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STUDIES ON THE FIRST DERIVATIVE OF THE VENTRICULAR PRESSURE PULSE IN MAN

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The rate at which the ventricular pressure rises has been of interest to investigators for many years (1, 2). Wiggers demonstrated that when ventricular end-diastolic filling pressure was elevated by increasing the venous return to the heart or the resistance to ventricular ejection, the rate of rise of ventricular pressure also increased (3). When epinephrine (4) or digitalis (5) was administered the rate of pressure rise increased despite a fall in ventricular end-diastolic pressure. Conversely, when myocardial ischemia was induced, the slope of the ventricular pressure rise decreased in the face of a rising end-diastolic pressure (6). More recently, although further observations have been made in the dog on the determinants of the slope of the ventricular pressure pulse (7–11), there have been no systematic studies of the effects of physiologic stresses, pharmacologic agents, and various types of heart disease on the slope of the ventricular pressure pulse in man.

Accurate determinations of the instantaneous rate of ventricular pressure change in intact human subjects have been prevented by the technical limitations imposed by the pressure-recording systems that are usually employed in cardiac catheterization. These systems, which consist of a fluid-filled catheter and an external manometer, have a very limited range in which the frequency response is uniform (usually to less than 15 cycles per second) and they are subject to frequent artifacts related to motion of the catheter within the heart. Such artifacts may be manifest as sudden changes in pressure and will therefore be greatly exaggerated when their first derivative is computed. These difficulties have been largely eliminated by obtaining the ventricular pressure tracings with a catheter that has a high-frequency micromanometer mounted at its tip, or by direct needle puncture of the ventricle.

METHODS

Percutaneous puncture of the left ventricle was carried out by the method of Brock, Milstein and Ross (12) as modified in this laboratory (13). All such tracings were obtained with a 3.5-inch no. 19 or 20 gage thin-walled needle attached directly to a Statham P23D pressure transducer without intervening tubing. All other studies from either the left or right ventricle were carried out with a Telco intracardiac manometer[1] (14, 15). This instrument consists of a double-lumen catheter, one lumen of which carries the electrical connection to the micromanometer mounted at the tip, the other serving as a conventional fluid-filled catheter system which is attached to a Statham P23D manometer. The sensitivities of the micromanometer and the external manometer were equalized with an air-pressure calibrating system prior to the introduction of the catheter into the heart. The catheter tip was placed in the right or left ventricle and simultaneous pressure pulses were recorded from the two manometers. The baseline for the micromanometer was made equal to that of the external manometer by superimposing the diastolic portions of the two ventricular pressure pulses.

The frequency responses of the micromanometer and of the needle directly attached to the strain gage were analyzed in a fluid-filled chamber in which a sinusoidal pressure wave of variable frequency was generated. The pressure produced was monitored by a Lilly capacitance manometer built directly into the chamber. Figure 1 illustrates a comparison of the pressures recorded simultaneously from the fluid-filled lumen of the Telco catheter, using a Statham P23D strain gage as the external manometer, the Lilly manometer, and the Telco micromanometer. It is apparent that, while the response of the conventional external manometer system resonates at 7 cycles per second (c/sec) and becomes significantly attenuated at frequencies above 10 c/sec, the micromanometer maintains an almost uniform response, indistinguishable from the Lilly manometer, to frequencies as high as 200 c/sec. With an identical method for comparison it was observed that the needle attached to the P23D gage maintained a uniform response to a frequency of 40 c/sec.

The rate of change of the ventricular pressure pulses (dp/dt) was continuously determined with an R-C differentiating circuit, consisting of a 47 kilo-ohm resistor and a 0.002 microfarad condenser as outlined elsewhere (16). The time constant of this circuit is 9.4×10^{-5} second, and it provides differentiation of linear amplitude without phase distortion to 50 c/sec. The differentiating circuit was calibrated by imposing a signal of constant and known slope from an integrating amplifier and measuring the resulting response of the differentiator.

[1] Telco, Inc., Gentilly, France. Distributed in the U.S.A. by Dallons Laboratory, Inc., Los Angeles, Calif.

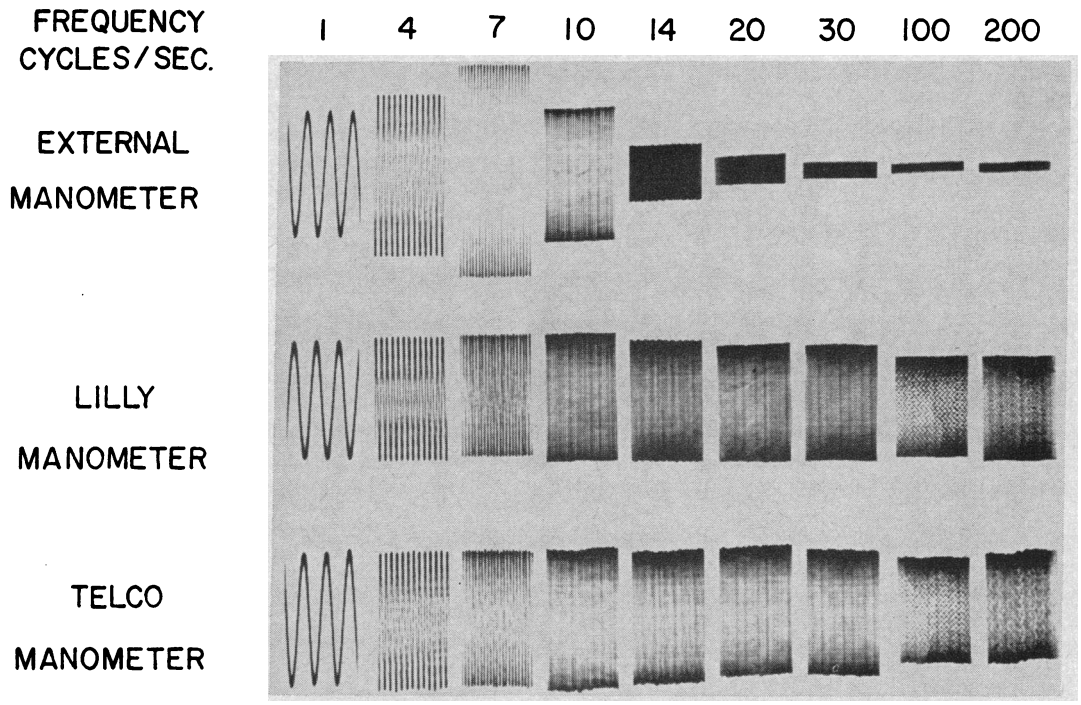

FIG. 1. SIMULTANEOUS RECORDINGS OF PRESSURES FROM A FLUID-FILLED CHAMBER THROUGH THREE TRANSDUCERS AT FREQUENCIES RANGING FROM 1 TO 200 CYCLES PER SECOND. The external manometer resonates at 7 c/sec and its response falls off rapidly thereafter. It is likely that the equal diminution of the amplitude responses of both the Lilly and Telco manometers at 100 c/sec reflects a decrease in the amplitude of the generated sine wave.

The first derivative of the ventricular pressure pulse was determined in a total of 40 patients, in some of whom it was recorded in both ventricles. In 13 patients percutaneous puncture of the left ventricle was carried out (13) and in a total of 21 patients, including all 17 patients in whom right ventricular dp/dt was recorded, the Telco micromanometer was used. Four patients with patent ductus arteriosus and 2 patients with mitral stenosis were studied by direct puncture of the left ventricle at the time of thoracotomy. In the patients with patent ductus arteriosus the effects of clamping and of releasing the ductus were observed. Congenital or rheumatic heart disease was present in most of the patients studied in the catheterization laboratory (Tables I and II). Eight patients had experienced congestive heart failure prior to study and had roentgenographic evidence of ventricular enlargement; in 6 of these the ventricular end-diastolic pressure was distinctly elevated. Thirty-two of the patients studied were in sinus rhythm and 8 had atrial fibrillation.

The cardiac abnormalities present were divided by the type of hemodynamic burden which they imposed on the ventricle. It is fully recognized that considerable variation in the state of ventricular function existed in different patients in the same group and that alterations in ventricular performance were induced by anethesia and thoracotomy in the patients who were studied under these conditions. Nonetheless, it was felt that by dividing the

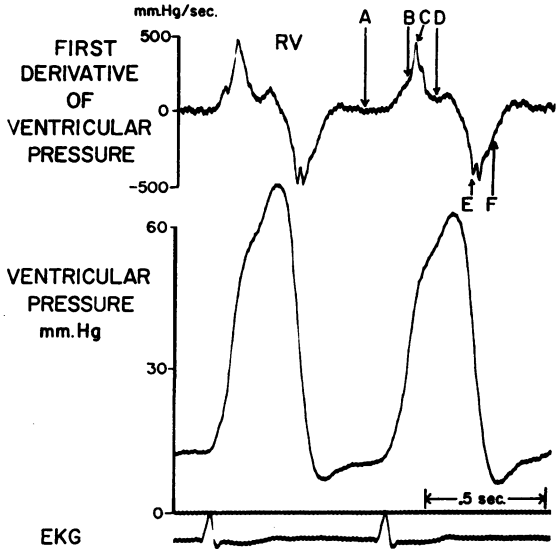

FIG. 2. SIMULTANEOUS RECORDINGS OF THE RIGHT VENTRICULAR PRESSURE PULSE, THE FIRST DERIVATIVE OF THE RIGHT VENTRICULAR PRESSURE, AND THE ELECTROCARDIOGRAM IN A PATIENT WITH MITRAL REGURGITATION, ATRIAL FIBRILLATION AND PULMONARY HYPERTENSION. The various portions of the first derivative are labeled and discussed in the text.

patients into three groups the gross effects of chronic elevations of systolic pressure and of stroke volume on dp/dt could be discerned. Group A consists of 15 patients in whom the ventricle in which dp/dt was determined did not have an abnormally increased hemodynamic burden and includes 4 patients with mitral stenosis, 5 with atrial septal defect, and 1 after complete abolition of an aortic pressure gradient in whom the left ventricle was studied. In addition, in group A there were 3 patients without hemodynamic evidence of heart disease and 2 with abnormalities involving the left side of the heart but without pulmonary hypertension, in whom dp/dt was determined in the right ventricle. Group B consists of 18 patients in whom the ventricle which was studied was subject to a chronically augmented flow load. In this group there were 5 patients with mitral regurgitation, 5 with aortic regurgitation, and 4 with patent ductus arteriosus in whom the left ventricular dp/dt was recorded, as well as 3 patients with atrial septal defect and 1 with ventricular septal defect in whom the right ventricular dp/dt was determined. Group C consists of the 11 patients in whom the dp/dt was determined in ventricles which developed a distinctly elevated systolic pressure (increased pressure load). This group consists of 3 patients with aortic stenosis in whom the left ventricle was studied, and 5 patients with pulmonary hypertension and 3 patients with pulmonic stenosis in whom the right ventricle was studied.

During the control observations the patients were asked to relax and to suspend respiration briefly while the electrocardiogram, ventricular pressure and dp/dt were recorded with a multichannel photographic oscilloscopic recorder. In a number of patients without abnormal hemodynamic burdens the effects of a variety of acute in-

TABLE I

Peak left ventricular dp/dt *

Patient Method	Diagnosis	Peak dp/dt	Heart rate	LV pressure s/d
	Group A, normal LV load			
A.T. OR	MS; TS; AF	1,032	67	120/8
O.M.H. LVP	MS; AF	1,439	96	97/9
G.L.W. OR	MS; AF	1,385	89	118/9
N.E.D.† LVP	MS; AF; dilated LV			
	Preop.	1,300	90	114/15
	Postop.	878	86	108/21
J.P.H. TC	ASD; normal LV	1,009	88	99/7
J.Y. TC	ASD; normal LV	841	71	83/8
D.A.T. TC	Postop. AS; no gradient	1,696	107	103/3
A.B.C. TC	ASD; normal LV	1,611	105	95/8
C.W.C. TC	ASD; normal LV	943	58	87/6
M.J.S. TC	ASD; normal LV	938	86	96/6
	Group B, increased LV flow load			
G.R.P. LVP	MI; AF	1,355	108	96/8
	Group B, increased LV flow load			
J.E.S. TC	MI; ASD	1,615	95	110/9
A.R.L. LVP	MI; AF	1,276	73	109/7
V.E.R. LVP	MI; AI; AF	1,076	79	120/3
W.W.G.† LVP	AI severe	1,252	90	141/9
L.M.L. LVP	AI moderate	1,284	87	127/10
E.J.I.† LVP	AI very severe	1,223	102	160/35
B.J.McC.† LVP	AI severe	1,308	92	138/10
J.M.B. LVP	MI; AF	975	86	98/5
W.R.A.† LVP	AI severe	920	74	116/29
	Group C, increased LV pressure load			
J.L.W. LVP	AS, gradient 41 mm Hg	2,150	107	155/9
R.A.Z. LVP	AS, gradient 62 mm Hg	3,239	103	186/15
L.D.S. LVP	AS, gradient 50 mm Hg	2,080	94	156/24

* Abbreviations: dp/dt = first derivative of pressure pulse; s/d = systolic/diastolic in mm Hg; LV = left ventricle; MS = mitral stenosis; TS = tricuspid stenosis; AF = atrial fibrillation; ASD = atrial septal defect; MI = mitral insufficiency; AI = aortic insufficiency; AS = aortic stenosis; † = patients with clinical evidence of myocardial failure; LVP = percutaneous left ventricular puncture; OR = study done in operating room at time of thoracotomy; TC = Telco catheter study.

terventions on the ventricular dp/dt were also determined. The pharmacologic agents studied included isoproterenol, norepinephrine, methoxamine, and atropine. Whenever the effects of more than one drug were examined, sufficient time was allowed between studies for the results of the previously injected drug to disappear completely. The effects of exercise in the supine position were studied in 2 patients who were asked to pedal a stationary bicycle ergometer vigorously for 2 minutes.

RESULTS

1. *Contour of dp/dt*

The contour of the first derivative of the ventricular pressure pulse is, in general, similar in both ventricles. During ventricular diastole, when the rate of change of ventricular pressure is slow, dp/dt is flat and at a level of 0 or slightly greater (point A in Figure 2). With the onset of isometric ventricular contraction in the left ventricle, dp/dt increases slowly for several milliseconds and then rises smoothly to reach its peak (PD_{LV}) near the midpoint of the isovolumetric contraction period. In the right ventricle, dp/dt exhibits either a notch or an inflection on its ascending limb (B, Figure 2) and usually reaches its peak (PD_{RV}) at a point higher (C) than the midpoint of the ascending limb of the ventricular pressure pulse; during early ventricular ejection dp/dt descends to a level either slightly above or below the baseline and then remains relatively flat during mid and late ejection (D). It begins to fall abruptly to values far below zero during late systole, reaching its nadir early during isovolumetric relaxation (E). Later during isovolumetric relaxation the rate of pressure fall diminishes and dp/dt again returns to the baseline (F).

2. *Values for PD_{LV}*

The peak values of the ascending limb of dp/dt in the left ventricular pressure pulse recorded during the control period are presented in Table I; these values ranged from 841 to 3,239 mm Hg per second. In the ten patients without an abnormal hemodynamic load on the left ventricle (group A), PD_{LV} varied from 841 to 1,696, with an average of 1,219 mm Hg per second. In the patients in whom the left ventricular stroke volume was chronically augmented (group B) the values for PD_{LV} were in a similar range (920 to 1,615; average, 1,228.) The PD_{LV} in patients with an elevation of left ventricular systolic pressure (group C) tended to be much higher (2,080 to 3,239) than in groups A and B.

TABLE II

Peak right ventricular dp/dt *

Patient	Diagnosis	Peak dp/dt	Heart rate	RV pressure s/d
	Group A, normal RV load			
J.E.W.	AS; AI	263	87	22/6
F.W.M.	Hyp	229	79	22/3
L.C.J.	MS; TS	230	77	25/3
L.B.H.	Funct M	223	111	23/3
J.V.G.	Postop. ASD	296	83	33/0
	Group B, increased RV flow load			
J.E.S.	ASD; MI	520	92	42/5
R.F.	VSD	309	86	31/0
A.B.C.	ASD	459	107	34/6
J.P.H.	ASD	334	85	34/7
	Group C, increased RV pressure load			
G.S.†	Idiopathic PH	382	77	53/7
L.D.C.	PS	823	64	121/7
O.F.C.	MS; PH	646	71	58/6
S.K.H.	PS; VSD	639	87	69/2
K.M.M.	PS	489	87	51/9
T.S.†	Hodgkin's dis.; myocard. infilt.; PH	422	107	53/11
J.M.B.	MI; PH	472	81	59/12
M.J.S.†	ASD; PH	471	85	77/8

* Abbreviations same as in Table I, plus: VSD = ventricular septal defect; PS = pulmonary stenosis; PH = pulmonary hypertension; Hyp = systemic hypertension; Funct M = functional murmur.

3. *Values for PD_{RV}*

The peak values for the first derivative of the ascending limb of the right ventricular pressure pulse recorded during the control period in patients without an abnormal hemodynamic load on the right ventricle (Table II, group A) ranged from 223 to 296 mm Hg per second. In patients with right ventricular stroke volume greatly augmented but only a slight elevation of right ventricular systolic pressure (group B), these values ranged from 309 to 520. In patients with an increase in the pressure load on the right ventricle (group C) the PD_{RV} ranged from 382 to 823 mm Hg per second.

It is thus apparent that the values for the PD of the ventricular pressure pulse varied widely among various patients and that the values in the left ventricle exceeded those observed in the right ventricle. The large variations of PD are attributable,

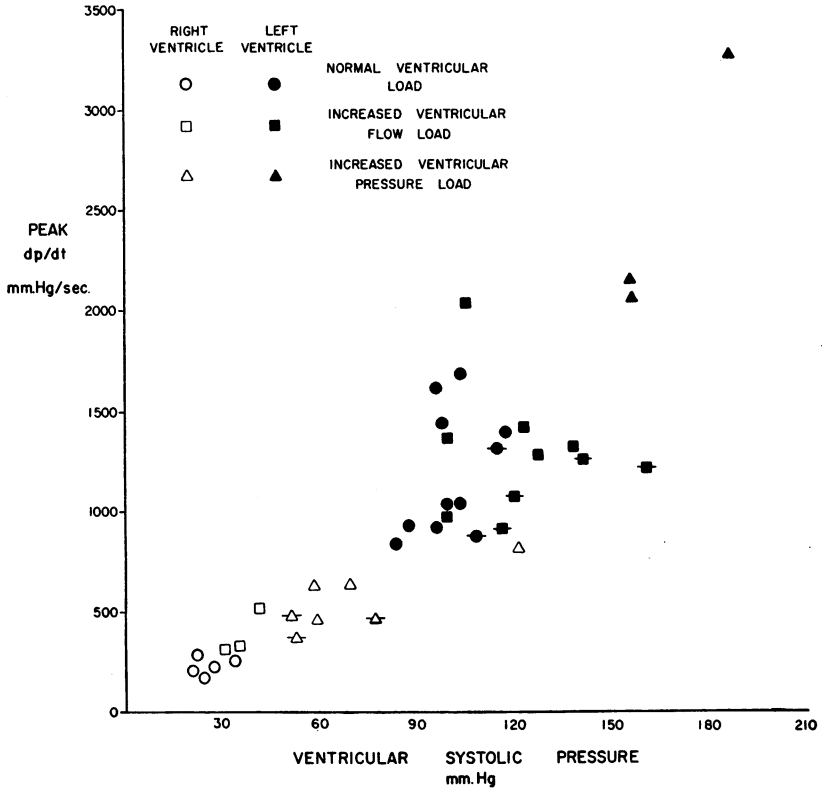

FIG. 3. RELATIONSHIP BETWEEN PD AND THE VENTRICULAR SYSTOLIC PRESSURE. The symbols with the horizontal lines represent the patients who had marked ventricular enlargement and had experienced congestive heart failure, as described in the text. The correlation coefficient and regression lines were calculated without inclusion of the data from these patients; the formula for the regression line is: PD = 15.3 systolic pressure − 254.

at least in part, to the diversity of cardiovascular abnormalities present in the patients who were studied, as well as the conditions existing at the time of study. Nonetheless, it was observed in both ventricles that the PD tended to be higher in patients with elevation of intraventricular systolic pressure than in those without. When the PD was related to the peak ventricular pressures, a significant correlation ($r = 0.85$) was evident (Figure 3). It was also observed that at any given ventricular systolic pressure, the PD was a function of the heart rate. Accordingly, when PD was related to the product of the systolic pressure and heart rate, a somewhat better correlation ($r = 0.92$) was evident (Figure 4). The data obtained from the patients with clinical evidence of marked myocardial failure tended to fall to the right of the regression lines in Figures 3 and 4; i.e., their PD's were relatively low for their systolic pressures and heart rates. When these patients were excluded from analysis, the coefficient of correlation between systolic ventricular pressure and PD rose to 0.91 (Figure 3) and between the product of systolic pressure and heart rate and PD it rose to 0.97 (Figure 4).

4. *Effects of acute intervention*

a) *Drugs.* Isoproterenol (1.5 μg intravenously) resulted in a striking increase in the PD in all four patients to whom it was administered (Table III and Figure 5). A clear-cut increase in heart rate was produced in only one of these four patients. Methoxamine, in doses that raised left ventricular systolic pressure between 25 and 37 mm Hg, and slowed the heart rate by an average of 11 beats per minute, had no significant effect on

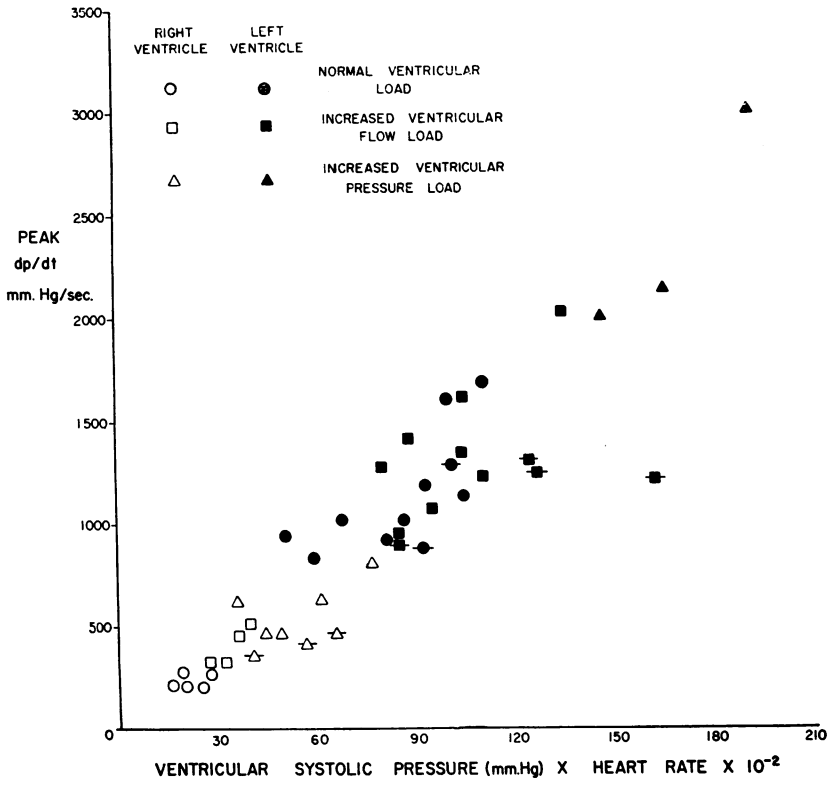

FIG. 4. RELATIONSHIP BETWEEN PD AND THE PRODUCT OF VENTRICULAR SYSTOLIC PRESSURE AND HEART RATE. The symbols indicating the patients who had experienced heart failure are the same as in Figure 3, and the correlation coefficient and regression line which are shown were calculated without inclusion of the data from these patients; the formula for the regression line is: PD = 0.157 (systolic pressure × heart rate) − 149.

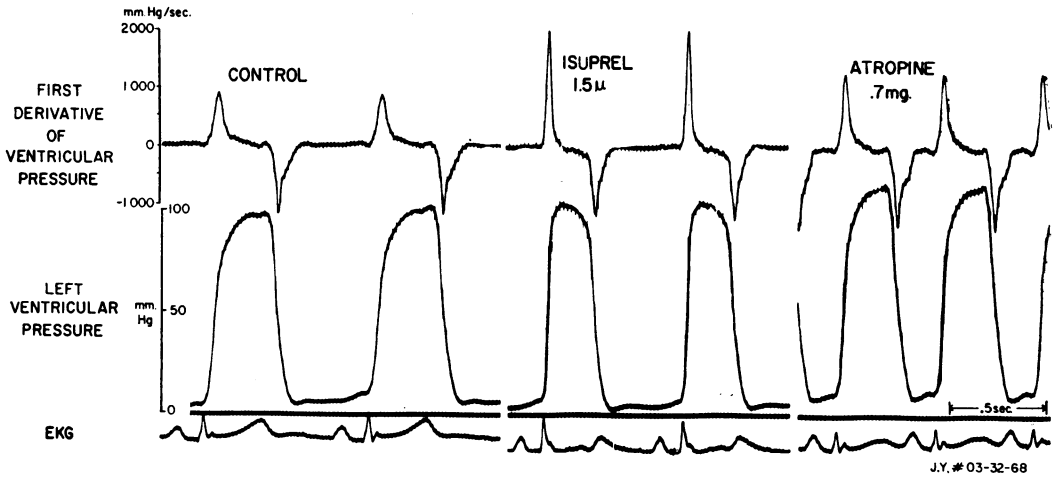

FIG. 5. SERIAL RECORDINGS OF LEFT VENTRICULAR PRESSURE AND OF DP/DT IN A 12 YEAR OLD GIRL WITH MILD PULMONIC VALVULAR STENOSIS. The first record (control) is in the basal state, the middle record after the administration of 1.5 μg isoproterenol (Isuprel), and the final record after 0.7 mg atropine.

TABLE III

Acute interventions *

Patient Diagnosis	Ventricle studied Method of study	Intervention	Peak dp/dt	Peak −dp/dt	Heart rate	Ventricular pressure s/d
J.Y. ASD	LV TC	Control	841	1,110	71	83/8
		Methoxamine, 2.4 mg	881	1,260	45	122/18
		Control	863	1,260	72	93/6
		Isuprel, 1.5 μg†	2,425	1,230	100	100/6
		Control	920	1,220	74	99/11
		Norepineph., 2.4 μg	1,456	1,330	50	151/11
		Control	845	1,180	72	93/8
		Atropine, 0.7 mg	1,370	1,500	119	109/11
C.W.C. ASD	LV TC	Control	943	661	58	87/9
		Isuprel, 1.5 μg	1,228	675	59	105/8
		Control	835	780	58	101/11
		Methox., 2 mg	737	960	51	126/9
		Control	750	870	54	115/11
		Atropine, 1 mg	1,372	1,290	112	138/5
M.J.S. ASD	LV TC	Control	938	915	86	96/6
		Methox., 2 mg	994	980	79	111/5
		Isuprel, 1.5 μg	1,197	1,040	86	111/3
		Atropine, 1 mg	1,008	1,060	111	98/1
J.V.G. Postop ADS	RV TC	Control	295	249	83	33/0
		Atropine, 1 mg	318	267	106	29/0
L.C.J. MS; TS	RV TC	Control	230	220	77	25/3
		Isuprel, 1.5 μg	453	254	79	32/3
		Control	196	230	68	23/0
		Methox., 1 mg	189	225	63	25/2
		Control	239	228	75	22/−2
		Atropine, 1 mg	298	304	95	23/0
J.P.H. ASD	LV TC	Control	1,009	1,070	88	99/7
		2 min. exercise	1,948	1,390	111	122/7
L.B.H. Funct M	RV TC	Control	165	126	99	22/5
		2 min. exercise	297	214	130	26/3
J.G.P. ASD	LV TC	Control	960		73	105/9
		2 min. exercise	1,520		102	120/9
J.B. PDA; coarc.	LV OR	Ductus closed	2,629	3,850	89	191/12
		Ductus opened	2,950	3,520	103	178/18
T.B. PDA	LV OR	Ductus closed	1,300	1,390	65	145/12
		Ductus opened	1,410	1,520	80	120/12
C.M.F. PDA	LV OR	Ductus closed	2,030	2,920	128	111/9
		Ductus opened	2,040	2,840	129	105/11
M.Y.J. PDA; MI	LV OR	Ductus closed	968	1,510	94	90/16
		Ductus opened	768	1,210	98	78/17

* Abbreviations same as in Tables I and II, plus: PDA = patent ductus arteriosus; Coarc. = coarctation of aorta; −dp/dt = maximum rate of fall of ventricular pressure.

† Isoproterenol.

the PD in the four patients to whom it was administered, in spite of raising the left ventricular end-diastolic pressure (Figure 6). One patient received norepinephrine in addition to isoproterenol and methoxamine; this drug elevated the PD but to a lesser degree than isoproterenol (Patient J. Y., Table III, Figures 5 and 6). Atropine, administered intravenously to five patients in doses of 0.7 to 1.0 mg, raised the heart rate by an average of 33 beats per minute and elevated the PD by values ranging from 7 to 83 per cent of the control values; the magnitude of the increase in the PD was related to the increase in heart rate (Table III).

b) *Exercise.* In the patients in whom the effects of exercise were studied, the PD_{LV} (two patients) and the PD_{RV} (one patient) were greatly augmented (Table III).

c) *Effects of opening a patent ductus arteriosus.* Immediately after the ductus was opened a significant increase in heart rate occurred in two patients, and in them a modest augmentation of PD_{LV} was observed. In the other two patients no significant change in heart rate occurred; PD_{LV} fell slightly in one, and remained unchanged in the other (Table III).

d) *Beat-to-beat changes in PD in atrial fibrillation.* It was consistently observed that the PD_{LV} varied with the interval between successive QRS complexes. Furthermore, the peak left ventricular systolic pressure and the aortic pulse pressure were directly proportional to the PD_{LV}; i.e., when the rate of left ventricular pressure rise was rapid, the peak systolic pressure and pulse pressure which were developed tended to be greater than when the PD_{LV} was relatively low. The results obtained in one patient are plotted in Figure 7 and are representative of those observed in the eight patients with atrial fibrillation who were studied.

e) *Ventricular premature contractions.* Four patients developed an occasional premature ventricular contraction in the course of the study. In each instance the PD of the premature contraction was significantly smaller than that observed during normal beats.

5. *Negative PD*

The maximum rate of decline of the ventricular pressure (negative PD) was usually of an order of magnitude similar to the PD of the ascending limb of the same ventricular pressure pulse. Interventions that increased myocardial contractility (e.g., intravenous isoproterenol, Figure 5) had little effect on the negative PD in spite of their striking augmentation of the positive PD. On the other hand, an acutely induced increase in the peak ventricular pressure or increase in heart rate tended to augment the negative PD (Table III).

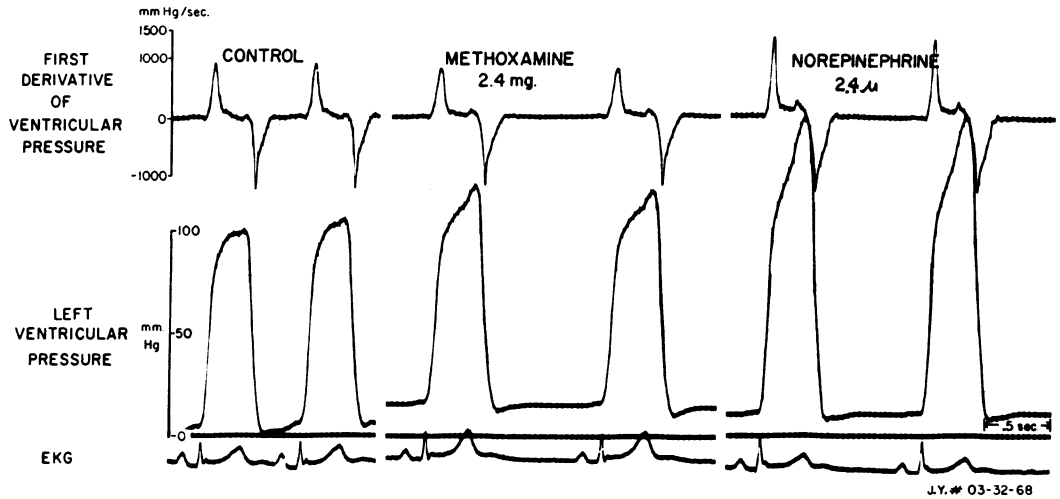

FIG. 6. SERIAL RECORDINGS OF LEFT VENTRICULAR PRESSURE AND OF DP/DT IN THE SAME PATIENT AS IN FIGURE 5. The tracings obtained in the control state are on the left, after methoxamine injection in the middle, and after norepinephrine injection on the right. These recordings were obtained at a slower paper speed than those reproduced in Figure 5.

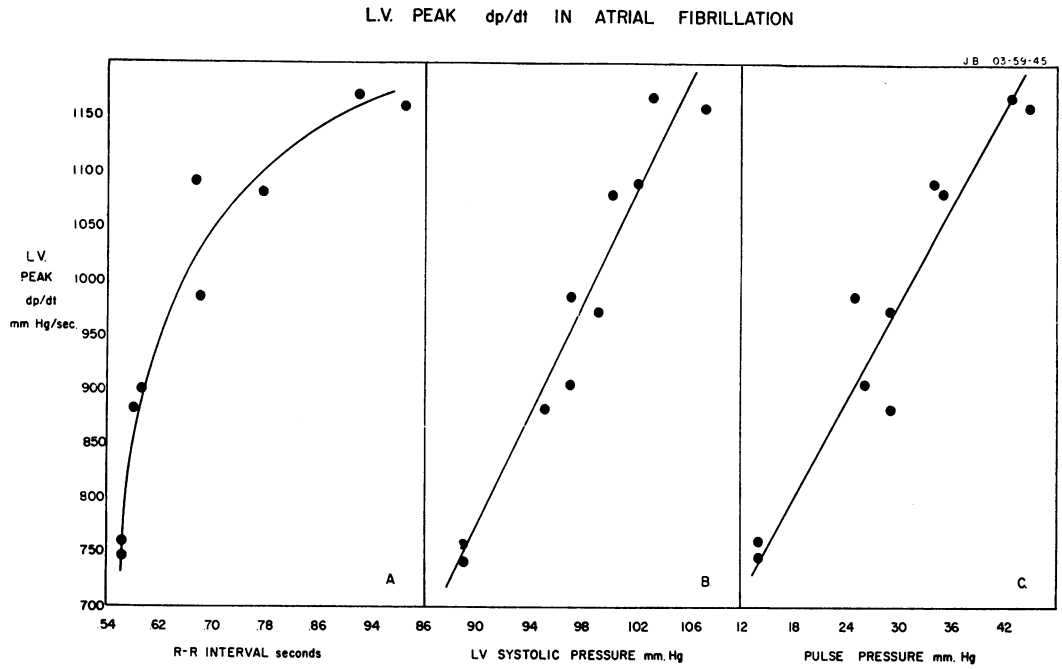

FIG. 7. GRAPHS ILLUSTRATING THE RELATIONSHIP BETWEEN THE LEFT VENTRICULAR PD AND (A) THE PRECEDING R–R INTERVAL; (B) THE LV SYSTOLIC PRESSURE; (C) THE BRACHIAL ARTERIAL PULSE PRESSURE OF THE SAME BEAT IN A PATIENT WITH RHEUMATIC MITRAL VALVE DISEASE AND ATRIAL FIBRILLATION.

DISCUSSION

Sarnoff and Mitchell have recently defined an increase of myocardial contractility as occurring "when from any given end-diastolic pressure or fiber length, the ventricle produces more external stroke work and more stroke work per systolic second. Implicit in this definition is an increased rate of development of tension when contractility increases" (17). Rushmer, Smith and Franklin have demonstrated an increase in the rate of pressure development in the left ventricle when myocardial contractility was augmented by the administration of catecholamines, by muscular exercise, or by hypothalamic stimulation (18). The observations of these and other investigators (1–11) are all compatible with the view that the rate at which ventricular pressure is developed reflects a fundamental property of contracting myocardium. Accordingly, it was thought that measurement of this parameter would provide an approach to the study of ventricular contractility in intact, unanesthetized man.

It is well established that certain sympathomimetic amines, such as isoproterenol and norepinephrine, augment myocardial contractile force, while others, such as methoxamine, fail to do so (19, 20). It could thus be anticipated that if changes in the PD reflected changes in myocardial contractility, the rate of pressure rise should be elevated by administration of the cardioactive sympathomimetic amines, but not modified by the drugs that have no direct cardiac effects; this indeed was found to be the case (Figure 5). It was also demonstrated that muscular exercise and atropine-induced tachycardia raised the PD. The increase noted with tachycardia may be analogous to the so-called "treppe" phenomenon, described by Bowditch (21).

Siegel and Sonnenblick, utilizing an isovolumetrically-beating ventricle, as well as a cat papillary muscle preparation, have demonstrated that rate of development of tension is dependent on the length of the muscle fiber at the onset of contraction (8). In patients with mitral valve disease and atrial fibrillation, variations in the duration of diastole result in alterations in the degree of ventricular filling and, therefore, in the ventricular end-diastolic volume and fiber length (22). In the present study good correlations between the PD and the duration of the filling period (Figure

7, A), the peak sytolic ventricular pressure (B) and the arterial pulse pressure (C) were observed. These observations suggest that in these patients with mitral stenosis and atrial fibrillation, the PD correlates closely with the end-diastolic fiber length during a series of consecutive cardiac cycles.

Unlike the effects of acute elevations of ventricular end-diastolic volume, hemodynamic abnormalities which result in a chronic augmentation of ventricular stroke volume did not result in abnormal values of the PD. In contrast, the PD correlated well with the peak systolic pressure chronically developed by the ventricle, and in this correlation both ventricles fell on the same regression line (Figure 3). A number of factors may be involved in this relationship. Sandler, Dodge and Hay have recently presented evidence indicating that the thickness of the ventricular wall increases in proportion to the systolic pressure which is chronically developed by the ventricle (23). Taking the chamber size and wall thickness into consideration they have calculated that the tension developed by each unit of myocardium tends to remain constant, regardless of the level of systolic pressure which the ventricle sustains. In patients with a ventricular "pressure load" and an increased muscle mass of hypertrophied myocardium, the elevated systolic pressure is developed in the same time interval that is required by the normal myocardium to reach a normal ventricular systolic pressure. In view of these findings of Sandler and co-workers, it is possible that the rates of development of tension of each myocardial unit are similar in the normal and in the hypertrophied heart. Accordingly, it may be postulated that the relatively high PD's observed in ventricles that developed elevated pressures reflect the increased muscle mass which is present. The differences in the PD's observed between the two ventricles in the patients without hemodynamic abnormalities could also be similarly explained.

The correlation between PD and peak systolic pressure was improved slightly when rate was also taken into consideration (Figure 4). It is likely that the sympathetic stimulation of myocardial contractility was greater in patients with rapid heart rates than in those with slower rates, and that this effect, as well as the stimulation of myocardial contractility provided by an increase in heart rate per se—i.e., by the "treppe" phenomenon (21, 24)—was responsible for the improvement in this correlation.

The patients who had experienced congestive heart failure and had roentgenographic evidence of left ventricular enlargement and elevation of the ventricular end-diastolic pressure, tended to have lower PD's than might have been anticipated by their systolic ventricular pressure and heart rate (Figures 3 and 4). Two explanations for this finding may be advanced. First, when the law of Laplace (25) is considered, it is apparent that any given rate of development of tension by the myocardium would result in a slower rate of pressure rise and, hence, in a lower PD in a dilated than in a normal-sized heart. Second, it is possible that the depression of myocardial contractility which may have been present in these patients is responsible for their lowered PD's. In support of this view are the demonstrations by Wiggers in the dog with an intact circulation (6) and by Buckley and Zeig in an isolated heart preparation (10) that acute left ventricular failure is accompanied by a decrease in the rate of ventricular pressure rise. Regardless of the specific mechanism responsible for lowering the PD in patients with congestive heart failure, it is possible that analysis of the first derivative of the ventricular pressure pulse may provide a simple means of quantifying depressed ventricular function in man.

The findings in this investigation are not consonant with the general impression (26) that the rate at which ventricular pressure falls usually parallels the rate at which it rises (26) (Table III). However, Zeig, Buckley and Porter have recently shown that contraction and relaxation can be altered independently by acutely changing ventricular work loads (11).

SUMMARY

Since observations in experimental animals have suggested that the rate at which ventricular pressure rises is a function of myocardial contractility, it was thought that determination of the rate of change of ventricular pressure might permit study of myocardial contractility in intact man. The first derivative of the ventricular pressure pulse was continuously computed by means of an electronic differentiating circuit in 40 patients. In order to avoid the artifacts inherent in pressures

measured by means of standard catheter-manometer systems, these studies were confined to pressures obtained from a catheter with a high-fidelity micromanometer mounted at its tip or by puncture of the ventricle with the manometer directly attached to the needle. The peak first derivative (maximum rate of pressure rise) in patients without hemodynamic abnormalities ranged between 841 and 1,696 mm Hg per second in the left ventricle, and between 223 and 296 in the right ventricle. Interventions which acutely augmented myocardial contractility, such as muscular exercise, isopropyl norepinephrine, norepinephrine, and atropine, resulted in striking increases in the peak derivative. Beat-to-beat changes in ventricular filling in patients with atrial fibrillation produced changes in the peak derivative which suggested that the latter parameter was also dependent upon ventricular end-diastolic volume. In the control state the peak derivative in both ventricles demonstrated a linear correlation with the peak systolic pressure and a somewhat better correlation with the product of systolic pressure and heart rate.

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