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Left and right heart haemodynamics during spontaneous angina pectoris

Comparison between angina with ST segment depression and angina with ST segment elevation

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The function of both right and left sides of the heart was studied during spontaneous attacks of angina pectoris at rest in 7 patients showing ST depression (type I) and 4 showing ST elevation (type II) during the attack.

In none of the 44 type I attacks and 29 type II attacks which were recorded did circulatory changes precede the cardiographic changes; the latter were invariably the initiating events. The subsequent haemodynamic changes were different in the two groups.

Type I attacks showed: a) a brief fall in arterial pressure, accompanied by b) a rise of right atrial and pulmonary wedge pressures and c) a decrease of cardiac output, right and left stroke work, the mean rate of systolic ejection, and indirect left ventricular pre-ejection dP/dt. In the course of the attack a hypertensive phase followed, which was paralleled by an increase of heart rate, cardiac output, left and right stroke work, and mean systolic ejection rate, left dP/dt; right atrial pressure and wedge pressure remained raised. All of the circulatory functions started to revert towards the pre-attack levels coincident with the waning phase of the electrocardiographic alteration, the latter occurring either spontaneously or after nitroglycerin.

Type II attacks for the entire duration of the electrocardiographic changes showed : a) a reduction of arterial pressure, cardiac output, right and left stroke work, mean systolic ejection rate, and left dP/dt, b) a rise of right atrial and wedge pressures, and c) quite small changes of heart rate. When the electrocardiogram started to revert to the pre-attack aspect, the cardiac function rapidly improved and, after a supernormal phase, returned to the basal levels in about 2 minutes.

It is concluded: 1) that no circulatory factor interfering with the mechanical effort of the heart is responsible for eliciting spontaneous angina: 2) that in type I attacks right and left ventricular impairment occurs which recovers rapidly, possibly through a sympathetic compensation; 3) that in type II attacks dysfunction of both sides of the heart occurs and persists throughout the episode of electrocardiographic alteration; 4) that the dynamic impairment is probably more severe in type I than in type II angina.

Anginal pain coming on at rest, unrelated to deliberately induced stress or any other identifiable eliciting factor is defined as 'spontaneous'. It may be associated with ST segment depression, the common pattern of angina pectoris, which we call angina type I, or with ST segment elevation on the electrocardiogram, Prinzmetal's variant form (Prinzmetal *et al.*, 1959), which we call type II.

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During the past decade the systemic and left ventricular haemodynamics of type I angina have been investigated by means of continuous monitoring (Roughgarden, 1966; Rosland, 1969), during heart catheterization (Müller and Rørvik, 1958; Cohen *et al.*, 1965; Gorlin, 1965), and also in unrestricted patients going about their normal lives (Littler *et al.*, 1973). It is generally agreed that type I angina is accompanied by a rise in arterial pres-

sure and that major changes in the greater and lesser circulation occur, consistent with impaired left ventricular function, but there are still areas that require further elucidation. Abundant data indicate that increased cardiac mechanical activity is the major precipitating mechanism in effort and in pacing-induced angina. The factors involved in, or responsible for, spontaneous type I angina are less certain. A correlation between the time of onset of systemic hypertension, increase in left ventricular end-diastolic pressure, and electrocardiographic abnormalities has not been fully established. It is also not clear whether anginal pain is responsible for the rise in arterial pressure and whether the latter contributes to left ventricular dysfunction; in addition there is lack of agreement as to whether the basis of such dysfunction is transient left ventricular failure, reduced ventricular compliance, or increased myocardial wall stiffness. Finally, the function of the right heart and its relation with that of the left has not been investigated. A purpose of this report is to present our observations which may contribute to the elucidation of these points.

As regards angina with ST segment elevation (our type II), some of the aspects listed above have been clarified in a previous report from this laboratory (Guazzi *et al.*, 1971). A comparison between the data on spontaneous angina with ST segment depression (Müller and Rørvik, 1958; Cohen *et al.*, 1965; Gorlin, 1965; Roughgarden, 1966; Littler *et al.*, 1973) and the results of our previous study of the Prinzmetal's form (type II) (Guazzi *et al.*, 1971) indicates that some differences exist between the two types. Another purpose of this report is to assess and to define more precisely, if possible, such differences. In our earlier study of the Prinzmetal form right heart function was not investigated; additional subjects suffering from this type of angina have been examined including this aspect of the circulation.

Subjects and methods

The more frequent the anginal attacks, the more detailed can the haemodynamic observations be, since various circulatory aspects can be analysed within the same individual in separate episodes of angina. Accordingly from 23 patients with type I and 9 with type II attacks, 7 and 4 subjects respectively who had a daily occurrence of at least 10 spontaneous episodes, were selected for the investigation.

Each subject gave a history of spontaneous praecordial pain of variable occurrence for periods ranging from 2 months to 3 years. None of them had symptoms or signs (clinical or radiological) of valvular disease. In patients with angina type I the basal electrocardiogram was normal in 2 cases; it showed an old myocardial infarction in 2 cases, and flat or negative T waves in the left-sided leads in 3 cases. In angina type II, in 1 case the electrocardiogram presented flat T waves in the inferior leads and was normal in the other 3 cases. In group I the main electrocardiographic abnormality during angina was ischaemic ST segment depression in the leads reflecting left ventricular epicardial potentials, sometimes accompanied by T wave inversion; in a few subjects, and only in some of their anginal episodes, ST segment sagging was preceded or accompanied by peaking of the T wave. In type II patients, ST segment elevation in the inferior leads in 3 cases, and in the left-sided leads in 1, was the major electrocardiographic feature during angina. In both groups, some patients in occasional anginal episodes developed cardiac arrhythmias, such as premature ventricular contractions or short runs of ventricular tachycardia.

Over a one-week period, daily recording in a diary of the time and circumstances of the attacks indicated the hours of the day when spontaneous angina occurred with the highest frequency for each individual patient. The haemodynamic studies were carried out during these hours. Each patient gave free consent to the investigation in the full knowledge of the procedures to be undertaken. In order to minimize the possible effect of emotion or tension, they were familiarized with the investigators and the laboratory before the study. Patients came to the laboratory on three consecutive days. On the first day they merely lay comfortably in bed for a few hours. On the second day they lay in bed for several hours while continuous electrocardiographic recordings were made.On the third day the circulatory investigation was performed for an average duration of 7 hours. Our object was to obtain as much information as possible using safe techniques without discomfort to the patients.

Haemodynamic studies

Studies were carried out in the fasting state without premedication in the supine position. The following variables were continuously recorded, at a variable paper speed, on a Hewlett-Packard 8-channel ink recorder: electrocardiogram, phonocardiogram, heart rate, carotid sphygmogram, systemic arterial pressure, pulmonary arterial or wedge pressure, and right atrial pressure. The electrocardiogram was also monitored on an oscilloscope; during low speed paper recordings the electrocardiographic pattern could be inspected on the oscilloscope tracing, which was set at a sweep speed of 25 mm/s. However, the changes occurring during angina were so clear that they could be consistently detected even at a speed as slow as 0.5 mm/s.

Under local anaesthesia, a balloon-tipped catheter (Swan *et al.*, 1970) was inserted percutaneously in an antecubital vein, floated under fluoroscopy to the pulmonary artery, and advanced, when necessary, to the wedge position. For the measurement of right atrial pressure a polyethylene catheter was also inserted into an antecubital vein and positioned into the right atrium. An 18-gauge 'teflon' catheter needle, introduced into the brachial artery, was used to sample indocyanine green for cardiac output and to monitor arterial pressure. Pressures were determined with Statham P23De and P23Db

strain gauge transducers. Dye dilution analyses of cardiac output were performed after injection of indocyanine green (5 mg) into the right atrium and withdrawal from the brachial artery. Blood withdrawn during inscription of the indicator dilution curves was immediately reinfused; at the end of the study only the amount (50 ml) necessary for calibrating the densitometer (Gilford) was retained. The area under each dye curve was measured by a planimeter as well as by a digital computer (Gilford), and cardiac output was calculated by the standard Hamilton method. Systemic peripheral resistance was calculated from the formula: SPR (dynes. sec. cm^{-5} = $\frac{(mAP - mRAP) \times 1332 \times 60}{CO\ (ml/min)}$, where mAP and mRAP are, respectively, the mean arterial and mean right atrial pressures in mmHg. The electrocardiographic leads recorded were those that showed the most evident repolarization alterations during the attacks. Beat-to-beat variations of heart rate were detected by a Cardio-Tach Preamplifier (Hewlett-Packard 350–3400 A). Left ventricular pre-ejection period and ejection time were calculated from the electrocardiogram, carotid sphygmogram (through a Sanborn APT/16/1 transducer), and phonocardiogram taken at end-expiration, recorded at a paper speed of 100 mm/s, according to the method indicated by Weissler, Harris, and Schoenfeld (1968). The right ventricular ejection time was measured from the pulmonary arterial tracing (from the beginning of upstroke to the trough of the incisura) recorded at a speed of 100 mm/s. The indirect mean pre-ejection dP/dt of the left ventricle was calculated by subtracting from the diastolic arterial pressure the left ventricular filling pressure (pulmonary wedge pressure), and dividing by the simultaneous values of the pre-ejection period (Diamond *et al.*, 1972). Right and left ventricular mean rates of systolic ejection (index) were determined by dividing the stroke index by the ejection times of the two ventricles. Right and left ventricular stroke work (index) were calculated, respectively, from the following formulae:

$$RSW\ (g\ m\ per\ m^2) = (mSPP - mRAP) \times SI \times 0.136$$
$$LSW\ (g\ m\ per\ m^2) = (mSAP - mWP) \times SI \times 0.136$$

where SI = stroke index in ml/m^2; mSPP = mean systolic pulmonary pressure in mmHg; mRAP = mean right atrial pressure in mmHg; mSAP = mean systolic arterial pressure in mmHg; mWP = mean pulmonary wedge pressure in mmHg.

The patients held a push button for the remote control of a marker of the recording system. They were instructed to keep it pressed for the entire duration of the pain, so that a good time relation between pain and electrocardiographic and circulatory alterations could be recorded. Each episode of the electrocardiographic abnormality was followed by detailed questioning of the patient in order to assess his pain.

From the continuous record, measurements of brachial, right atrial, pulmonary arterial and wedge pressures, and heart rate were made during the four 20-second intervals (indicated as A, B, C, D) which just preceded the onset of the electrocardiographic changes. During the ST segment depression or elevation, measurements were taken at the following times: onset of the electrocardiographic abnormality (E); waxing period (F, G); beginning of the steady state (H); during the steady state (I, L); beginning of the waning period (N, O); at the moment when the electrocardiogram reverted to its usual appearance (P); 30 seconds (Q) and 90 seconds (R) after reversion of the electrocardiogram to its original aspect. Measurements of the left ventricular systolic time intervals and of the right ventricular ejection time were made at all the times previously indicated. Cardiac output was determined at the times shown in the Figs.

Results

In 3 patients with type I and in 2 with type II angina, episodes of typical electrocardiographic abnormalities were recorded which were completely unperceived by the patients. Because no qualitative difference was detected in the haemodynamic pattern between such episodes and those accompanied by pain, the related circulatory data have been pooled together in both groups.

Angina type I

Altogether 44 episodes of type I anginal attacks were recorded during the circulatory investigations. The averages ($\pm$ SD) of the circulatory measurements carried out at the various moments during the anginal attacks, as described above, are given in Table 1. The most detailed study was accomplished in patient L.F. in whom 12 episodes of electrocardiographic alteration were recorded. The observations made in this subject have been taken as an example representative of the entire group and have been presented graphically in Fig. 1. Arterial pressure, heart rate, and right atrial pressure show the means of 12 episodes of electrocardiographic abnormality analysed at selected times as indicated under the Methods section. The graph of the pulmonary wedge pressure represents the mean of measurements done on 6 episodes. The values of cardiac index were obtained by the mean of two measurements at time A and L and by a single measurement of cardiac output at the other times indicated in Fig. 1.

From the onset of the abnormalities on the electrocardiogram a brief fall of arterial pressure was observed which was paralleled by a reduction of cardiac output and an increase of peripheral resistance. The initial hypotensive phase was followed by a rapid and progressive rise of arterial pressure (towards levels definitely higher than the preanginal ones), due to both an increase of output and a further increase of resistance. An increase of heart rate accompanied the pressure rise. The circulatory pattern then remained unchanged for the entire

TABLE 1 *Averages (± standard deviation) of the circulatory values at subsequent moments during angina in*

	A	*B*	*C*	*D*	*E*	*F*	*G*	*H*
HR	74±6	74±6	72±9	72±6	74±8	80±5	86±8	88±7
(b/min)	(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
SAP	141±18	140.7±19.1	142.4±17.5	140.3±18.2	142.3±19.2	129.8±18.2	128.5±17.3	141.3±19.2
(mmHg)	(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
DAP	82.2±9.8	82.3±10	83±9.3	82.2±9	83±9.7	70.5±10.9	69.3±12.2	83±11.6
(mmHg)	(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
mRAP	6±1.2	6±1.4	5.7±2	5.8±1.8	5.9±2	7.8±2.3	9±1.7	11.4±3.6
(mmHg)	(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
mWP	11.2±3.3	10.8±4	10.9±3.7	11±3	11.3±2.6	15.3±3.7	17±4	18±4.4
(mmHg)	(21)	(20)	(17)	(21)	(18)	(23)	(23)	(20)
RSW	5.88±2.4	—	—	—	5.56±2	3.23±1.44	—	—
(g m/gm²)	(14)				(11)	(9)		
LSW	48.9±17.4	—	—	—	47.6±19.5	32.5±13.4	—	—
(g m/gm²)	(14)				(11)	(9)		
RMSEJR	123.4±16.4	—	—	—	122.4±15.2	94.5±15.3	—	—
(ml s⁻¹m⁻²)	(15)				(11)	(11)		
LMSEJR	150.8±19.9	—	—	—	151±20.6	107±13	—	—
(ml s⁻¹m⁻²)	(15)				(11)	(11)		
dP/dt	0.79±0.2	—	0.77±0.16	—	0.78±0.13	0.61±0.1	0.69±0.1	0.77±0.15
(mmHg/ms)	(16)		(16)		(15)	(16)	(16)	(14)
CI	3566±723	—	—	—	3580±690	2472±513	—	—
(ml min⁻¹m⁻²)	(15)				(11)	(11)		

A, B, C . . . . Q, R = intervals during the period of observations, as defined in the text.
HR = heart rate; SAP = systolic arterial pressure; DAP = diastolic arterial pressure; mRAP = mean right atrial pressure; (index); RMSEJR = right ventricular mean rate of systolic ejection (index); LMSEJR = left ventricular mean systolic ejection, numbers of observations at the various moments. CI = Cardiac index. See text for details.

TABLE 2 *Averages (± standard deviation) of the circulatory values at subsequent moments during angina in*

	A	*B*	*C*	*D*	*E*	*F*	*G*	*H*
HR	80±8	82±6	80±8	80±7	82±8	84±5	85±7	84±6
(b/min)	(29)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
SAP	147.6±15.5	145.5±16.5	148.7±15.6	146.5±17.2	146.7±18.5	141.4±16.4	137.7±13.5	133.5±14.2
(mmHg)	(29)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
DAP	83.4±7.9	82.3±6.7	83.5±8.6	83.4±7	85±8.2	80.1±7.8	76.7±7.5	75.4±8
(mmHg)	(29)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
mRAP	5.5±1.3	5.3±1.4	5±1.2	5±1.4	5±1	7.1±0.9	9.5±1.6	11.3±1.8
(mmHg)	(28)	(26)	(25)	(28)	(24)	(28)	(24)	(24)
mWP	7.5±1.4	7±1.2	7.8±2.6	7.7±2.3	7.6±1.3	9.7±1.5	12±1.7	13.9±1.7
(mmHg)	(13)	(13)	(13)	(13)	(13)	(13)	(12)	(13)
RSW	3.8±0.7	—	—	—	3.9±0.6	—	—	2.7±0.5
(g m/m²)	(9)				(8)			(6)
LSW	79.2±19.8	—	—	—	74.7±17.9	—		51.2±10.2
(g m/m²)	(9)				(8)			(6)
RMSEJR	142±20.4	—	—	—	150±15.8	—	—	118.7±13.4
(ml s⁻¹m⁻²)	(9)				(7)			(5)
LMSEJR	150.5±21.5	—	—	—	153±13.3	—	—	115.8±15.2
(ml s⁻¹m⁻²)	(9)				(7)			(5)
dP/dt	0.85±1	—	0.83±9	—	0.86±0.6	0.80±0.12	0.72±0.1	0.66±0.1
(mmHg/ms)	(11)		(11)		(9)	(10)	(10)	(11)
CI	3872±428	—	—	—	3841±350	—	—	2440±321
(ml min⁻¹m⁻²)	(9)				(8)			(6)

Abbreviations as in Table 1.

patients with type I angina pectoris

I	*L*	*M*	*N*	*O*	*P*	*Q*	*R*
92±9	93±10	92±8	92±6	90±7	86±8	80±10	77±7
(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
150.6±21.2	169.2±19.7	176.1±20.3	169.1±19.5	155.1±18.4	151.5±18.1	146.3±18.6	142.2±18.1
(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
93.3±9.3	95.8±7.5	98.4±7.7	98.3±75	96.1±8.6	91.1±7.5	86.7±7.6	82.6±9.4
(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
11.7±2.8	12.5±3	11.7±1.8	12±2	10.4±1.5	8.1±3	7.5±2.2	6.4±1.3
(44)	(44)	(44)	(44)	(44)	(44)	(44)	(44)
17.4±4.4	18.5±4.2	18.3±3.4	16.9±3.5	15.5±3.5	14±3.3	13.1±3.2	11.4±3.3
(19)	(19)	(18)	(21)	(19)	(18)	(21)	(21)
5.17±1.65	5.52±1.63	—	—	—	—	5.98±2.13	5.88±2
(9)	(8)					(14)	(14)
52.0±16.3	61.4±20.8	—	—	—	—	52.9±16.9	49.7±17
(9)	(8)					(14)	(14)
120.6±20.6	126.4±17.8	—	—	—	—	127±18.9	123.8±17.7
(10)	(11)					(15)	(14)
139.9±19.8	151.3±20.7	—	—	—	—	153±20.2	148.4±20.3
(10)	(11)					(15)	(14)
0.83±0.12	0.87±0.14	0.89±0.18	0.94±0.06	0.88±0.11	0.85±0.12	0.82±0.15	0.78±0.09
(16)	(16)	(14)	(16)	(15)	(13)	(16)	(16)
3349±658	3746±673	—	—	—	—	3582±655	3513±703
(10)	(11)					(15)	(14)

mWP = mean pulmonary wedge pressure; RSW = right ventricular stroke work (index); LSW = left ventricular stroke work rate (index); dP/dt = left ventricular indirect mean pre-ejection dP/dt; CI = cardiac index. Figures in parenthesis represent the

patients with type II angina pectoris

I	*L*	*M*	*N*	*O*	*P*	*Q*	*R*
84±6	82±7	84±8	82±7	80±6	81±5	80±6	82±6
(29)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
131.8±15.6	130.7±14.8	131.4±16.5	142.3±12.6	153.5±18.2	158.4±14.7	155.7±13.2	147.5±16
(29)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
74.5±7.3	74.1±9.2	73.8±6.7	82.1±10.6	87±9.8	88.5±8.9	85.8±6.5	83.2±7.3
(29)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
10.8±2.6	11±3.1	10.5±2.8	8.6±1.8	8.4±1.2	7.2±2.6	6.8±2	6.1±1.3
(28)	(29)	(29)	(29)	(29)	(29)	(29)	(29)
15.3±1.9	16±1.9	16.7±2.2	12.8±1.9	9.8±0.8	9.5±1.3	8±1	6.7±1.4
(13)	(12)	(11)	(13)	(13)	(12)	(13)	(13)
—	2.5±0.6	—	5±1.2	—	—	—	3.7±0.8
	(6)		(7)				(9)
—	50.3±11.6	—	92.3±14.2	—	—	—	78.4±18.8
	(6)		(7)				(9)
—	109.1±12	—	159.2±14.8	—	—	—	144±19.7
	(5)		(7)				(8)
—	111.2±11.1	—	176±15.8	—	—	—	151.2±21.3
	(5)		(7)				(8)
0.59±0.07	0.61±0.06	0.60±0.08	0.88±0.09	0.95±0.12	0.99±0.11	0.94±0.14	0.85±0.10
(11)	(11)	(10)	(11)	(11)	(9)	(10)	(11)
—	2491±413	—	4116±311	—	—	—	3770±310
	(6)		(7)				(9)

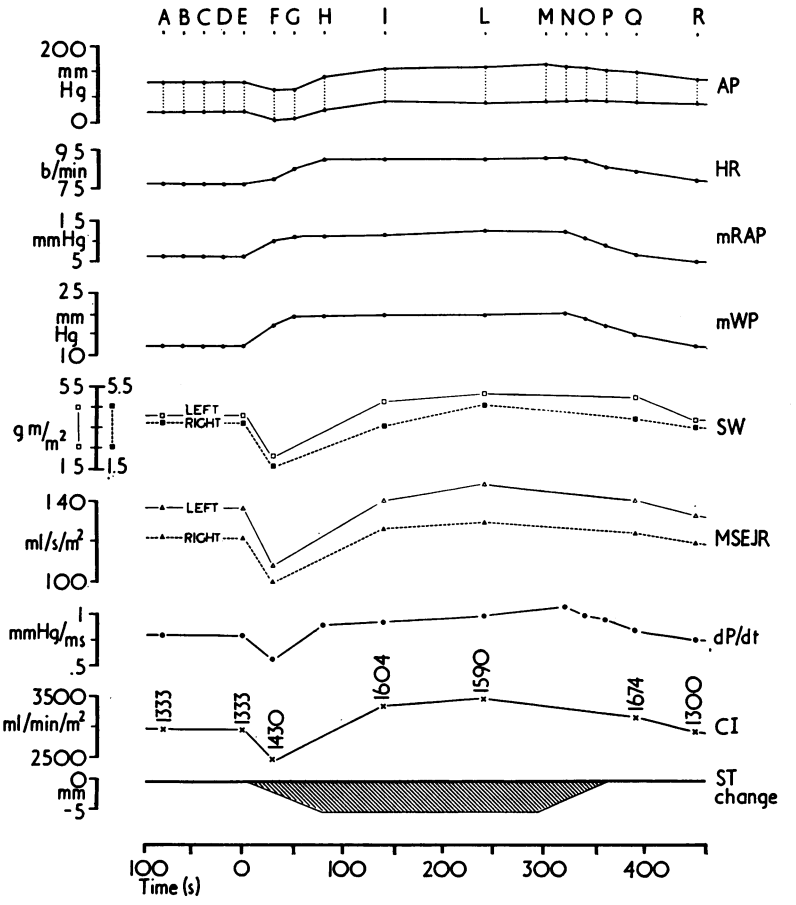

FIG. 1 *Schematic representation of the pattern of some circulatory functions during anginal attacks (type I) in the patient L.F. The measurements were made at selected times indicated at top, as described under Methods. From top: AP, arterial pressure; HR, heart rate; mRAP, mean right atrial pressure; mWP, mean pulmonary wedge pressure; SW, stroke work index (left and right); MSEJR, mean systolic ejection rate (left and right); dP/dt, left ventricular mean pre-ejection dP/dt; CI, cardiac index. Together with the values of CI the simultaneous values of systemic peripheral resistance (dynes. sec. cm^{-5}) are reported. The shaded area indicates the duration, the extent, the waxing, and the waning periods of ST segment depression. See text for further details.*

duration of the steady period of the electrocardiogram alteration. The following changes were simultaneously observed. From the beginning (time E) through the waxing and the steady period (until time M) of the ST segment depression, the right and left ventricular filling pressures (mean right atrial and pulmonary wedge pressures) rose, remaining constant or showing a further rise at the same time as, or preceding, the onset of pain. As compared to the preanginal state, right and left ventricular function, evaluated through the relation between filling pressure and stroke work, showed a clear reduction concomitant with the initial arterial pressure fall, and a subsequent increment during the hypertensive phase. A pattern similar to that of stroke work was shown by the right and left ventricular mean rates of systolic ejection, and the left mean pre-ejection dP/dt. Contemporaneously with the beginning of normalization of the electrocardiogram (time M), either occurring spontaneously or after nitroglycerin, the various circulatory functions reverted towards the preanginal values.

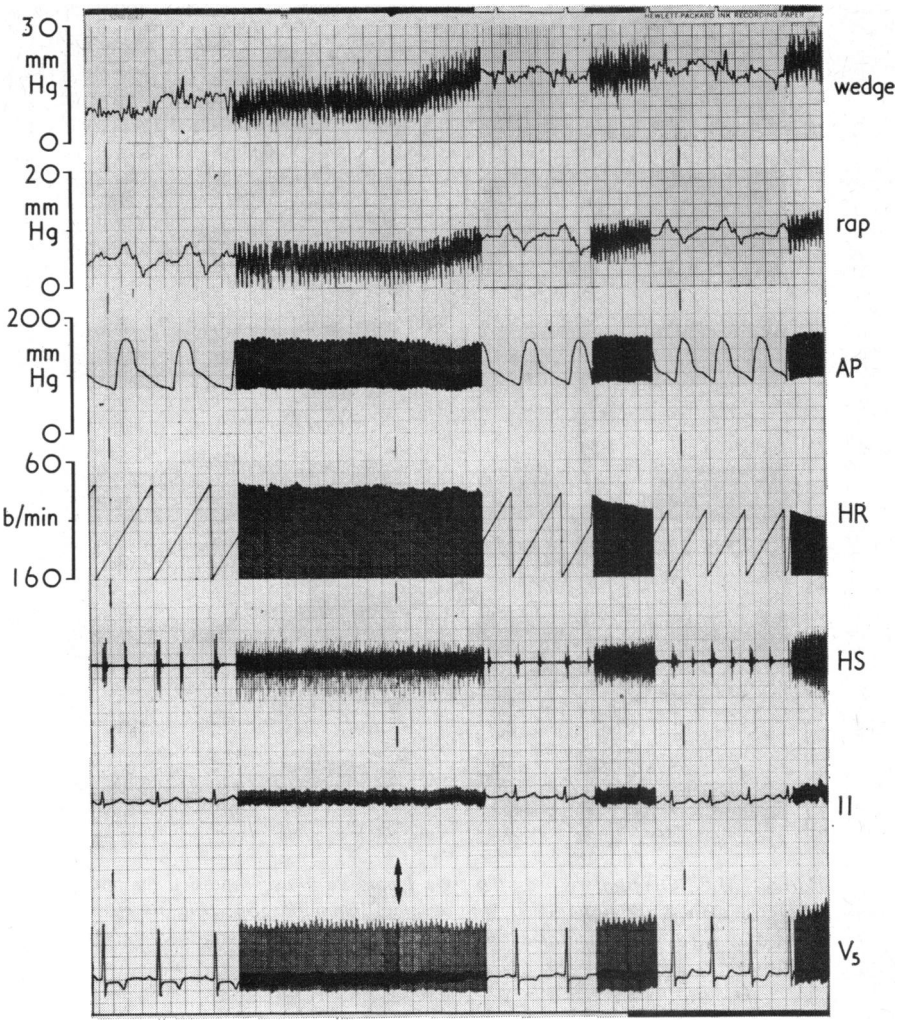

FIG. 2 *Patient L.F. Original record showing the waxing and part of the steady period of a type I anginal episode. Time marker; wedge, pulmonary wedge pressure; rap, right atrial pressure; AP, brachial arterial pressure; HR, heart rate; HS, heart sounds; II, lead II of the electrocardiogram; V5, lead V5 of the electrocardiogram. The heavy line at the bottom indicates pain. The onset of the attack is signalled by the arrow. Note the progressive depression of the ST segment.*

Fig. 2 reproduces original records from the same patient as Fig. 1, taken during an episode of electrocardiographic abnormality accompanied by pain. Transient electrocardiographic abnormalities of myocardial ischaemia without anginal pain are shown in Fig. 3 (patient M.C.); the circulatory behaviour is qualitatively similar to that of the painful episode reproduced in Fig. 2. An example of cardiac arrhythmias which accompanied some of these anginal attacks is represented in Fig. 4; the electrocardiographic and circulatory changes caused by nitroglycerin are also recorded. In this episode of angina, sagging of the ST segment is accompanied by peaking of the T wave.

A curious phonocardiographic feature was observed in patient M.F.: during the periods of pain he developed a systolic non-ejection click interpretable as a sign of mitral dysfunction. The click was not

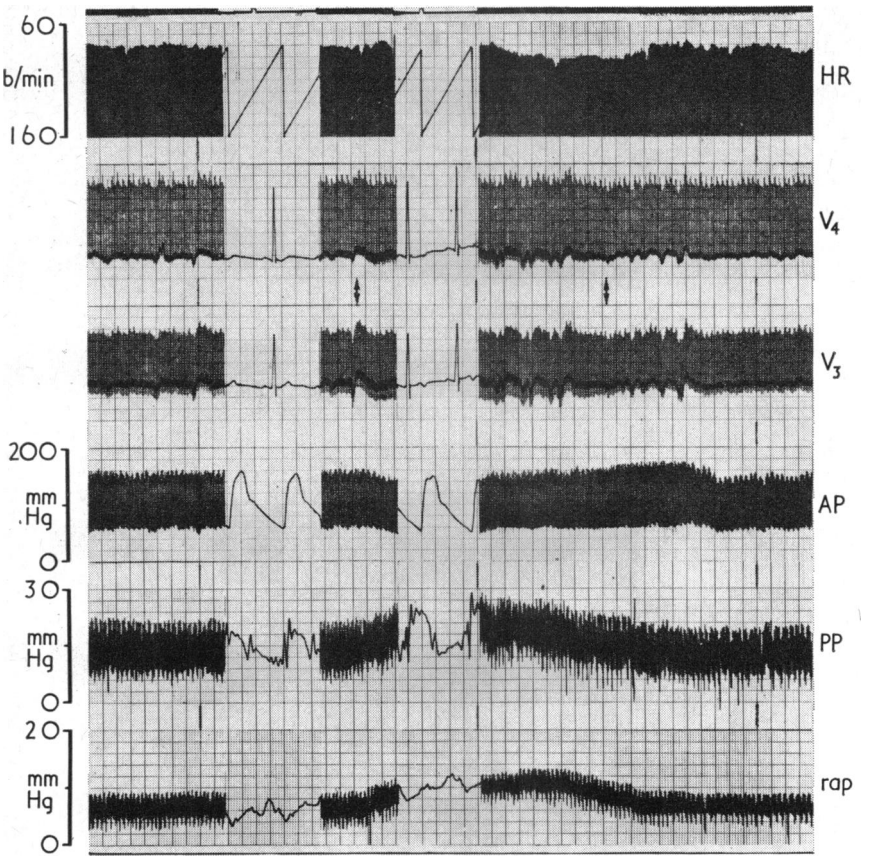

FIG. 3 *Patient M.C. Original record of a type I episode unaccompanied by pain. The onset and the end of the attack are signalled by the arrows. From the top: time marker; HR, heart rate; leads V4 and V3; AP, brachial arterial pressure; PP, pulmonary arterial pressure; rap, right atrial pressure.*

detected, as shown in Fig. 5, when pain was absent, even though there were equal electrocardiographic alterations before the onset of pain.

Angina type II

Twenty-nine episodes of type II angina were investigated in this study. Table 2 reports, for the entire group of these patients, the averages (± SD) of the haemodynamic values measured at the various moments of their anginal attacks. An example of the circulatory pattern of this group is presented schematically in Fig. 6, taken from patient R.M. who developed 10 episodes of electrocardiographic alteration during the study. Arterial pressure, heart rate, and right atrial pressure show the means of the 10 episodes. The graph of the wedge pressure represents the mean of measurements done in 4 of them; in the other 6 episodes the catheter was pulled back from the wedge position.

From the onset of the electrocardiographic alteration, during its waxing and steady period (from time E to M), a progressive reduction of arterial pressure was observed, which was paralleled by a conspicuous reduction of cardiac index and a rise of systemic peripheral resistance. The following changes were simultaneously observed from time E through time M: 1) rise of right atrial and pulmonary wedge pressures; 2) quite moderate increase of heart rate; 3) definite reduction of right and left ventricular stroke work, right and left mean rate of systolic ejection, mean pre-ejection dP/dt of the left ventricle.

At the beginning of the waning period, which occurred spontaneously in most of the episodes of

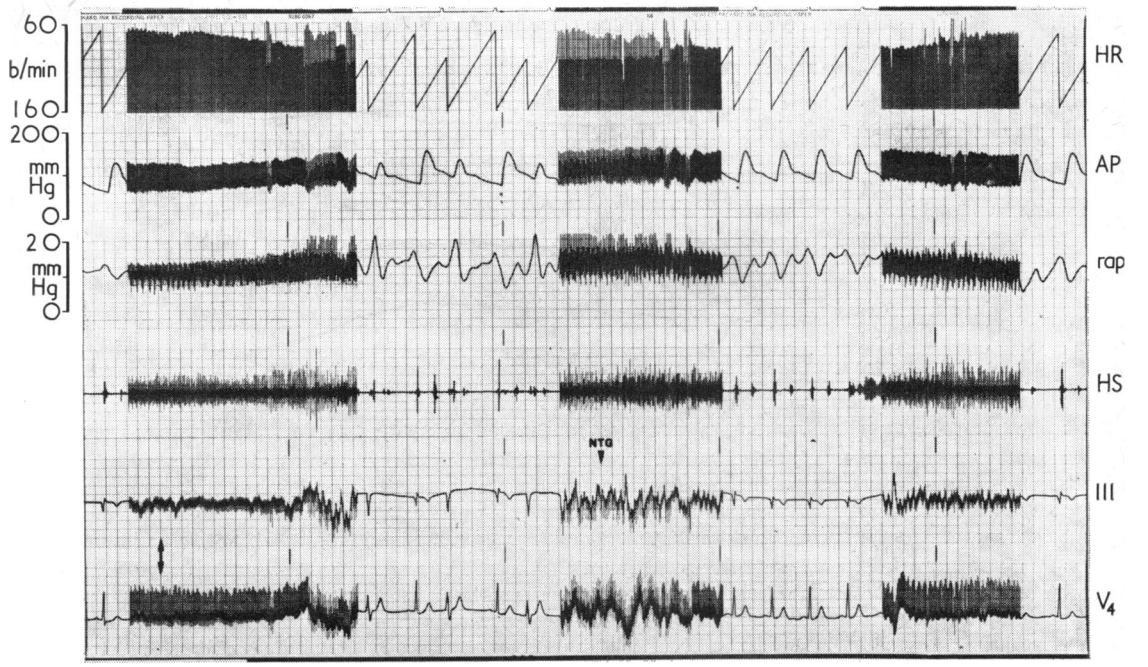

FIG. 4 *Patient G.C. Original record of a type I anginal episode accompanied by pain. The onset of the episode is signalled by the arrow. NTG indicates the moment when nitroglycerin was administered. Abbreviations as in the previous figures.*

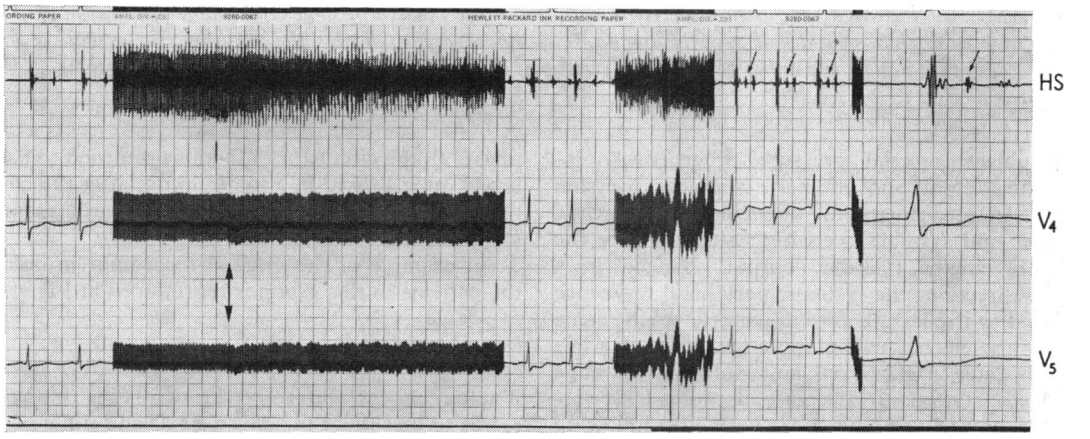

FIG. 5 *Patient M.F. Original record of a type I anginal episode the onset of which is signalled by the large arrows between leads V4 and V5. The small arrows indicate a systolic non-ejection click which appeared only with pain (indicated by the heavy line at the bottom). In the initial part of the anginal attack, when pain was absent, the systolic click was undetectable.*

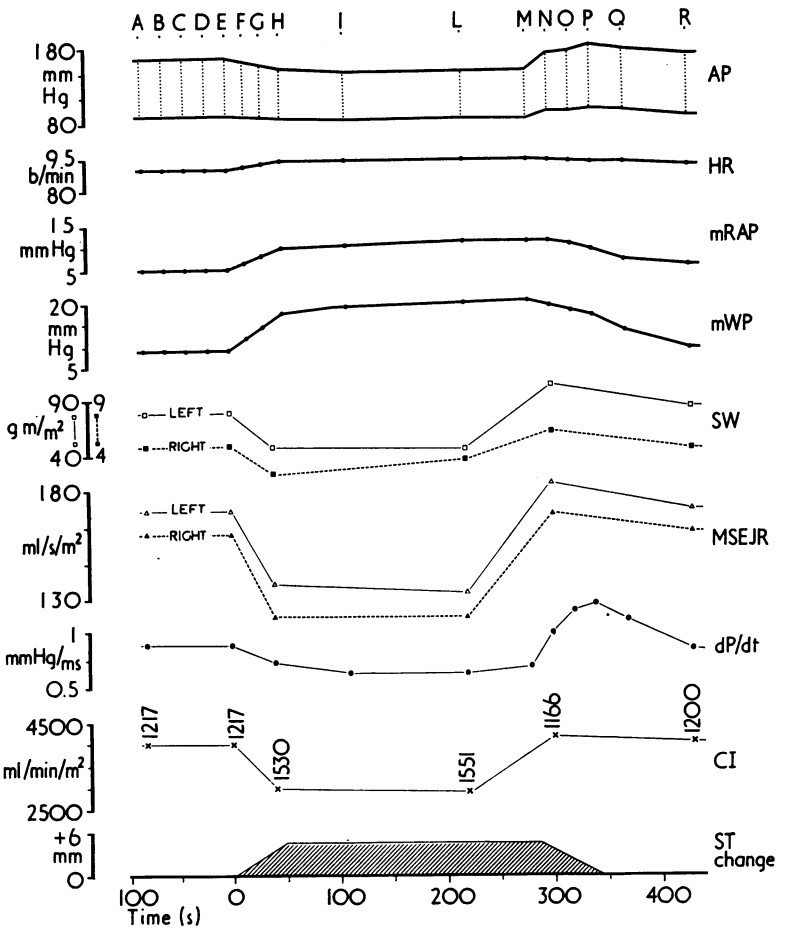

FIG. 6 *Patient R.M. Schematic representation of the pattern of some circulatory parameters during anginal episodes of type II angina. The shaded area indicates the duration, the extent, the waxing and the waning periods of ST segment elevation. See text for details. Abbreviations as in Fig. 1.*

this subject, arterial pressure progressively increased; a few seconds after the complete reversion of the electrocardiographic abnormality, it reached diastolic and systolic levels higher than before the onset of angina. Cardiac output changed in a similar direction; the systemic peripheral resistance returned to the level before the attack. At the same time as the electrocardiographic reversion, or a few seconds later, right atrial and pulmonary wedge pressures started to decrease, progressively returning towards pre-attack values. The following changes were also seen during this period of electrocardiographic reversion: the stroke work and the mean rate of systolic ejection of both ventricles, as well as the left ventricular mean pre-ejection dP/dt rose over control values. After this 'supernormal' phase, all the circulatory functions returned to basal levels (time R) within 2 to 3 minutes after the complete disappearance of the electrocardiographic abnormalities.

An example of the original recordings in one of the patients in this group is reproduced in Fig. 7.

Discussion

The circulatory pattern of the two types of angina seems to be similar in some aspects and different in several others. The major feature which is shared by the two types is that in neither group of patients did haemodynamic changes precede, and consequently precipitate the electrocardiographic abnormalities. If these abnormalities reflect, as it is

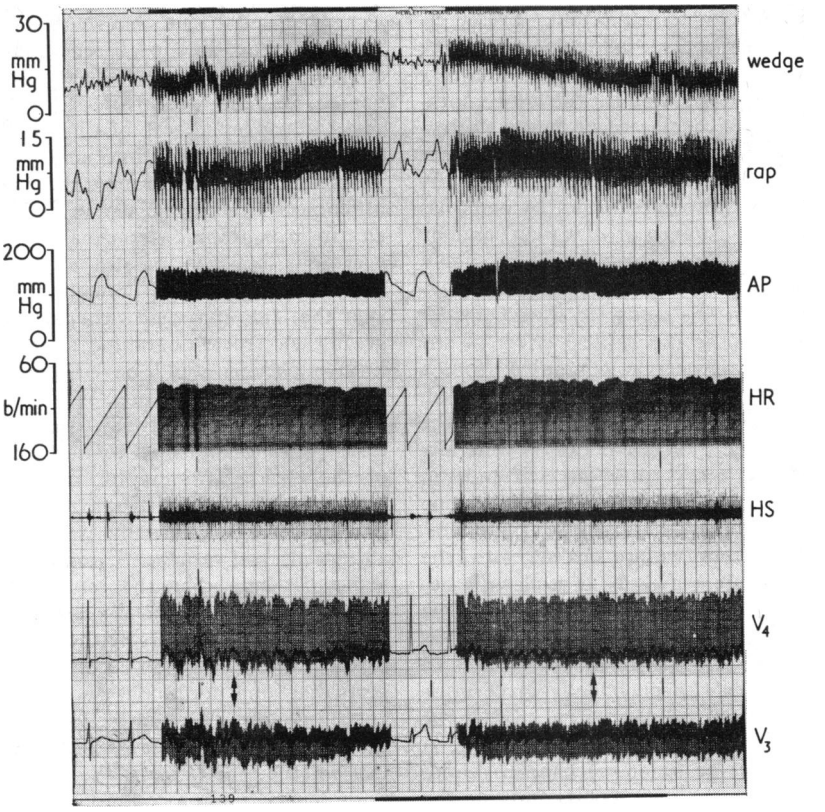

FIG. 7 *Patient L.D. Original recording of a type II anginal episode accompanied by pain .The onset and the end of the episode are indicated by the arrows. From the top: time marker; wedge, pulmonary wedge pressure; rap, right atrial pressure; AP, brachial arterial pressure; HR, heart rate; HS heart sounds; leads V4 and V3. The heavy line at the bottom indicates pain.*

reasonable to conceive, acute myocardial ischaemia, the latter was the initiating event, which was immediately followed by circulatory variations of different quality in the two groups.

In angina with ST segment depression the initial hypotensive response was associated with considerable increase of the filling pressures, and a decrease of stroke work, mean rate of systolic ejection of both ventricles, and left dP/dt. These responses, which are representative of changes usually described in ventricular failure (Braunwald, Sarnoff, and Stainsby, 1958; Diamond *et al.*, 1972) indicate that during the very early stage of angina overt failure occurs, which involves both sides of the heart. The circulatory pattern follows an opposite direction in the time course of the attack: stroke work and mean rate of systolic ejection of both ventricles, left dP/dt, arterial pressure, and heart rate rapidly increase, all of them reaching levels higher than in the pre-attack period. It seems unlikely that Starling's mechanism is responsible for such improvement of cardiac function, since in many instances the filling pressure was at the same level in the early stage of functional depression as in the subsequent stage of functional improvement. We would rather suggest, in agreement with Littler *et al.* (1973), that a sympathetic compensatory mechanism becomes active during the attacks of this angina. The triggers of the sympathetic activation might be at the level of the reflexogenic areas of the vascular system, or of the heart itself (Malliani, Schwartz, and Zanchetti, 1969). It seems unlikely that pain is the primary factor involved in the sympathetic activation, since the latter becomes manifest also in the episodes unaccompanied by pain.

Right atrial and pulmonary wedge pressures

reflect the ventricular end-diastolic pressures, which one would expect to fall coincident with improved ventricular function; on the contrary these pressures remained raised for the entire duration of the ST segment displacement on the electrocardiogram. An altered ventricular compliance during severe ST segment depression induced by atrial pacing, both accompanied or not by pain, has been documented by Linhart *et al.* (1969) and by Dwyer (1970); such a mechanism could provide a reasonable explanation for the discrepancy above.

The observations in this study led us to consider the relation between the mechanical effort of the heart and the acute ischaemia of angina from a viewpoint opposite to that commonly suggested. The increased effort of the heart, caused by the rise in arterial pressure and cardiac rate, is generally considered as the primary cause of ischaemia in exercise (Robinson, 1967) or pacing-induced angina (Sowton *et al.*, 1967; Lau *et al.*, 1968). In spontaneous angina of the type we are dealing with, the electrocardiographic abnormalities of ischaemia become evident first, the overload of the heart appears a consequent phenomenon. These considerations bring on, once more, the disputed question as to whether the beneficial effect of nitroglycerin is primarily at the level of coronary circulation or the consequence of the reduced load of the heart. A contributory effect of the latter mechanism cannot be excluded in our cases, but the data indicate the former mechanism as the primary one in interrupting spontaneous angina. Support for this interpretation is provided by the fact that nitroglycerin is effective in the Prinzmetal form of angina, during which the work of the heart has been shown to be lower than in the pre-anginal periods.

The observations in this study of Prinzmetal's angina confirm the data of our previous report (Guazzi *et al.*, 1971). The results indicate that cardiac failure occurs during the anginal attacks and that both sides of the heart are involved. Contrary to type I angina, the function of the heart remains depressed throughout the ST segment elevation, and functional recovery occurs only at the time when the electrocardiographic signs of ischaemia start to disappear. The compensatory mechanism which comes into action in angina type I does not seem to be elicited, or, what appears more likely, to become effective in the Prinzmetal form. The second hypothesis, in agreement with the experimental demonstration that ST segment elevation is associated with more severe ischaemia than ST segment depression (Ekmekci *et al.*, 1961), implies a more severe dynamic impairment in type II than in type I angina.

Finally, as far as pain is concerned, we have already discussed its role in relation to the circulatory effects. The occurrence in both types of angina of episodes either accompanied or unaccompanied by pain, within the same patient, suggests that the trigger factors of this symptom, whatever they are, do not come into action in all of the episodes of electrocardiographic abnormalities. Possible differences in the magnitude and duration of the electrocardiographic abnormalities and circulatory variations between painful and non-painful episodes were examined. Though we had the impression that the episodes with pain were those with greater electrocardiographic abnormalities, no definitive pattern could be established. A constant feature in our experience, similar to that of other authors (Lau *et al.*, 1968), was that in all of the cases pain was signalled to start in the steady state of the electrocardiographic alteration, and in no case before or during its waxing phase. The symptom disappeared usually when the circulatory alterations had returned completely to normal, i.e. somewhat later than the return to normal of the electrocardiogram. The appearance, in a patient, of a systolic click only during those periods of electrocardiographic alteration accompanied by pain, suggests that some additional disorder (Pasternac *et al.*, 1972) in ventricular contraction occurs, or becomes greater, during pain; it is hard, however, to establish whether the latter is the cause of the pain, or both depend upon a common cause.

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