THE EFFECTS OF ACUTELY INCREASED SYSTEMIC RESIST-
ANCE ON THE LEFT ATRIAL PRESSURE PULSE: A
METHOD FOR THE CLINICAL DETECTION OF
MITRAL INSUFFICIENCY

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In 1921, Wiggers and Feil in a study of experimental mitral insufficiency observed an elevation of left atrial pressure when the aorta was constricted (1). This finding has subsequently been confirmed both in experimental animals (2, 3) and in a circulatory model (4). In recent experiments "mitral" regurgitant flow was produced and measured by permitting blood to pass from the left ventricle through a flow meter into the left atrium (5). It was observed that with any given mitral regurgitant orifice the regurgitant flow could be substantially increased by elevating the resistance to left ventricular ejection with graded aortic constriction.

The experimental observations listed above suggested that acutely increased resistance to left ventricular ejection in patients with mitral regurgitation should also result in an elevation of left atrial pressure. It was further reasoned that such elevations of left atrial pressure would not occur in patients without mitral valve disease or with pure mitral stenosis and that this difference in response might therefore be of value in the clinical detection of mitral regurgitation. In addition to such observations in patients, it was considered desirable to determine the effects of elevated aortic pressure on the left atrial pressure pulse in animals before and after the production of experimental mitral regurgitation.

EXPERIMENTAL OBSERVATIONS

Methods. Dogs weighing 14.5 to 20.4 Kg. were studied with intravenous pentobarbital anesthesia and positive pressure respiration. The left chest was entered through the fifth intercostal space. A perforated tygon tube was placed into the left atrium through the appendage; by advancing the end of the tube through the mitral valve into the left ventricle mitral regurgitation was induced and could be abolished by withdrawal of the tube (Figure 1). Resistance to left ventricular ejec-

tion was increased either by an infusion of norepinephrine (0.008 mg. per ml. isotonic saline), or by means of graded constriction of the ascending aorta with an aneurysm clamp. Pressures were recorded from the left atrium and from the aorta proximal to the constriction. In two experiments a Potter turbine flow meter (6) was introduced into the aorta for the continuous registration of systemic flow. All recordings were made on a multichannel oscillograph.

RESULTS

Results representative of 26 experiments performed in eight dogs are illustrated in the experiment shown in Figure 2A. In the absence of mitral regurgitation, striking elevations of aortic pressure raised the v point of the left atrial tracing relatively little. A degree of mitral insufficiency which produced only slight elevation of the v point was then induced. A striking elevation of the left atrial v point occurred when aortic pressure was then raised by aortic constriction. This finding was consistent regardless of whether aortic pressure was elevated by aortic constriction or by norepinephrine infusion.

In two experiments systemic flow was recorded while norepinephrine was infused. A greater depression of systemic flow and greater elevation of left atrial mean and v point pressures occurred when mitral regurgitation was present than when absent.

CLINICAL OBSERVATIONS

Selection of patients and methods. A total of 20 patients has been studied. Group I consists of seven patients without mitral insufficiency, of whom six had "pure" mitral stenosis on the basis of clinical findings, the demonstration at left heart catheterization of a diastolic pressure gradient between left atrium and left ventricle, and by palpation of the valve at operation. The seventh patient in this group, J. T., had an atrial septal defect without associated mitral insufficiency; this diagnosis
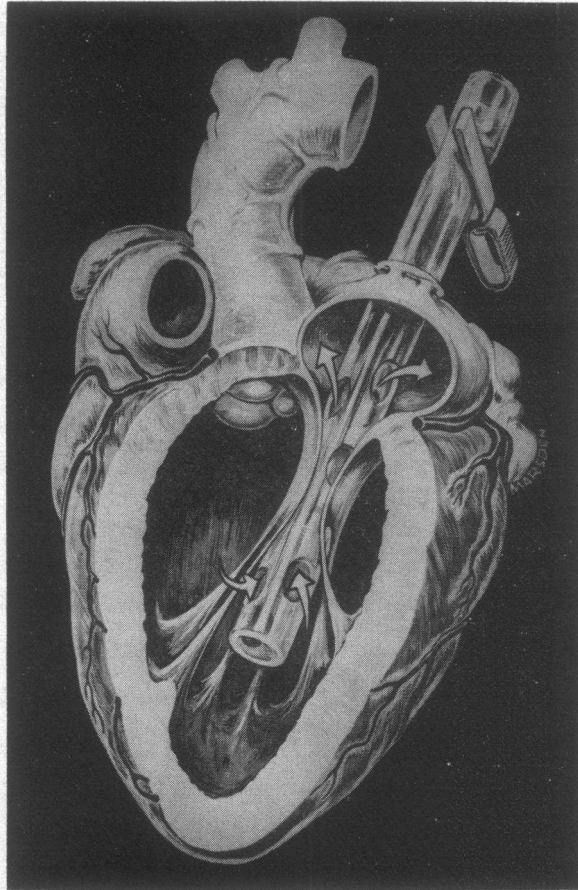
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FIG. 1. DIAGRAM OF THE EXPERIMENTAL METHOD OF
PRODUCTION OF REVERSIBLE MITRAL INSUFFIENCY

and left ventricle and by operative findings, but in all
of these patients a definite regurgitant jet was also palp-
able. The seven patients in Subgroup IIB presented the
clinical picture of "pure" mitral insufficiency; the presence
of a left to right shunt was excluded by right heart
catheterization.

Left atrial pressures were measured by the technique
of transbronchial left heart catheterization, which has
been described in detail (7). In the first eight patients
norepinephrine was infused while the bronchoscope was
in place and left atrial pressure was recorded through
the transbronchial needle. In the other twelve patients,
following measurement of left ventricular pressure with
a polyethylene catheter threaded through the trans-
bronchial needle, both the bronchoscope and needle were
removed and the catheter was left *in situ*. After a 20 to
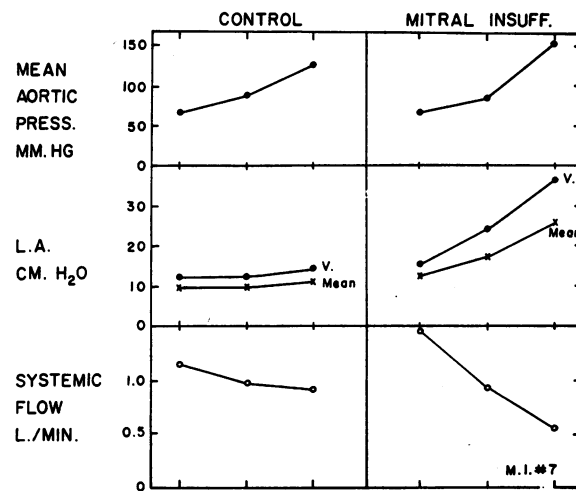
FIG. 2B. ALTERATIONS IN FORWARD SYSTEMIC FLOW
ACCOMPANYING ELEVATION OF AORTIC PRESSURE BEFORE
AND AFTER THE PRODUCTION OF MITRAL INSUFFICIENCY

Aortic pressure elevated by norepinephrine infusion.

was confirmed at operation. Group II consists of thir-
teen patients with mitral insufficiency. The six patients
in Subgroup IIA had mitral stenosis proved by the pres-
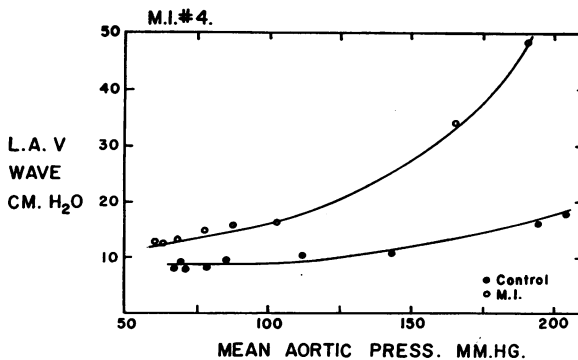ence of a diastolic pressure gradient between left atrium

FIG. 2A. RELATION BETWEEN LEFT ATRIAL v POINT
PRESSURE AND MEAN AORTIC PRESSURE IN DOGS BEFORE
AND AFTER THE PRODUCTION OF MITRAL INSUFFIENCY

Aortic pressure elevated by aortic constriction.

30 minute period during which the patient returned to
a more basal state, the catheter was withdrawn into the
left atrium and the norepinephrine then infused.

In the measurement of left atrial pressures, a Statham
P23 A strain gauge was employed with the transbronchial
needle, and a P23 D gauge with the polyethylene catheter.
Left atrial and systemic arterial pressures and the elec-
trocardiogram were continuously recorded and visually
monitored on a multichannel photographic recorder.

Following control observations, norepinephrine was in-
fused at approximately 10 to 20 γ per minute. The infu-
sion was continued until systolic arterial pressure be-
came significantly elevated (approximately three to five
minutes). The infusion was then stopped and meas-
urements continued until the arterial pressure returned to
control levels. Pressure measurements were averaged
over two respiratory cycles. Mean pressures were ob-
tained either by electrical or planimetric integration.

TABLE I

Hemodynamic observations before and during norepinephrine infusion

Patient	Before norepinephrine infusion*					During norepinephrine infusion					Elevation L. A. v × 100
	F. A.		L. A.		Heart rate	F. A.		L. A.		Heart rate	Elevation F. A. syst. (%)
	s/d	m	v	m		s/d	m	v	m		
Group I—No mitral insufficiency											
D. G.†	114/54	76	34	29	96	156/79	104	36	25	40	5
D. S.†	138/61	93	12	9	64	186/73	113	22	14	50	21
I. W.	80/46	60	13	14	100	166/67	116	15	22	64	2
J. G.	136/68	91	10	10	76	164/75	103	14	13	60	14
B. C.	104/55	78	19	19	80	163/72	100	23	21	68	7
J. B.†	124/66	80	22	19	88	151/58	98	23	19	50	4
J. T.	116/77	88	10	8	68	172/88	120	14	11	52	7
Group IIA—Mitral insufficiency and stenosis											
E. C.†	133/72	91	10	9	104	182/91	122	14	11	68	8
J. M.†	123/49	84	10	5	60	206/78	110	35	21	40	30
G. S.	128/75	91	38	35	92	163/88	110	47	41	100	26
E. P.	151/74	102	33	23	104	200/80	123	58	34	80	51
N. M.†	179/78	109	26	20	58	225/85	132	38	25	68	26
H. C.†	128/64	81	25	16	72	181/79	128	42	23	68	32
Group IIB—Pure mitral insufficiency											
L. G.†	134/77	103	20	13	96	198/105	134	45	26	65	39
J. L.†	98/60	76	21	19	66	128/79	97	36	30	52	50
M. S.†	131/71	92	3	3	96	184/105	126	31	13	72	53
W. B.	127/76	94	12	10	84	187/89	120	35	20	64	38
K. S.	135/69	95	38	17	88	203/91	148	92	42	77	79
W. C.	111/67	87	48	28	96	146/83	102	92	46	92	126
M. T.†	167/91	122	32	24	72	197/104	152	48	32	80	53

* F. A., femoral artery pressure; L. A., left atrial pressure; s, systolic; d, diastolic; m, mean; v, v point pressures. All pressures are in mm. Hg.

† Observations made 20 to 30 minutes following bronchoscopy.

RESULTS

The majority of the patients described a brief sensation of pounding in the chest and head accompanying the norepinephrine infusion. Several patients developed occasional premature ventricular contractions during the infusion and one had a brief period of bigeminal rhythm. No complications resulted from the left heart catheterizations.

The results of the clinical studies are summarized in Table I. In the patients without mitral regurgitation (Group I) only a slight elevation of left atrial pressure occurred as systolic arterial pressure was raised (Figures 3 and 4). The ratio of the elevation of the left atrial v point pressure to the rise in systemic arterial systolic pressures ranged from 2 to 21 per cent, averaging 9 per cent. In contrast, in all but one of the patients with mitral regurgitation (Group II) a substantial rise in left atrial pressure occurred as systemic pressure was elevated (Figures 3 and 5). The ratio of the elevation of the left atrial v point

pressure to the rise in systemic arterial systolic pressure ranged from 8 to 126 per cent, averaging 47 per cent. In all but one of these patients (E. C.), this ratio exceeded the highest ratio obtained in patients without mitral insufficiency. The ratios tended to be lower in the patients with combined mitral stenosis and insufficiency (Group IIA) than in the patients with pure mitral insufficiency (Group IIB). In Group IIA the ratios ranged from 8 to 51 per cent, with an average of 30 per cent, while in Group IIB the range was from 38 to 126 per cent, with an average of 63 per cent.

DISCUSSION

When norepinephrine is infused in the absence of mitral insufficiency, left atrial pressure is increased only slightly. The stroke work of the left ventricle is increased by both the elevation of aortic pressure and by the bradycardia. The increase in left ventricular stroke work elevates left ventricular end-diastolic and left atrial pres-
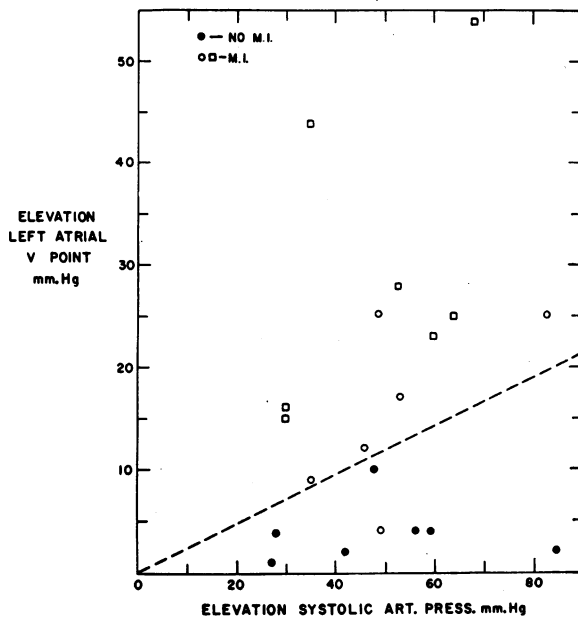
FIG. 3. RELATIONSHIP OF ELEVATION OF LEFT ATRIAL
V POINT PRESSURE TO ELEVATION OF FEMORAL ARTERIAL
SYSTOLIC PRESSURE IN PATIENTS WITH AND WITHOUT
MITRAL INSUFFICIENCY

Closed circles represent patients without mitral in-
sufficiency; open circles, patients with mitral stenosis
and insufficiency; open squares, patients with pure mitral
insufficiency.

sure (8). However, the elevation of the left ven-
tricular function curve by norepinephrine (9) acts
in the opposite direction and tends to decrease left
atrial pressure. When mitral insufficiency is pres-
ent, norepinephrine also increases the systolic

pressure gradient across the regurgitant orifice
and thereby results in increased mitral regurgitant
flow and a substantially greater increase in left
atrial pressure. In the dogs in which forward
systemic flow was metered (Figure 2b) this ele-
vation of left atrial pressure was accompanied by
a fall in forward cardiac output. Other experi-
ments on metered mitral regurgitant flow have
shown that total cardiac output, i.e., the sum of
regurgitant flow and forward cardiac output, re-
mains relatively constant as forward cardiac output
and regurgitant flow vary reciprocally with aortic
constriction (5). Thus, in the presence of mitral
regurgitation, if left ventricular emptying across
the aortic valve is hindered, the blood seeks the
other path available to it and mitral regurgitant
flow is increased.

It would seem to follow that with any given
regurgitant orifice, any mechanism operating to
increase the left venrticular systolic pressure,
such as systemic hypertension or aortic stenosis,
would augment mitral regurgitant flow. Simi-
larly, when ventricular systolic pressure is ele-
vated by aortic insufficiency, coexistent mitral re-
gurgitation is poorly tolerated (10, 11).

Norepinephrine was the agent chosen to in-
crease peripheral resistance acutely because its
effects are transient and the arterial pressure level
could therefore be precisely controlled by the
speed of infusion. Since it is well recognized that
this drug increases myocardial contractility as well
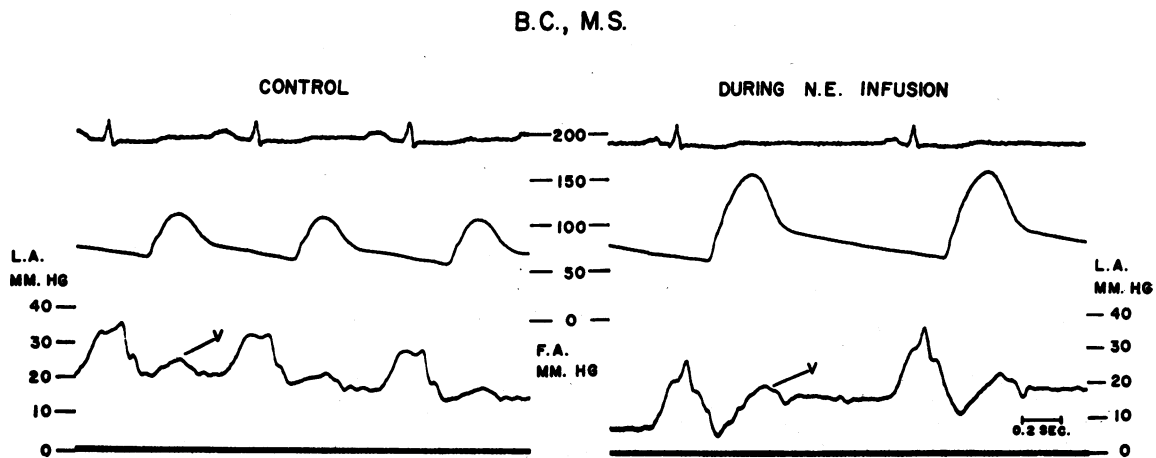as peripheral resistance (9, 12), it is likely that

FIG. 4. FEMORAL ARTERIAL (F.A.) AND LEFT ATRIAL (L.A.) PRESSURES BEFORE AND DURING NOREPINEPHRINE
(N.E.) INFUSION IN PATIENT B. C. WITH PURE MITRAL STENOSIS
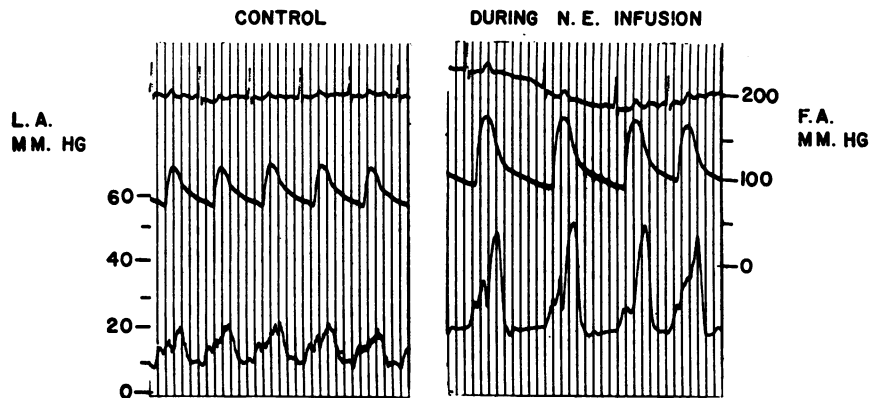
L. G., MITRAL INSUFFICIENCY

FIG. 5. FEMORAL ARTERIAL AND LEFT ATRIAL PRESSURES IN PATIENT L. G. WITH PURE MITRAL INSUFFICIENCY

Vertical time lines indicate 0.1 second.

if an agent such as methoxamine, which acts predominantly on the periphery, had been employed the elevation of atrial pressure would have been greater in both groups of patients.

The extent to which left atrial pressure is elevated during norepinephrine infusion would appear to be of diagnostic value. The presence of severe, pure mitral insufficiency can generally be recognized in the left atrial pressure tracing (13). When mitral regurgitation is associated with mitral stenosis, the pressure pulse is modified and sometimes is indistinguishable from that obtained in patients with "pure" stenosis. However, in the present study, the elevation of arterial pressure resulted in greater elevation of left atrial pressure in patients with combined mitral stenosis and insufficiency than in patients with "pure" mitral stenosis. Therefore, the technique described affords opportunity for the detection of mitral insufficiency in patients with associated mitral stenosis.

Patients who present apical systolic murmurs without elevation of left atrial pressure may present difficult diagnostic problems. While an elevated left atrial v point may suggest the presence of mitral regurgitation, it should be emphasized that this point is often the highest in the left atrial pressure pulse during the cardiac cycle in normal man (14). The effect on left atrial pressure of increasing resistance to aortic ejection may be of value in establishing or excluding the presence of mitral insufficiency in such patients.

SUMMARY

The effects of increased resistance to ventricular ejection on the left atrial pressure pulse were studied in eight dogs with reversible mitral insufficiency. In the absence of mitral insufficiency, elevated aortic pressure resulted in only slight elevations in the left atrial v point. Similar increases in aortic pressure in the presence of mitral insufficiency resulted in striking elevations of mean and v point pressures.

Utilizing the techniques of transbronchial left heart catheterization and norepinephrine infusion, similar observations were made in 20 patients. In the absence of mitral insufficiency (seven patients) the average ratio of increase of v point pressure to increase in systolic peripheral arterial pressure was only 9 per cent. In contrast, in 13 patients with mitral insufficiency this ratio averaged 47 per cent. Although the highest ratios were observed in patients with "pure" mitral insufficiency, striking increases in left atrial pressure were seen in patients with both mitral stenosis and insufficiency. The physiologic mechanisms involved and the usefulness of this technique in the clinical recognition of mitral insufficiency are discussed.

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