211	7320	57.0	20.0	5.1	2.3
R. Q.	H.H.D.	1.81	288	5.22	5.52	3.05	24.8	48.8	2280	1440	8100	79.5	28.6	13.4	0.6
L. G.	H.H.D.	1.82	290	5.81	4.99	2.74	22.2	33.5	1850	1144	7080	86.7	56.7	23.1	1.9
E. T.	R.H.D.—A.I.	1.82	279	5.58	5.00	2.75	18.0	31.8	1500	1116	6170	54.6	29.9	21.9	9.0
H. G.	R.H.D.—A.S. A.I.	1.84	223	4.63	4.82	2.62	24.4	20.8	1960	1289	6800	73.8	40.0	29.0	1.8
C. M.	S.H.D.—A.I.	1.85	279	4.71	5.92	3.20	17.2	35.9	1700	1260	—	67.8	41.9	25.0	5.8
G. R.	H.H.D.	1.93	293	4.50	6.51	3.37	15.2	24.3	1650	1163	7030	88.8	40.0	17.5	4.2
H. B.	R.H.D.—A.S.	1.93	254	3.68	6.90	3.58	12.0	16.2	1380	915	5550	62.7	29.2	12.5	4.9
C. B.	H.H.D.	1.94	300	4.61	6.51	3.36	22.0	15.0	2390	1192	7490	116.3	29.3	15.1	5.4
A. B.	H.H.D.	2.04	219	5.87	3.73	1.83	21.6	22.8	1340	854	6530	84.4	22.3	8.8	5.1
M. K.	R.H.D.—A.I.	2.06	336	5.04	6.67	3.24	24.8	31.4	2760	1953	—	97.1	26.3	14.7	8.5
Mean		1.81	273	5.66	5.07	2.78	21.4	27.8	1750	1251	6440	77.5	38.3	18.9	4.5
Standard deviation		±0.13	±34	±0.39	±1.28	±0.59	±5.0	±9.6	±420	±281	±1090	±16.1	±14.7	± 7.8	±3.1

* H.H.D.—Hypertensive Heart Disease.
R.H.D.—Rheumatic Heart Disease.
S.H.D.—Syphilitic Heart Disease.
A.S.—Aortic Stenosis.
A.I.—Aortic Insufficiency.

RESULTS

In order to determine the significance of the findings in the patients with heart disease it was necessary to compare them with the findings previously obtained in a group of 12 normal subjects (2). The dye concentration curves in patients with heart disease differed in most instances from the normal curve in that they were more prolonged than the normal and the maximal dye concentration was lower in the former than in the latter (Figure 1). Because recirculation usually began before the completion of the primary curve, a small error may have occurred in the determination of the mean circulation time. The mean circulation time was prolonged in the group with mitral disease and in the group with left ventricular failure, the increase being greater in the latter group (Table I). The mean cardiac index was significantly reduced in both groups as compared with the normal subjects.

The mean value for Q in 10 patients with mitral stenosis was 1230 cc. as compared with 1160 cc. in the group of 12 normal subjects ([2] Table I). This difference is not significant statistically. Adjusting the individual values to 1.73 sq. m. body surface resulted in a larger difference between the two means but the statistical significance of the difference remained doubtful.

The mean value for Q in the group of 18 patients with left ventricular failure was 1750 cc. which is
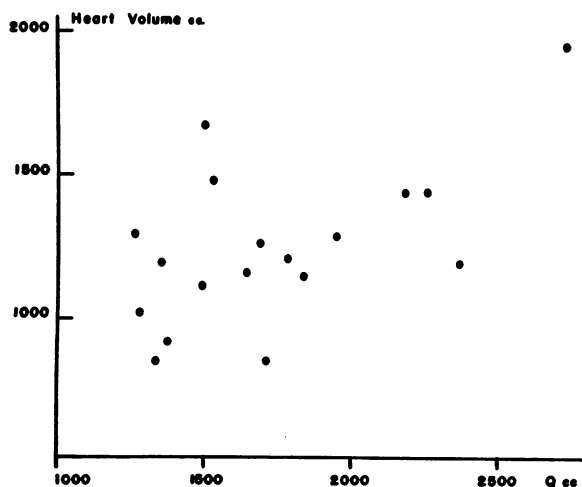
TABLE III

Comparison of mean increase in Q with mean increase in volume of the heart in 18 patients with left ventricular failure

	Left ventricular failure	Predicted normal	Mean increase
Volume of heart (cc.) Estimated from teleroentgenogram	1251	675	576
Q (cc.)	1750	1160	590

significantly greater than the mean value for Q in normal subjects (Table II). It was immediately apparent that the increase in Q in the group with left ventricular failure could be due to an increase in volume of blood in the left ventricle. In order to evaluate this possibility, the volume of the heart in the individual cases was plotted against Q (Figure 2). There was a moderate correlation ($r = 0.6954$ p $< .01$). In Table III the difference between the mean volume of the heart in the group with left ventricular failure and the predicted mean normal heart volume for the group is compared with the difference between the mean value for Q in the group with left ventricular failure and the mean value for Q in the group of normal subjects. The two values were very similar.

The pulmonary arterial pressure was moderately elevated in the group with left ventricular failure and more strikingly elevated in the group with mitral stenosis (Tables I and II). There was no correlation between Q and the vital capacity in either group.

DISCUSSION

The prolongation of the circulation time from a peripheral vein to an artery in heart disease is well known and is widely used in the clinical assay of congestive heart failure. In most studies of the circulation time, a method is used which gives a single end point. The means of detecting the end point differs, both in technique and in sensitivity, from method to method. For example, in the determination of the circulation time by the use of radium as performed by Blumgart and Weiss (10), the end point depends on the sensitivity of the detecting device and the concentration of the radium in the blood flowing through the brachial artery. Hamilton *et al.* (11) have demonstrated that this end point does not represent the mean

FIG. 2. CHART SHOWING CORRELATION BETWEEN HEART VOLUME AND Q IN PATIENTS WITH LEFT VENTRICULAR FAILURE

circulation time but merely approximates the earliest circulation time. A study of the dye concentration curve determined in patients with heart disease, makes it apparent that the measurement of the circulation time by the usual method will give a value which is quite remote from the true mean circulation time.

The importance of the determination of the mean circulation time lies in the fact that it is a function of the rate of blood flow and the volume of blood contained in a given portion of the circulation. According to Stewart (4) and Hamilton (11), the mean circulation time from the pulmonary artery to the left auricle should be inversely proportional to the cardiac output and directly proportional to the volume of blood in the pulmonary vessels. Unfortunately, it is impossible to measure the circulation time from the pulmonary artery to the left auricle so that this approach to the estimation of the pulmonary blood volume is closed. It is possible, however, to measure the mean circulation time from the pulmonary artery to the femoral artery. Using Stewart's formula, one finds that this mean circulation time is inversely proportional to the cardiac output and directly proportional to the value Q, which represents the amount of circulating blood in the lungs, left heart, aorta, and certain other arteries as defined above. Hence, if the cardiac output and the mean circulation time are known, Q can be calculated. If the volume of blood in the aorta and left heart remains constant, variations in the pulmonary blood volume will cause corresponding variations in Q. Blood in the lungs which is stagnant or circulating very slowly would not be measured by this method.

There was no significant increase in Q in the group of patients with mitral stenosis and pulmonary hypertension as compared with the group of normal subjects, and it can be concluded, therefore, that there was no large increase in pulmonary blood volume. Moreover, a marked increase in pulmonary arterial pressure can occur in mitral stenosis without an increase in Q and, consequently, without a large increase in pulmonary blood volume. None of the patients studied had severe orthopnea or evidence of pulmonary congestion and edema roentgenologically. It is quite possible that a marked increase in pulmonary

blood volume does occur in patients with these findings.

There was a marked increase in Q in the group of patients with left ventricular failure. Gernandt and Nylin (12) have observed a relationship between increase in circulation time from peripheral vein to peripheral artery and increase in size of the heart. All patients with left ventricular failure in this study had varying degrees of left ventricular enlargement, and the largest increase in Q occurred in those patients with the largest hearts. A positive correlation existed between the heart volume and Q. If the mean increase in heart volume is compared with the mean increase in Q, the similarity of the two values suggests that they have a common cause, namely, an increase in the amount of blood in the left ventricle. In roentgenological studies of heart volume, it is impossible to distinguish between the effects of hypertrophy and dilatation but it is generally conceded that the increase in the size of the heart in heart failure is primarily due to cardiac dilatation (13, 14). Because of the contribution of the blood in the dilated left ventricle to Q, it is difficult to evaluate changes in pulmonary blood volume in patients with left ventricular failure.

The reduction in vital capacity in patients with heart disease has been attributed to pulmonary congestion with consequent changes in pulmonary distensibility and elasticity (15, 16). It has been suggested that prolongation of the circulation time in association with reduced vital capacity is due to an increase in the volume of blood in the lungs (17). From the present study, it does not appear that reduction of vital capacity is of necessity accompanied by a large increase in pulmonary blood volume, nor does it appear that an increase in pulmonary blood volume is the major factor in prolonging the circulation time.

SUMMARY AND CONCLUSIONS

1. The mean circulation time from the pulmonary artery to the femoral artery and cardiac output were determined on 10 patients with mitral stenosis associated with pulmonary hypertension and 18 patients with left ventricular failure.

2. From the mean circulation time and the cardiac output the volume of blood in the pulmo-

nary vessels, left heart, aorta and certain other arteries (Q) was calculated.

3. The mean circulation time was prolonged and the cardiac output was reduced in both groups as compared with normal subjects. The value for Q in the group of patients with mitral stenosis and pulmonary hypertension did not differ significantly from the value in normal subjects and hence, there was no evidence of a large increase in circulating blood in the lungs.

4. A marked increase in Q was present in the group of patients with left ventricular failure. Because of evidence which suggested that the increase in Q was largely due to an increase in the amount of blood in the left ventricle, it was impossible to evaluate changes in pulmonary blood volume in this group.

5. There was no correlation between the reduction in vital capacity and Q. This suggests that the reduction in vital capacity in patients with heart disease is not a direct function of increase in pulmonary blood volume.

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