Haemodynamic Changes After Angiocardiography

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The injection of angiocardiographic contrast medium into the left side of the heart or the aorta is a common diagnostic procedure, and recent studies have described some of the haemodynamic responses which are produced (Brown *et al.*, 1965; Friesinger *et al.*, 1965; Rahimtoola, Duffy, and Swan, 1966, 1967). This study arose from the recognition of considerable increases in left ventricular end-diastolic pressure and left atrial pressure after injection of Hypaque 85 per cent (sodium and methylglucamine diatrizoate) during left heart catheterization. The purpose of this paper is to present data concerning the pressure changes in a series of 133 patients after the injection of radio-opaque dye, and to assess the value of taking serial pressure records.

To help in the interpretation of the pressure changes, the alterations in blood volume, haematocrit, and cardiac output after injection of Hypaque have been measured in smaller groups of patients, and we have recorded pressures after exercise in some of these patients.

PATIENTS AND METHODS

Serial pressure changes after injection of radio-opaque material were recorded and analysed from 133 patients during diagnostic catheterization, and these patients are grouped as follows: 7 with minimal heart disease regarded as "Normals"; 18 with mitral stenosis; 30 with mitral regurgitation; 18 with combined mitral stenosis and regurgitation; 19 with aortic stenosis; 23 with aortic regurgitation; and 18 with cardiomyopathy.

Combined right and left heart catheterization was performed for diagnostic purposes in all patients. Left atrial and left ventricular catheterization was performed by transseptal puncture of the atrial septum. A second catheter was inserted percutaneously into the femoral artery, passed to the aortic root, and where possible into the left ventricle.

Pressures were recorded immediately before the in-

jection of the radio-opaque dye and at intervals for 20 minutes after the injection, using equisensitive induction manometers and a multi-channel, oscilloscopic recorder (Cambridge Instrument Company). The zero baselines were set at 5 cm. below the sternal angle. The radio-opaque dye used in all patients was 85 per cent Hypaque in a dose of $\frac{1}{2}$ –1 ml./kg. body weight. The Hypaque was injected using a Gidlund power injection syringe at a pressure of 6–8 kg./cm.²

In 7 patients pressures were recorded serially after successive angiograms during the same catheter session. In 8 patients pressure changes after angiography have been compared with pressure changes after exercise. The degree of exercise was mild to moderate, and consisted of arm exercise for 3 to 5 minutes.

Haematocrit estimations were made in 35 patients, and 18 of these are included in the group of 133 patients in whom serial pressure changes were recorded. Three baseline samples were taken before the angiogram, and determinations in duplicate were made within the first 3 minutes, and again at 5, 10, and 15 minutes after the injection of Hypaque. Seventeen of the patients also had serial blood volume estimations before and after angiography using ¹³¹I-labelled serum albumin (Veall and Vetter, 1958).

Cardiac outputs were measured before and at intervals after angiography in 9 patients using 5 mg. injections of indocyanine green dye as indicator, and the dilution curves were inscribed with a Gilford cuvette densitometer (1031R) and constant flow system (105S). After amplification the output from the photomultiplier of the densitometer was fed into a linear pen recorder (Cambridge Instrument Company). The curves from each patient were calibrated by drawing known concentrations of dye in whole blood (2.5 mg./l.; 5.0 mg./l.; and 7.5 mg./l.) through the cuvette densitometer with the constant flow system, the deflection of each concentration being registered by the pen recorder. Cardiac output calculations were made by the method of Hamilton *et al.* (1932).

In view of the effects of Hypaque on the blood haematocrit, calibration studies were carried out on the Gilford densitometer using various concentrations of indocyanine green and Hypaque in whole blood. This showed that Hypaque, in concentrations comparable to

Received August 26, 1968.

* In receipt of a grant from the British Heart Foundation.

TABLE I
PRESSURE CHANGES IN LEFT ATRIUM AND LEFT VENTRICLE BEFORE AND AFTER SUCCESSIVE ANGIOGRAMS

Patient No., age (yr.), and sex	Diagnosis	Angiogram	LA mean (mm. Hg)		LA "v" peak (mm. Hg)		LV end-diast. (mm. Hg)	
			Before	After	Before	After	Before	After
(1) H.L. 54 F	Mitral and aortic regurgitation	{LV cine	10	28	10	58	—	—
		{Aortic cine	8	25	8	40	—	—
(2) R.J. 52 M	Lone atrial fibrillation	{Aortic cine	5	15	6	20	4	14
		{LV cine	5	14	6	24	4	14
(3) E.O. 54 M	Aortic stenosis; hypertension	{Aortic cine	—	—	—	—	5	9
		{Renal angiogram	—	—	—	—	5	9
(4) J.M. 43 F	Mitral and aortic valve disease	{Aortic cine	15	26	17	30	10	22
		{LA cine	18	40	21	50	—	—
(5) C.B. 45 M	Aortic and mitral regurgitation	{LV cine	17	23	23	28	7	15
		{Aortic cine	—	—	—	—	8	20
(6) H.J. 60 M	Post-infarction ventricular aneurysm	{LA cine	7	19	7	29	—	—
		{LA biplane	6	15	6	25	—	—
(7) J.C. 48 F	Mitral stenosis and regurgitation	{LV cine	25	35	40	50	10	16
		{Aortic cine	25	36	40	57	12	20

TABLE II
COMPARISON OF PRESSURE CHANGES IN LEFT ATRIUM AND LEFT VENTRICLE AFTER EXERCISE AND ANGIOGRAPHY

Patient No., age (yr.), and sex	Diagnosis	Exercise						Angiography					
		LA mean (mm. Hg)		LA "v" peak (mm. Hg)		LV end-diast. (mm. Hg)		LA mean (mm. Hg)		LA "v" peak (mm. Hg)		LV end-diast. (mm. Hg)	
		Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
(1) J.R. 53 M	Mitral stenosis	12	16	13	17	—	—	12	23	13	25	—	—
(2) M.H. 58 F	Mitral stenosis and regurgitation	22	28	27	38	7	9	23	42	27	60	6	18
(3) G.B. 35 M	Mitral stenosis	10	12	14	20	2	3	10	15	14	22	3	5
(4) M.J. 32 F	Mitral regurgitation	13	19	25	38	12	18	13	25	25	48	12	20
(5) S.W. 41 M	Mitral regurgitation; tricuspid disease	18	22	23	27	5	10	18	26	23	27	4	13
(6) N.D. 51 F	Aortic stenosis	—	—	—	—	5	12	—	—	—	—	5	13
(7) J.M. 30 M	Aortic stenosis	—	—	—	—	11	16	—	—	—	—	11	17
(8) M.W. 49 M	Aortic regurgitation; mitral stenosis	13	27	15	33	—	—	13	35	17	50	—	—

that produced by angiography, resulted in a 2 per cent underestimation of cardiac output, which is not significant.

RESULTS

General Observations

Pressure Changes. Pressure changes were maximal 1 to 3 minutes after the injection of the radio-opaque dye and returned to pre-angiogram levels within 15 to 20 minutes. In the 7 patients who had successive angiograms performed the pressure changes after the second angiogram were similar to those after the first angiogram, regardless of the site of injection in the left heart or aorta (Table I).

Post-exercise and post-angiography pressure changes were compared in 8 patients (Table II). The average rise in left atrial mean pressure post-exercise was 5.5 mm. Hg, compared with an average rise of 14 mm. Hg after angiography. The average rise in left ventricular end-diastolic pressure after

exercise was 4.5 mm. Hg, whereas the rise after injection of Hypaque averaged 7.5 mm. Hg.

Haematocrit Estimations. A sudden fall in haematocrit occurred immediately after the injection, and return to control levels took about 15 minutes (Fig. 1). The maximum average fall was 11 per cent (range 5 to 20%) and occurred 3 minutes after the injection.

Blood Volume Estimations. The results of blood volume determinations in 17 patients, before angiography and at intervals up to 15 minutes after angiography, are shown in Fig. 2. The maximum average rise in volume was 14 per cent (range 7 to 27%) which was recorded 1 minute after the injection.

Cardiac Output Studies. The results in 9 patients are shown in Table III and Fig. 3. The cardiac output increased in 8 patients and the maximum

FIG. 1.—Serial changes in haematocrit in 35 patients after angiocardiology. In this and subsequent figures, the thick central line represents the mean change as a percentage of control and the shaded area represents the range. The maximal fall occurred 3 minutes after injection of Hypaque (-11%), and in most patients had returned to pre-angiography values within 20 minutes.

average rise was 43 per cent (range -2 to $+71\%$) occurring 1 to 3 minutes after the injection. In 3 patients the output fell to control level within 15 minutes. The stroke volume increased in 8 patients and the maximum average rise was 25 per cent (range -30 to $+48\%$) occurring 1 to 3 minutes

FIG. 2.—Serial changes in blood volume in 17 patients after angiocardiology. The maximal rise occurred between 1 and 3 minutes after injection of Hypaque ($+14\%$), and in most patients returned to control values within 20 minutes.

after the injection. There was a rise in heart rate in 8 patients (average 18% ; range 9 to 33%), maximum at 1 to 3 minutes. One patient with gross mitral and tricuspid regurgitation showed a fall in cardiac output and stroke volume after the injection.

Observations in Specific Groups of Patients

Normal Patients. Seven patients were investigated (Table IV). After angiography the highest

FIG. 3.—Serial changes in cardiac output in 9 patients after angiocardiology. The percentage change is shown at 1 to 3, 5, and 10 to 15 minutes after the injection of Hypaque. In 1 patient cardiac output fell. The maximal rise occurred 1 to 3 minutes after injection of Hypaque ($+43\%$), and usually returned to control levels within 20 minutes.

left ventricular end-diastolic pressure was 13 mm. Hg and the highest left atrial mean pressure was 12 mm. Hg.

Mitral Stenosis. The pressure changes in 18 patients are shown in Fig. 4. The Hypaque was injected into the left ventricle in 12 patients, the left atrium in 5 patients, and into the aorta in 1 patient.

Left ventricular end-diastolic pressure increased in all patients but in no case did it exceed 12 mm. Hg (Fig. 4). The average left ventricular end-diastolic pressure before angiography was 4.6 mm. Hg (SD ± 1.8 ; range 0 to 7 mm. Hg), and after angiography the average left ventricular end-diastolic

TABLE III
CHANGES IN HEART RATE, CARDIAC OUTPUT, AND STROKE VOLUME AFTER INJECTION OF HYPAQUE

Patient	Diagnosis	Site of hypaque injection	Rhythm	Heart rate				Cardiac output (l./min.)				Stroke volume (ml.)			
				0	1-3 min.	5 min.	10-15 min.	0	1-3 min.	5 min.	10-15 min.	0	1-3 min.	5 min.	10-15 min.
(1) W.W. 63 M	Aortic aneurysm	Pulm. art.	Sinus	76	99	78	75	4.1	7.0	6.8	4.2	54	71	87	55
(2) T.M. 31 F	Mitral and tricuspid regurgitation	RV	Atrial fib.	60	80	80	66	4.2	4.2	3.9	3.5	70	53	49	53
(3) H.M. 29 F	Mitral and tricuspid regurgitation	RV	"	120	126	120	110	4.5	5.9	4.3	3.7	38	47	35	33
(4) I.K. 32 M	Normal	Pulm. art.	Sinus	96	106	84	85	6.8	11.1	9.0	7.8	72	105	107	92
(5) A.C. 43 M	Mitral regurgitation	LV	Atrial fib.	96	106	99	—	5.1	6.5	5.8	—	53	62	59	—
(6) M.S. 55 F	Aortic stenosis and regurgitation	Aorta	Sinus	102	126	105	96	5.0	8.4	6.5	6.4	49	67	62	66
7 W.W. 40 M	Mitral stenosis	LV	"	99	123	102	75	9.1	11.7	10.2	7.2	92	95	100	96
(8) J.W. 29 M	Coarctation	LA	"	114	138	108	102	6.5	9.8	6.9	5.8	57	71	64	57
(9) F.B. 55 F	Chronic pericardial effusion	RV	"	93	93	74	80	5.3	7.7	6.6	5.6	58	83	79	70

TABLE IV
PRESSURE CHANGE IN "NORMAL" PATIENTS AFTER ANGIOGRAPHY

Patient No., age (yr.), and sex	Diagnosis	LA mean (mm. Hg)		LA "a" peak (mm. Hg)		LA "v" peak (mm. Hg)		LV end-diast. (mm. Hg)	
		Before	After	Before	After	Before	After	Before	After
(1) M.W. 12 M	Small ventricular septal defect	—	—	—	—	—	—	6	13
(2) J.R. 36 M	Normal heart	—	—	—	—	—	—	7	7.5
(3) D.F. 18 F	Peripheral pulmonary artery stenosis; previous closure patent ductus arteriosus	2	6	3	5	6	11	1	6
(4) A.R. 23 F	Slight mitral regurgitation; previous closure patent ductus arteriosus	8	8	8	8	12	13.5	6	7
(5) G.C. 47 M	Small atrial septal defect and mild mitral stenosis	8	12	—	—	7	10	7	10
(6) M.L. 17 F	Small atrial septal defect	—	—	—	—	—	—	4	12
(7) V.G. 43 F	Small atrial septal defect	—	—	10	10	10	12	7	7

FIG. 4.—Effects of angiocardiology on left atrial and left ventricular pressures in 18 patients with pure mitral stenosis. Considerable rises in left atrial "v" peak and mean pressures are shown, but left ventricular end-diastolic pressure remains within normal limits.

FIG. 5.—Left atrial and left ventricular pressures in a patient with pure mitral stenosis before and 4 minutes after angiography. Mean left atrial pressure rises from 9 to 22 mm. Hg, and left ventricular end-diastolic pressure from 4 to 11 mm. Hg. The diastolic gradient across the mitral valve is considerably increased.

FIG. 6.—Effects of angiocardiography on left atrial and left ventricular pressures in 30 patients with pure mitral regurgitation.

pressure was 9 mm. Hg ($SD \pm 2.7$; range 3 to 12 mm. Hg).

Mean left atrial pressure averaged 23 mm. Hg ($SD \pm 4.9$; range 8 to 35 mm. Hg), with a "v" peak of 25 mm. Hg ($SD \pm 15.9$; range 9 to 46 mm. Hg). After injection of Hypaque the mean left atrial pressure rose to 36.5 mm. Hg ($SD \pm 6.1$; range 15 to 50 mm. Hg) and the "v" peak rose to 47.5 mm. Hg ($SD \pm 13.9$; range 22 to 60 mm. Hg).

In all cases with simultaneous left atrial and left

ventricular pressure recordings, the diastolic gradient was seen to rise after the angiogram (Fig. 5).

Pure Mitral Regurgitation. Thirty patients were investigated and the results are shown in Fig. 6. Hypaque was injected into the left ventricle in all except 3 patients in whom left atrial injection was performed.

The average left ventricular end-diastolic pressure before angiography was 9.5 mm. Hg ($SD \pm 3.3$;

FIG. 7.—Left atrial and left ventricular pressures in a patient with severe rheumatic mitral regurgitation before and 3 minutes after angiography. Left atrial “V” peak pressure rises from 30 to 60 mm. Hg, and left ventricular end-diastolic pressure rises from 10 to 20 mm. Hg.

range 5 to 17 mm. Hg), and after angiography the average left ventricular end-diastolic pressure was 19.3 mm. Hg (SD ± 4.8 ; range 11 to 32 mm. Hg). There were considerable rises in left atrial “v” peak pressures after angiography and the average rise in pressure was 20.3 mm. Hg. Left atrial mean pressure rose from an average of 15 mm. Hg (SD ± 7.7 ; range 6 to 27 mm. Hg) before the injection of Hypaque, to 30 mm. Hg (SD ± 7.6 ; range 15 to 41 mm. Hg) after the injection (Fig. 7).

Combined Mitral Stenosis and Regurgitation. All these 18 patients had grade 2 or 3 mitral regurgitation, as demonstrated by left ventricular cine-angiography using the three grades suggested by Rees, Jefferson, and Harris (1965). Also, they each had a persistent diastolic gradient on simultaneous left atrial and left ventricular pressure records. The haemodynamic responses to angiography are shown in Fig. 8.

After the injection of radio-opaque dye, left

FIG. 8.—Effects of angiography on left atrial and left ventricular pressures in 18 patients with combined mitral stenosis and regurgitation.

FIG. 9.—Effects of injection of Hypaque on left ventricular end-diastolic pressure in the 3 groups of patients with mitral valve disease. Abnormal increases of end-diastolic pressure occur in patients with combined mitral stenosis and regurgitation and in those with pure mitral regurgitation. Left ventricular end-diastolic pressure remains normal after angiography in mitral stenosis.

ventricular end-diastolic pressure rose from an average of 8 mm. Hg (SD ± 2.5 ; range 5 to 13 mm. Hg) to an average of 15 mm. Hg (SD ± 3.9 ; range 9 to 23 mm. Hg). Left atrial mean pressure rose from an average of 20.5 mm. Hg to 31.5 mm. Hg, and the average “v” peak pressure rose from 28.5 mm. Hg to 45 mm. Hg.

The changes in left ventricular end-diastolic pressure after angiography in the three types of mitral valve lesion are shown for comparison in Fig. 9.

Aortic Stenosis. The results in 19 patients are shown in Fig. 10. In 16 patients Hypaque was injected into the aorta via a retrograde femoral artery catheter. Dye was injected through a trans-septal catheter into the left ventricle in 2 patients and into the left atrium in 1 patient. The average left ventricular end-diastolic pressure before angiography was 10.8 mm. Hg (SD ± 3.6 ; range 5 to 15 mm. Hg) and after angiography 21 mm. Hg (SD ± 8.2 ; range 9 to 50 mm. Hg).

Systolic gradients over the aortic valve were increased in 8 of the 10 patients in whom records were made before and after Hypaque. In one patient the gradient remained unchanged and in one patient the gradient fell from 60 to 45 mm. Hg, but the post-angiogram record in this patient was not obtained until 12 minutes after the injection of Hypaque.

FIG. 10.—Effects of angiocardiology in 19 patients with aortic valve stenosis. The left-hand column shows the abnormal left ventricular end-diastolic pressures after angiography with only 1 exception. The right-hand column shows the changes in peak systolic gradient in 10 of the 19 patients.

FIG. 11.—Effects of angiography on left atrial and left ventricular pressures in patients with aortic regurgitation. In half the patients left ventricular end-diastolic pressure does not rise above normal (12 mm. Hg) after angiography.

Aortic Regurgitation. Fig. 11 shows the pressure changes in the 23 patients studied. All except 2 patients had dye injected into the aorta. In 1 patient left ventricular injection was performed and in the other patient left atrial injection was used. The left ventricular end-diastolic pressure averaged 9.3 mm. Hg (SD ± 5.3 ; range 5 to 26 mm. Hg) before the injection of Hypaque and 16.5 mm. (SD ± 8.8 ; range 6 to 38 mm. Hg) after the injection. Mean left atrial pressure rose from an

average of 10 to 17.5 mm. Hg and the "v" peak average from 13 to 24 mm. Hg after the injection of Hypaque (Fig. 12).

Cardiomyopathy. The pressure changes after angiography in 18 patients with obscure heart disease, 7 of whom were considered to have hypertrophic obstructive cardiomyopathy, are shown in Table V. In the 7 patients with obstructive cardiomyopathy left ventricular end-diastolic pressure

FIG. 12.—Left atrial pressures in a patient with severe aortic regurgitation before and after cine-aortography. Pre-angiography: a = 28, v = 30, mean = 22 mm. Hg; post-angiography: a = 40, v = 60, mean = 40 mm. Hg. Note the tall "v" waves after angiography, though there was no evidence of mitral regurgitation on the left ventriculogram.

TABLE V
PRESSURE CHANGES IN LEFT VENTRICLE AND LEFT ATRIUM AFTER ANGIOGRAPHY IN PATIENTS
WITH OBSCURE HEART DISEASE

Patient No., age (yr.), and sex	Diagnosis	LA mean (mm. Hg)		LA "a" peak (mm. Hg)		LA "v" peak (mm. Hg)		LV end-diast. (mm. Hg)	
		Before	After	Before	After	Before	After	Before	After
(1) T.K. 27 M	Hypertrophic obstructive cardiomyopathy	12	22	18	36	9.5	26	13	22
(2) A.C. 25 M	" "	8	13	10	16	6	8	12	14
(3) M.R. 47 F	" "	27	37	31	42	40	63	20	—
(4) M.M. 20 F	" "	9	—	12	—	7	—	12	25
(5) L.M. 29 F	" "	6	17	9	11	11	22	—	—
(6) D.H. 34 F	" "	21	32	—	—	30	47	14	23
(7) E.D. 28 M	" "	12	20	15	24	13	21	13	30
(8) J.H. 36 F	Thyrototoxic cardiomyopathy: mild mitral stenosis	8	14	13	25	8	25	8	14
(9) M.L. 16 F	Mild mitral stenosis with obscure LV disorder	11	26	15	27	14	30	9	28
(10) R.M. 23 F	Non-obstructive familial cardiomyopathy	6	—	8	15	8	13	5	16
(11) M.N. 33 F	Familial heart block and cardiomyopathy	—	—	35	35	—	—	10	18
(12) M.S. 55 F	Idiopathic cardiomyopathy	2	—	5	—	2	—	6	15
(13) H.P. 55 F	" "	10	26	16	33	7	23	13	25
(14) D.C. 32 F	" "	8	19	6	21	12	24	7	20
(15) E.S. 48 F	Cardiomyopathy and Meig's syndrome	10	23	14	35	14	25	9	38
(16) I.C. 33 F	Idiopathic cardiomyopathy	23	28	22	29	29	55	20	—
(17) A.P. 53 F	" "	3	29	10	43	1	20	5	23
(18) K.C. 19 F	" "	12	23	17	31	14	25	13	—

averaged 14 mm. Hg before angiography (SD ± 3 ; range 12 to 20 mm. Hg) and 23 mm. Hg after angiography (SD ± 8 ; range 15 to 38 mm. Hg).

In the other 11 patients with non-obstructive cardiomyopathy left ventricular end-diastolic pressure averaged 10 mm. Hg before angiography (SD ± 4 ; range 6 to 20 mm. Hg) and 22 mm. Hg after angiography (SD ± 8 ; range 15 to 38 mm. Hg).

DISCUSSION

The changes in cardiac pressures after injection of radio-opaque dye depend on the physiological effects of the contrast medium on the heart and circulation. The initial part of this study was, therefore, concerned with the physiological consequences of injection of the radio-opaque dye Hypaque. A fall in haematocrit value (-11%), a rise in circulating blood volume ($+14\%$), and an increase in cardiac output ($+43\%$) have been shown in the present study (Fig. 1, 2, and 3). The rise in blood volume coincided in time with the changes in cardiac output and haematocrit. These changes were maximal 1 to 3 minutes after angiography and returned to normal within 20 minutes.

Giammona, Lurie, and Segar (1963) showed an increase in body fluid osmolality after injection of contrast medium and concluded that hypertonicity of the injected solution was a major factor in producing reactions after angiography. Similar rises in plasma osmolality associated with an increase in plasma volume and a fall in blood haematocrit have been demonstrated by Iseri *et al.* (1965). A con-

comitant rise in cardiac output was shown by Brown *et al.* (1965) who suggested that the raised cardiac output after angiography was caused by a combination of the increased blood volume, mainly due to hypertonicity of the radio-opaque dye, and peripheral vasodilatation. Our observations suggest that the main determinant of the increased cardiac output after the injection of Hypaque is the increase in circulating blood volume.

A direct myocardial depressant action of the radio-opaque dye has been invoked by some authors as a cause of pressure alteration after angiography (Rainey and Edmonds, 1965), but this is unlikely, in view of the temporary nature of the changes, the absence of significant electrocardiographic abnormalities, and the similar changes in pressure caused by exercise. Furthermore, Friesinger *et al.* (1965) have shown that contrast medium injected directly into the coronary arteries does not produce haemodynamic changes like those after injection into the left heart chambers. Cardiac output does not alter after small injections of radio-opaque dye into the coronary arteries for selective coronary arteriography (Benchimol and McNally, 1966). Thus any direct depressant effect on the myocardium is likely to be small and insufficient to produce the pressure changes.

The site of injection into the left heart or aorta did not alter the pressure responses to the injection of Hypaque. Right heart injections of Hypaque also produced similar haemodynamic and physiological changes. These findings are similar to

those of Brown *et al.* (1965). In the patients who had successive angiograms, the pressure changes were reproducible if sufficient time elapsed to allow a return to basal levels before the second angiogram was performed (Table I). This time interval was consistently between 15 and 20 minutes after angiography. It is therefore necessary to allow at least 15 minutes between injections of dye if more than one angiogram is performed, to enable physiological and haemodynamic status to approach the baseline.

We have shown that the changes in pressure after injection of Hypaque are caused mainly by a rise in cardiac output. The increased cardiac output results principally from a rise in circulating blood volume. Since the volume of injected fluid is insufficient to explain the increase in blood volume, a transfer of fluid from the extravascular space to the intravascular space must have occurred because of the hyperosmotic character of the Hypaque.

The pressure changes after angiography serve as a useful "stress" test, and provide a convenient alternative to exercise studies. This applies particularly during transseptal catheter studies when leg exercise is difficult to perform. Mild arm exercise has provoked a rise in left atrial and left ventricular end-diastolic pressure which is similar but of a lesser degree than the rise after injection of Hypaque (Table II).

The effect of these physiological responses to the injection of Hypaque on left ventricular end-diastolic pressure and the relation of the changes in left ventricular end-diastolic pressure to altered left ventricular function have been our special interest in this study. The normal upper limit of left ventricular end-diastolic pressure is 12 mm. Hg (Braunwald *et al.*, 1961), and this value is not exceeded during exercise in patients with normal hearts (Ross *et al.*, 1966). In our group of patients considered to have insignificant cardiac lesions (Table IV) the highest value for left ventricular end-diastolic pressure after angiography was 13 mm. Hg—this in an asymptomatic patient with a small ventricular septal defect. An abnormal rise in left ventricular end-diastolic pressure by itself does not establish a diagnosis of left ventricular failure, but measurement of end-diastolic pressure before and during exercise may allow the recognition of abnormal left ventricular function (Braunwald and Ross, 1963; Ross *et al.*, 1966). In patients with a raised left ventricular end-diastolic pressure, two types of exercise response have been defined. A rise in end-diastolic pressure associated with an increase in stroke volume is termed "abnormal left ventricular dynamics", and a rise in end-diastolic pressure associated with a fall or no change in stroke volume is termed "depressed left ventricular func-

tion". Fig. 13 shows the changes in stroke volume and left ventricular end-diastolic pressure in 5 patients after angiography. One patient (No. 8) showed a normal response in that end-diastolic pressure remained virtually unchanged while stroke volume increased. Three patients (No. 3, 5, and 6) showed "abnormal left ventricular function", and one patient (No. 2) showed "depressed left ventricular function". A raised left ventricular end-diastolic pressure after angiography differentiates

FIG. 13.—Maximal change in stroke volume and left ventricular end-diastolic pressure in 5 patients following angiography. The numbers in parentheses correspond to the patient numbers in Table III. ○ = Before angiography; ● = after angiography. Patient (8) shows normal left ventricular function; patients (3), (5), and (6) show "abnormal left ventricular dynamics"; patient (2) shows "depressed left ventricular function".

the abnormal from the normal left ventricle. However, a change in end-diastolic pressure without knowledge of alteration in stroke volume will not distinguish "abnormal left ventricular dynamics" from "depressed left ventricular function".

There are conflicting views on left ventricular function in mitral stenosis, and though left ventricular dysfunction has been regarded as a cause of

failure to improve after operation (Harvey *et al.*, 1955), other authors doubt the importance of abnormal left ventricular dynamics (Bishop and Wade, 1963). Ross *et al.* (1966) have shown normal left ventricular end-diastolic pressures after exercise in 13 patients with mitral stenosis. However, in the series reported by Feigenbaum *et al.* (1966), 8 out of 32 patients with mitral stenosis had raised end-diastolic pressures after exercise. None of our 18 patients with pure mitral stenosis has shown resting or post-angiographic left ventricular end-diastolic pressures greater than 12 mm. Hg (Fig. 4 and 5), but 2 other patients with mitral valve obstruction have had increased left ventricular end-diastolic pressure. Data concerning these patients (No. 8 (J.H.) and No. 9 (M.L.)) are shown in Table V. Patient No. 8 (J.H.) had a closed mitral valvotomy two and a half years previously, and clinical findings, with full left heart studies, showed minimal mitral valve disease despite persistence of severe symptoms. She has been shown to have hyperthyroidism, and the haemodynamic findings may be explained by a thyrotoxic cardiomyopathy. The other patient, No. 9 (M.L.), had a cardiectomy at which no significant mitral stenosis could be detected and was subsequently referred for cardiac catheterization studies. Though only mild mitral obstruction was shown by left heart catheterization, her symptoms remain disabling, and a diagnosis of obscure cardiomyopathy with left ventricular dysfunction has been suggested.

Persistent gradients between the left atrium and left ventricle in long diastoles clearly indicate significant mitral valve obstruction (Nixon and Wooler, 1963), and in our patients with pure mitral stenosis end-diastolic pressure gradients invariably increased after angiography. Significant mitral stenosis may become apparent with the rise in end-diastolic gradient after angiography, and this may be particularly valuable diagnostically in patients who have been sedated before cardiac catheterization (Fig. 5).

We considered whether end-diastolic gradients between left atrium and left ventricle would help in differentiating patients with mixed lesions of the mitral valve. Rahimtoola *et al.* (1966), using pulmonary artery wedge pressures, demonstrated a rise in end-diastolic gradient in 8 patients with mitral stenosis after angiography, and concluded that regurgitant and stenotic orifices may be differentiated by the diastolic gradient changes. We have been unable to substantiate this, and some patients with severe mitral regurgitation have developed end-diastolic pressure gradients between left atrium and left ventricle after the injection of Hypaque, due in part to tachycardia. Also, a large left atrial "v"

wave after the injection of Hypaque cannot be taken to indicate dominant mitral regurgitation, as we have found similar left atrial tracings in patients with pure mitral stenosis and in patients with normal mitral valves (Fig. 12).

With aortic valve disease, as in some patients with mitral regurgitation, an abnormal left ventricular end-diastolic pressure may only become evident after angiography (Fig. 9, 10, and 11). Only one of our patients with severe aortic valve stenosis failed to show an abnormal left ventricular end-diastolic pressure after angiography, and this may have been due to recent intensive treatment with digitalis and diuretics.

In patients with pure aortic regurgitation, the severity of the reflux, as shown by retrograde aortic cine-angiography, correlated well with the clinical features, but not with the changes in left ventricular end-diastolic pressure after angiography. Three of the 23 patients with aortic regurgitation had normal end-diastolic pressures before and after the injection of Hypaque into the aortic root, but were considered to have severe reflux on clinical and radiological grounds. An operation was recommended, and in each case aortic regurgitation was considered by the surgeon to be severe, and the aortic valve was replaced.

It is difficult to generalize about the haemodynamic responses in the group of patients classified as cardiomyopathies since they are a mixed group of varied aetiology. Two of the 7 patients with obstructive cardiomyopathy had measurement of left ventricular outflow tract pressure gradients before and after angiography, and in both an increase in systolic gradient was noted, but this is of no differential diagnostic value, since most of our patients with valvar aortic stenosis have shown a similar rise in gradient after angiography (Fig. 10).

Patient No. 10 (R.M.) (Table V) is the propositus from a family in which several of the relatives have shown evidence of obscure myocardial disease with a tendency to early death (Brown *et al.*, 1967). Cardiac catheterization demonstrated a non-obstructive cardiomyopathy with a resting left ventricular end-diastolic pressure of 5 mm. Hg which rose to 16 mm. Hg after angiography. Earlier in the same study the patient developed anginal pain when left ventricular end-diastolic pressure was recorded at 20 mm. Hg.

All of the 18 patients with obscure cardiomyopathy were considered to have abnormal left ventricular function on the basis of routine clinical, radiographic, and electrocardiographic assessment. Left ventricular end-diastolic pressure after angiography was abnormal in all patients in whom it was recorded, but it is stressed that 7 of these patients

had normal end-diastolic pressures before the injection of Hypaque.

Ischaemic pain has not been induced by the injection of Hypaque in any of the patients in this series, despite a history of effort angina in several of them.

It is important to record pressures before as well as after angiography, since post-angiographic pressures represent maximal and not resting values. If only post-angiographic measurements are considered the severity of the cardiac lesion may be overestimated.

SUMMARY

Haemodynamic changes after injection of Hypaque into the left side of the heart or aorta during cardiac catheterization have been recorded in a series of patients, and the physiological processes involved have been investigated.

The injection of Hypaque, a hypertonic solution, caused an increase in circulating blood volume (+14%), with a rise in heart rate (+18%), stroke volume (+25%), and cardiac output (+43%). The changes were maximal within the first 3 minutes after angiography, and returned to normal within 20 minutes. Haemodynamic responses were unrelated to the site of injection. Pressures recorded during this period were compared with resting values, and hence the injection of dye served as a useful stress test.

Fifteen minutes should be allowed to elapse between successive angiograms to ensure a return to baseline conditions before the second angiogram.

Patients with pure mitral stenosis showed an increased diastolic pressure gradient between left atrium and left ventricle after injection of Hypaque. Similar increases in gradient were also found in patients with significant mitral regurgitation, and this feature therefore did not help in assessing mixed mitral valve lesions.

Patients with pure mitral stenosis had normal left ventricular end-diastolic pressures. Raised left ventricular end-diastolic pressure, either before or after angiography, in patients with mitral valve disease usually denoted significant mitral regurgitation. If there was insignificant mitral reflux then other causes of left ventricular dysfunction were likely to be present.

The severity of valvar aortic stenosis judged by the systolic gradient across the aortic valve correlated well with the high levels of left ventricular end-diastolic pressure after angiography. In patients with predominant aortic regurgitation the correlation was poor, and patients with severe aortic reflux may

have normal left ventricular end-diastolic pressure before and after angiography.

Patients with cardiomyopathy have invariably shown abnormal end-diastolic pressures in the left ventricle, though in 7 of the 18 patients in the present series this was only evident after angiography.

Measurement of left atrial and left ventricular pressures before and in the 5 minutes after angiography gives useful information about the function of the left side of the heart, while adding minimally to the complexity of cardiac catheterization. This information is similar to that obtained by recording pressure changes on exercise, and is both simpler and quicker to obtain.

We wish to thank Mrs. B. Lea, Senior Cardiographic Technician, and Sister J. Davies, in charge of the Catheter Laboratory, and their respective staffs for invaluable technical help. We are also grateful to Miss Lillian Harwood, of the Department of Haematology, for the haematocrit estimations.

This work was aided by Research Grant No. 92 from the Medical Research Committee of the United Liverpool Hospitals.

Dr. J. M. Clarke was holding a Research Grant from the British Heart Foundation and we are most grateful for their assistance.

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