HEMODYNAMIC ALTERATIONS IN ACUTE MYOCARDIAL INFARCTION. I. CARDIAC OUTPUT, MEAN ARTERIAL PRESSURE, TOTAL PERIPHERAL RESISTANCE, "CENTRAL" AND TOTAL BLOOD VOLUMES, VENOUS PRESSURE AND AVERAGE CIRCULATION TIME [1, 2]

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(Submitted for publication June 18, 1951; accepted August 20, 1951)

Despite its importance little is known of the hemodynamic abnormalities which accompany acute myocardial infarction in man. Aside from clinical observations, the measurement of venous pressure (1) and total blood volume (1, 2), few systematic studies have been carried out in clinical cases. The reason for this has been the impossibility of subjecting such acutely ill patients to difficult or time-consuming technical procedures. However, recent studies (3, 4) indicated that the values for cardiac output obtained with the Hamilton dye injection method were not significantly different from those obtained with the intravenous catheterization method using the Fick principle. It seemed probable, therefore, that the Hamilton dye method suitably modified could be used to determine cardiac output at the bedside in acutely ill patients. This report describes the changes observed using the dye injection method and other procedures in a series of cases with myocardial infarction as compared to a group of normal subjects and hypertensive patients.

METHODS

Fourteen hemodynamic studies were carried out in 11 patients with acute myocardial infarction, eight determinations in seven normal male medical students, and five in a similar number of hypertensive patients. It was essential in the cases of acute myocardial infarction to carry out the experimental procedures rapidly at the bedside and without serious disturbance to the patient. For this reason the dye injection method of Hamilton and colleagues (5) as modified by Werko and associates (4) was used for determining cardiac output. After novocainizing the skin and making a small incision through the dermis with a scalpel blade, a 15 gauge Robb type needle 5 cm. in length [4] was inserted into the femoral artery. This permitted excellent flows of 2 to 3 cc. of blood per second while the rate of flow could be controlled by the stopcock which forms a part of the hub of this needle. Despite the large size there was little difficulty with hematoma formation when the puncture site was compressed for 20 minutes after removing the needle.

The dye was injected into the central circulation by means of polyethelene tubing (1.12 mm. inner diameter),[5] previously sterilized by soaking in 1 to 1,000 aqueous zephiran solution. After nicking the novocainized skin over an antecubital vein situated on the medial aspect of the arm, a 13 gauge needle was introduced into the vein and using sterile precautions the polyethelene tubing was inserted through the needle to a level calculated to be midway between the axilla and the center of the sternum. The catheter always was advanced several inches further and then retracted to be certain that it was not in a venous tributary. Since the placement could not be determined by fluoroscopy it was decided not to attempt to reach the right auricle since in the process the catheter might pass over into the jugular or opposite subclavian veins. Following placement of the catheter the 13 gauge needle was removed and an 18 gauge needle inserted into the end of the catheter a distance of 1 inch.

Every effort was made to carry out these procedures calmly and quietly and towels were so draped that the patient could not see the insertion of the needles. The "team" of investigators was trained so that two men

[1] Supported in part by research grants from the National Heart Institute, U. S. Public Health Service, The Squibb Institute for Medical Research, New Brunswick, N. J. and Irwin Neisler & Co., Decatur, Ill.

Presented in part at the Southern Society for Clinical Research, Jan. 19, 1952.

[2] Sponsored (in part) by the VA and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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[4] Becton, Dickinson & Company, Rutherford, N. J.

[5] Clay-Adams Company, Inc., New York, N. Y.

would insert the catheter while another placed the Robb needle in the femoral artery. After some practice these procedures could be carried out in less than 10 minutes. Following this, the central venous pressure was measured through the catheter using a water manometer and the arterial pressure was measured using a strain gauge manometer,[6] a carrier-wave type amplifier[7] and single channel recorder.[8] Mean arterial pressure was determined by electronic integration of the pulse wave.

The injection of T-1824[9] in 0.5 per cent solution and collection of samples from the femoral artery were carried out according to method of Werko and associates (4). Following this the arterial pressure was measured again and additional arterial samples were withdrawn at 10, 15, and 20 minutes for determination of total plasma volume. In order to minimize hemolysis all samples were collected in parafined tubes containing a drop of dried heparin. Hemolyzed samples (rarely obtained) were discarded. The average circulation time and central blood volume were determined according to the method of Hamilton and co-workers (5). It was recognized that this method was not precise because of the variable contribution of blood from other large veins entering the right heart (6). However, it seemed that large discrepancies could be determined by this method especially since comparisons were made with normal and hypertensive controls who were studied using the same methods.

RESULTS

It was apparent that the hemodynamic changes found in cases of myocardial infarction varied with the clinical state of the patient. For this reason the cases have been divided into three groups: (*1*) mild, (*2*) moderately severe and severe and (*3*) cardiogenic "shock." The basis of such differentiation was made on clinical grounds. The mild cases were those who exhibited little or no evidence either of shock or of congestive heart failure and made a rapid and uneventful recovery. The moderately severe and severe group exhibited definite evidence of circulatory embarrassment, particularly prostration, and manifestations of congestive heart failure. The cardiogenic shock cases all were severely ill exhibiting extreme prostration, frequently with mental confusion as well as the clinical appearance of shock. All of the latter cases terminated fatally during the acute episode.

[6] Model P–23A, Statham Laboratories, Beverly Hills, Calif.

[7] Designed and built by Mr. Robert Wood, Tacoma Park, Md.

[8] Visocardiette, Sanborn Co., Boston, Mass.

[9] William Warner Co., New York, N. Y.

Mean Arterial Pressure, Cardiac Output, Heart Rate, Stroke Volume and Total Peripheral Resistance

In the normal group the mean pressure in the femoral artery ranged from 63 to 93 mm. Hg (average 84 mm. Hg), while in the hypertensive patients the average was 145 mm. Hg with a range of 104 to 189 mm. Hg (Table I). The mean arterial pressures in the cases with myocardial infarction were as follows: in the mild group the average was 95 mm. Hg (range 85 to 113 mm. Hg), in the moderately severe and severe cases it was 89 mm. Hg (range 68 to 120 mm. Hg) and in the patients with cardiogenic shock the average was 79 mm. Hg (range 73 to 88 mm. Hg). Extreme hypotension was not observed in the patients with coronary occlusion even in those cases who appeared clinically to be in "shock" and who later died.

Cardiac outputs were unusually high in the normal subjects, the mean cardiac index being 4.0 ± 0.81 L. per min. (Table I). The high values probably were due to the fact that all were healthy, young male individuals. These subjects were not unduly apprehensive as evidenced by the average heart rate of 64 per minute. In the hypertensive patients, who were more comparable in age to the cases with myocardial infarction, the mean cardiac index was 3.2 ± 0.4 L. In the patients with coronary occlusion the cardiac output was within the normal range in the mild cases, but was abnormally low in the cases exhibiting shock. The mean cardiac index in the mild group was 3.4 ± 0.8 L. per min., in the moderately severe and severe patients 2.9 ± 0.3 L. per min., and in the shock group 1.8 ± 0.4 L. per min.

The heart rate usually was increased in the patients with myocardial infarction but there was considerable variation from patient to patient. The average in the mild cases was 92 beats per minute and the range 64 to 124. In the moderately severe and severe group the heart rate ranged between 85 and 122 per minute (average 101), and in the cases exhibiting shock, it ranged from 74 to 160 per minute with an average of 128. Thus, in general the heart rate increased with increasing severity of the infarction.

The stroke volume was unusually high in the normal subjects averaging 118 ± 16 cc. In the

TABLE I

Hemodynamic data in normal subjects, hypertensive cases and patients with acute myocardial infarction of varying degrees of severity

Pt.	Age (*yrs.*)	Surface area (*sq. m.*)	Mean arterial pressure (*mm. Hg*)	Cardiac output (*liters per min.*)	Cardiac index	Heart rate (*per min.*)	Stroke volume (*cc.*)	Total peripheral resistance (*dynes cm.$^{-5}$ sec.*)	"Central" venous pressure (*mm. H_2O*)	"Central" blood volume (*liters*)	Total blood volume (*liters*)	Total blood volume (*liters per sq. m.*)	Average circulation time (*sec.*)	Time after infarction (*days*)	Outcome*
Normal young male subjects															
R. B.	29	1.72	83	9.1	5.3	70	130	725	88	2.1	5.6	3.3	13.9		
J. D.	26	1.96	93	8.9	4.6	60	149	775	68	3.4	8.2	4.2	23.2		
W. B.	28	1.92	63	7.0	3.7	68	103	725	76	2.5			21.1		
J. A.	21	1.84	88	8.1	4.4	66	123	875		2.9	5.6	3.1	21.5		
C. L.	26	2.09	84	7.2	3.4	68	105	950		2.3	5.0	2.4	19.7		
J. L.	22	1.87	78	8.9	4.8	73	122	700		4.5	6.1	3.3	30.4		
H. Bi.	36	1.89	91	5.2	2.8	54	98	1,386		2.3	4.9	2.8	26.5		
H. Bi.	36	1.89	94	6.2	3.3	56	110	1,200	56	2.1	5.6	3.0	20.4		
Mean and S.D.	28	1.90	84 ±10	7.6 ±1.35	4.0 ±.81	64	118 ±16	925 ±225	72	2.8	5.9	3.2	22.1 ±4.5		
Hypertensive cases															
E. J.	47	1.77	104	4.5	2.5	62	73	1,850		2.2	6.9	3.9	28.8		
A. M.	58	1.84	155	6.0	3.2	100	60	2,000	50	1.9	5.9	3.2	19.5		
M. F.	61	1.82	189	6.8	3.7	79	86	2,225		3.0	5.7	3.1	26.6		
B. L.	45	1.86	120	5.7	3.1	94	61	1,450		2.8	4.9	2.6	29.0		
A. F.	29	2.03	159	6.9	3.4	83	83	1,835		2.3	6.4	3.1	20.2		
Mean and S.D.	48	1.86	145 ±30	6.0 ±.87	3.2 ±.4	83	73 ±11	1,875 ±250	50	2.4	6.0	3.2	24.8 ±4.2		
Myocardial infarction patients															
Mild															
H. Bo.	60	2.14	95	6.3	2.9	64	98	1,225		3.5			33.4	1	R.
L. B.	57	1.90	86	5.3	2.8	67	79	1,300	117	3.1	6.4	3.4	34.7	1	R.
J. W.	45	1.83	87	6.0	3.3	124	49	1,150	84	1.8	4.7	2.6	18.3	1	R.
J. S.	37	1.85	113	8.7	4.7	114	76	1,050	70	2.2	5.3	2.9	15.3	0.5	R.
Mean and S.D.	50	1.93	95 ±11	6.6 ±1.3	3.4 ±.76	92	76 ±14	1,175 ±100	90	2.7	5.5	3.0	25.4 ±8.7		
Moderately severe and severe															
J. V.	54	1.91	103	5.0	2.6	103	36	1,650	144	2.4	6.2	3.5	29.6	3	R.
T. P.	63	1.80	78	4.8	2.7	85	57	1,300		3.4	4.3	2.4	41.6	1	R.
D. S.	64	1.80	75	5.1	2.9	86	60	1,175	160	2.9	5.2	2.8	33.8	0.5	D., 3 days later
R. E.	56	1.96	68†	5.2	2.7	108	48	1,000	81	2.8	4.7	2.4	32.0	1	R.
F. McC.	58	1.82	120	6.2	3.4	122	51	1,550	84	3.2	5.6	3.1	31.2	1	D., 11 days later
Mean and S.D.	59	1.86	89 ±20	5.3 ±.5	2.9 ±.31	101	50 ±9	1,325 ±250	120	2.9	5.2	2.8	33.6 ±4.1		
Cardiogenic "shock"															
F. McC.	58	1.82	72	4.4	2.4	160	28	1,300	115	2.0‡	6.4	3.5	27.3‡	3	D., 9 days later
P. C.	57	1.78	83	2.7	1.5	74	37	2,450	90	3.5			78.8	0.5	D., 7 days later
G. McK.	54	1.89	88	3.0	1.6	140	22	2,350		1.8	4.3	2.3	35.3	0.5	D., 6 days later
G. McK.	54	1.89	73	2.8	1.5	140	20	2,100	140	1.7	4.6	2.4	36.4	2	D., 4 days later
Mean and S.D.	56	1.84	79 ±11	3.2 ±.22	1.8 ±.37	128	27 ±7	2,050 ±450	115	2.3	5.1	2.7	44.5 ±21		
Mean for all infarctions	55		88	5.0	2.7	106	51	1,575	108	2.6	5.2	2.9	34.4		
J. V. (after recovery)	54	1.80	74	5.8	3.3	80	73	1,020	74	2.6	6.1	3.4	24.9	38	

S.D. (standard deviation) = $\sqrt{\frac{\Sigma d^2}{n}}$.

* R. signifies recovered while D. indicates death of the patient.

† Patient's blood pressure remained low following recovery. He did not present the clinical picture of shock.

‡ Values not comparable with prior data on this patient since in the second determination it was impossible to insert the catheter in an arm vein; it was inserted in the femoral vein and estimated by distance to be in the right auricle.

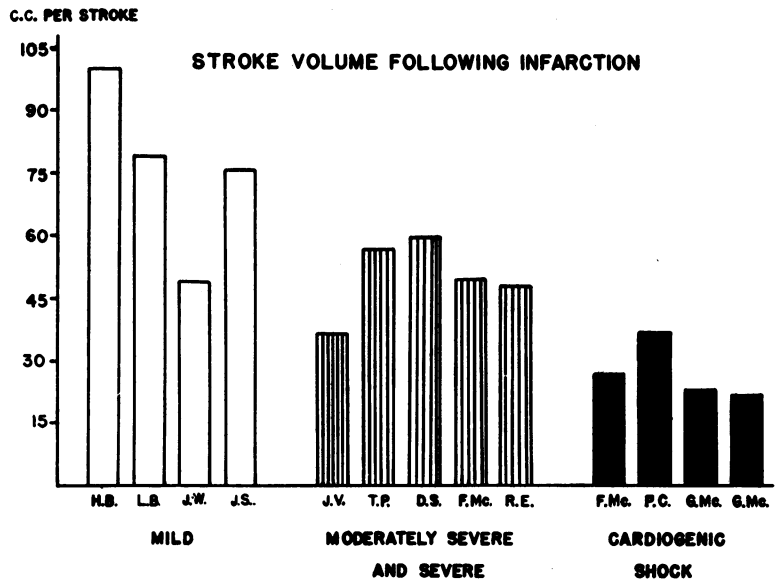

FIG. 1. RELATIONSHIP BETWEEN SEVERITY OF DISEASE AND DEGREE OF REDUCTION OF STROKE VOLUME IN THE PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

hypertensives the mean stroke volume was 73 ± 11 cc. and in the patients with myocardial infarction of mild degree the mean was 76 ± 14 cc. Stroke volume was slightly reduced in the moderately severe and severe group averaging 50 ± 9 cc., while in the patients with the shock syndrome there was a marked reduction of stroke volume to 27 ± 7 cc. (Table I, Figure 1).

The mean total peripheral resistance for the normal subjects was 925 ± 225 dynes cm.$^{-5}$ sec. and for the hypertensives was 1,875 ± 250 dynes cm.$^{-5}$ sec. In the patients with myocardial infarction of mild degree the total peripheral resistance was 1,175 ± 100 dynes cm.$^{-5}$ sec. However, it was slightly increased in the moderately severe and severe group being 1,325 ± 250 dynes cm.$^{-5}$ sec. and strikingly increased in the cardiogenic shock cases, averaging 2,050 ± 450 dynes cm.$^{-5}$ sec.

"Central" Venous Pressure, Average Circulation Time, "Central" Blood Volume and Total Blood Volume

The "central" venous pressure measured in the region of the subclavian or innominate veins averaged 90 mm. H_2O (range 70 to 117 mm.) in the patients with mild coronary occlusion. In the patients with moderately severe or severe myocardial infarction the venous pressure varied between 81 and 160 mm. H_2O (average 120 mm. H_2O). The average venous pressure for the cardiogenic shock cases was 115 mm. H_2O (range 90 to 140 mm.).

The average circulation time was 22.1 ± 4.5 sec. in the normal subjects, 24.8 ± 4.2 sec. in the hypertensive cases, and 25.4 ± 8.7 sec. in the patients with myocardial infarction of mild degree. The circulation time was prolonged in the more severe cases being 33.6 ± 4.1 sec. in the patients with moderately severe or severe attacks, and 44.5 ± 21 seconds in the cardiogenic shock group.

The "central" blood volume was not significantly different in the various groups, the average values being as follows: 2.8 L. in the normal subjects, 2.4 L. in the hypertensive patients, 2.7 L. in the patients with mild coronary occlusion, 2.9 L. in the moderately severe and severe group, and 2.3 L. in the patients with cardiogenic shock.

The total blood volume tended to be slightly reduced in the cases of severe myocardial infarction but the differences were not sufficiently marked to be significant in view of the small series of patients and there was considerable overlapping of individual values. The total blood volume ranged between 2.3 and 4.2 L. per sq. m. surface area (average 3.2 L.) in the normal subjects. In the hypertensives the average was 3.2 L. and the range

2.6 to 3.9 L. The total blood volumes in the patients with myocardial infarction were as follows: average 3.0 and range 2.6 to 3.4 L. per sq. m. in the mild group, average 2.8 and range 2.4 to 3.5 L. in the moderately severe and severe group, and average 2.7 and range 2.3 to 3.5 L. per sq. m. in the cardiogenic shock patients.

In patient F. McC. the typical picture of cardiogenic shock developed three days after the infarction and two days after the original studies (Table I and Figure 2). Hence, it was possible to compare the values obtained prior to and after the development of the shock-like state. In the interval between the tests, the electrocardiogram indicated extension of the infarct while the arterial pressure had fallen from hypertensive to hypotensive levels. The most striking change in this patient was the reduction of stroke volume from 51 to 28 cc. The venous pressure increased from 84 to 115 mm. H_2O and the heart rate from 122 to 160 beats per minute. Unfortunately during the shock phase it was impossible to thread the catheter into an arm vein. The femoral vein was entered and the catheter tip placed in the neighborhood of the right auricle. Hence, the measurements of average circulation time and central blood volume were not comparable in the two determinations.

In another patient (J. V.) the determinations were repeated approximately two months after the myocardial infarction when he had completely recovered (Table I). This patient was critically ill during the acute episode manifested by pulmonary edema, dyspnea and orthopnea. Following recovery the mean arterial pressure fell markedly from 103 to 74 mm. Hg while the cardiac output rose slightly from 5.0 to 5.8 L. per minute. The stroke volume, however, increased markedly from 36 to 73 cc. This was due in most part to the marked elevation of heart rate to 140 beats per minute during the acute episode which fell on recovery to 80 per minute. There also was a striking reduction in total peripheral resistance from 1,650 to 1,020 dynes $cm.^{-5}$ sec. The venous pressure also fell from 144 to 74 mm. H_2O, while the average circulation time became somewhat reduced from 29.6 to 24.9 seconds. However, despite the high venous pressure and evidence of cardiac failure at the time of the acute attack, the central blood volume was not significantly changed, being 2.4 L. initially and 2.6 L.

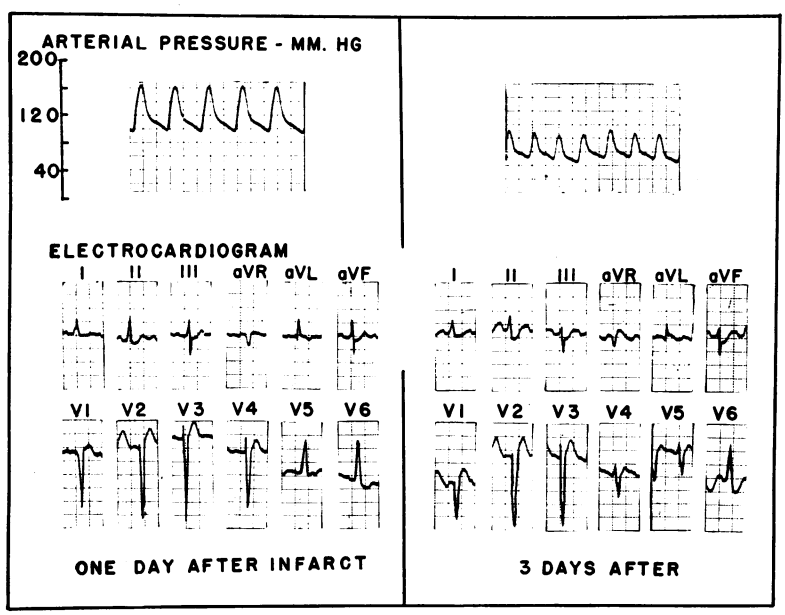

FIG. 2. CUTTINGS TAKEN FROM TRACINGS OF FEMORAL ARTERIAL PRESSURE AND ELECTROCARDIOGRAMS IN PATIENT F. McC., A WHITE MALE, AGE 58 YEARS, WITH ACUTE MYOCARDIAL INFARCTION

During the interim between the first and second determinations the patient developed the clinical picture of "shock." See text for further details.

after recovery. The total blood volume also remained essentially unchanged.

DISCUSSION

The disturbances in cardiovascular hemodynamics observed in the patients with myocardial infarction varied with the severity of the attack. The mild cases failed to exhibit significant abnormalities. In the patients with cardiogenic shock the most marked disturbances were the serious reduction of the stroke volume of the heart and the marked increase in total peripheral resistance. The moderately severe and severe cases formed an intermediate group between the mild and the shock patients so far as hemodynamic abnormalities were concerned. Thus, the severity of the attack as judged by clinical observations appeared to be correlated directly with the degree of depression of stroke volume.

Since the central blood volume was not significantly reduced it seemed reasonable to conclude that the depression of stroke output was due to failure of the heart as a pump and not to hypovolemia. These observations are in agreement with similar data obtained by Mendlowitz, Schauer and Gross (7) in dogs subjected to ligation of coronary arteries. In addition, Gilbert, Aldrich and Anderson, utilizing techniques similar to those used in the present study, found a reduction of cardiac output in two of three patients with acute myocardial infarction (8).

On the basis of the observed data the sequence of hemodynamic events following severe myocardial infarction appeared to be as follows: if the infarction was extensive or if it involved a previously damaged myocardium there was diminished contractility and hence a failure of stroke output. The consequent reduction of arterial pressure immediately resulted in the activation of neurogenic reflexes and possibly other compensatory mechanisms which produced an increase in total peripheral resistance and tachycardia. Thus, the hemodynamic response was not unlike the compensated phase of hypovolemic shock (9), except that the disturbance was due to ineffectual contraction of the myocardium rather than to blood loss.

This interpretation of the hemodynamic alterations accompanying myocardial infarction are in essential agreement with the classical studies of Wiggers and his colleagues on experimental coronary occlusion in animals. In his review of this work (10) Wiggers points out that the infarcted segment balloons out rather than contracts during systole. In some animals this is compensated for by an increase in diastolic ventricular volume with stretching of the muscle fibers and hence an increased contraction of the uninvolved portions of the myocardium. In others, however, this compensatory mechanism is insufficient to restore the cardiac output to normal. In these cases the arterial pressure falls progressively while the ventricles, atria, pulmonary vessels, and veins fill with blood.

Wiggers further states that, "the similarity of clinical syndromes following coronary occlusion and loss of blood or plasma is due to the fact that in both cases, cardiac output is decreased, but for different reason, hypovolemia in the case of shock due to blood loss and failure of the contractile capacity of the ventricle in the case of myocardial infarction. One of the consequences of lowering arterial pressure is that moderator vascular reflexes operate to cause generalized vasoconstriction . . . and constriction of skin reservoirs in cases of coronary occlusion . . . merely tends to intensify the engorgement and adds to the volume of blood that the defective myocardium cannot move."

Unlike the condition seen in congestive heart failure, the total blood volume tended to be slightly reduced and the central blood volume was not increased. This occurred even in those patients with elevations of venous pressure and, hence, the latter phenomenon cannot be ascribed to heart failure alone. The venous pressure, however, appeared to correlate with the total peripheral resistance, usually being high in the patients with elevated total peripheral resistances. These observations suggest that in addition to peripheral arterial constriction there also was venoconstriction. Elevation of venous pressure can be obtained in normal individuals following drugs which increase total peripheral resistance such as angiotonin (11) and norepinephrine (12). It seems not unlikely, therefore, that the increase in venous pressure observed in coronary occlusion is at least in part a reflection of the overall increase of total peripheral resistance.

It was surprising to find that the mean pressure as measured in the femoral artery was not usually significantly below normal in these patients, many of whom appeared to be in shock

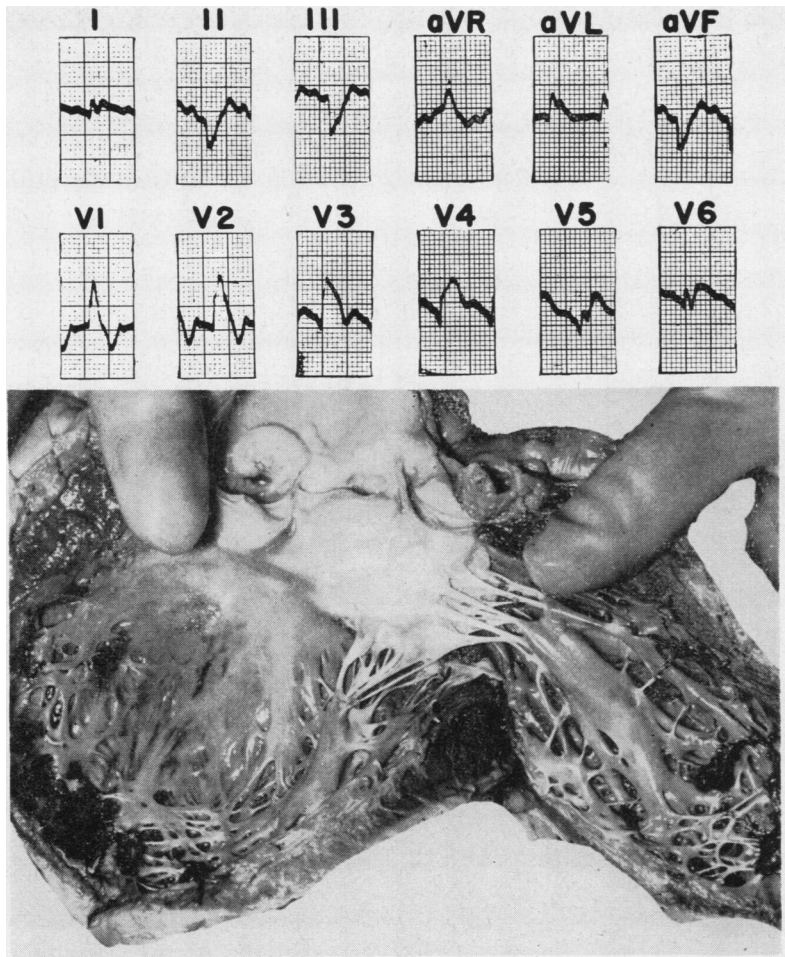

FIG. 3. CUTTINGS FROM ELECTROCARDIOGRAM AND PHOTOGRAPH OF THE HEART OF PATIENT G. MCK., A WHITE MALE, AGED 54 YEARS WHO EXHIBITED CARDIOGENIC SHOCK

The electrocardiogram is consistent with a diagnosis of acute anteroseptal infarction and intraventricular block, R.B.B.B. type. The photograph discloses extensive infarction and thinning of the left ventricular myocardium and "ballooning" of the intraventricular septum into the cavity of the right ventricle. See Table I for hemodynamic data.

clinically in that they were pale, mentally dulled and had weak and rapid pulses. Yet most of the patients who were judged to be in shock by clinical observations exhibited pressures in the femoral artery not markedly lower than in the normal subjects. The mean pressure as recorded directly from the femoral artery in shock due to skeletal trauma or blood loss is much lower, varying between 40 and 60 mm. Hg depending on the severity of the shock (13), as compared to an average value of 79 mm. Hg in the present series diagnosed clinically as being in cardiogenic "shock."

However, the level of arterial pressure probably was maintained at barely normal levels by means of the marked increase in total peripheral resistance. If the stroke volume fell further or persisted at low levels for long periods, eventually a limit would have been reached when the compensatory mechanisms of vasoconstriction and tachycardia could no longer compensate. This event apparently occurred in the case of G. McK. whose initial determination soon after the infarction revealed a mean arterial pressure of 88 mm. Hg despite a stroke volume of only 22 cc. However, two days later the mean arterial pressure had fallen to 73 mm. Hg with a stroke volume of 20

cc. It would appear in this case that the compensatory mechanisms began to fail after several days. A similar sequence seemed to have occurred also in patient F. McC.

One of the most puzzling aspects of the shock-like state accompanying acute myocardial infarction has been the presence on the one hand of the clinical features of hypovolemic shock, and on the other, of hypervolemic heart failure. Thus, the patient may exhibit at the same time pallor, moderate hypotension, and a thready pulse and also may have a high venous pressure, pulmonary edema, dyspnea and orthopnea. These discrepancies, however, can be fitted into a comprehensive schema. It is well known that if in hypovolemic shock the combination of low stroke volume and intense peripheral vasoconstriction is allowed to persist, there is fluid retention and eventually edema, *i.e.*, the so-called lower nephron nephrosis syndrome (14) associated with a reduction of renal blood flow and glomerular filtration rate (15).

It seems possible that a similar sequence may occur in acute myocardial infarction. Initially in this condition there is a shock-like state whereas the signs of congestive heart failure occur characteristically several days following the infarction (1). This pattern is similar to that observed in the lower nephron syndrome. However, in the patients with coronary occlusion, the signs of congestive heart failure are greatly exaggerated because of defective myocardial contractility. The administration of blood or plasma to such patients should only add to the insult since there is no deficiency of central blood volume but rather a failure of output. In G. McK., an attempt was made to transfuse the patient intra-arterially. The rapid administration of blood resulted almost immediately in increased dyspnea and substernal pain. The transfusion was stopped and the patient recovered. Further attempts at transfusing even small amounts of blood produced the same symptoms and, after 200 cc. had been administered, the attempt to transfuse this patient was abandoned. Several other subjects claimed that they derived definite relief of substernal pain and dyspnea following the cardiac output determination which entailed the withdrawal of 100 to 150 cc. of blood.

These observations are in agreement with those of Boyer who in a review of cardiogenic shock (16) concluded that, "The bulk of evidence both direct and theoretical is overwhelmingly in favor of the concept that shock in myocardial infarction is largely, and probably solely, a manifestation of heart failure. . . . Indeed pulmonary edema may constitute a more immediate threat to life (by lowering the oxygen content of the blood) than does shock, and venesection may occasionally be life-saving." Stead and Ebert withdrew 500 and 650 cc. of blood, respectively, from two patients with myocardial infarction and shock with no evident harmful effects (17).

The hypovolemia and terminal heart failure observed in animals in the late stages of hemorrhage shock (18) no doubt lead to an insufficient coronary circulation as pointed out by Corday and his co-workers (19), but is not at all comparable to the hemodynamic situation existing in myocardial infarction. Corday and associates ligated coronary vessels and found that if the animals were then bled to shock levels, the non-contractile zone of myocardium became larger. Transfusion in this instance improved the contractility of the ischemic area. However, this experimental situation cannot be directly related to the patient with coronary occlusion since as determined by the present study there is no deficiency of central blood volume but rather a failure of the ventricle to expel the normal amount of blood presented to it.

The compensatory mechanisms activated by the reduction of stroke volume aid in the maintenance of aortic pressure and hence of coronary blood flow; but they also may have harmful consequences on the course of the disease, by adding extra burdens to an already damaged heart. Such deleterious influences include (*1*) an elevation of total peripheral resistance thereby increasing the work of the heart, (*2*) tachycardia which also adds to the work of the heart and results in a less effective stroke output, (*3*) increased venoconstriction resulting in increased venous filling pressure in the presence of a failing heart, and (*4*) a fluid retention syndrome secondary to renal vasoconstriction. It seems possible that such a series of compensatory reactions teleologically designed to tide a wounded animal over an emergency situation may be harmful in the patient with a weakened myocardium due to coronary occlusion.

SUMMARY AND CONCLUSIONS

The hemodynamic abnormalities associated with severe myocardial infarction were a reduction of cardiac output, especially stroke volume, an increase of total peripheral resistance, heart rate, central venous pressure and average circulation time, a slight and possibly insignificant reduction of total blood volume and an essentially normal central blood volume. The less severe cases did not exhibit these abnormalities.

It is suggested that the initial change after an extensive infarction is a reduction of stroke volume due to the myocardial insult. This is followed by a series of compensatory mechanisms characterized by generalized, intense vasoconstriction probably including venoconstriction, and by tachycardia producing a clinical picture resembling shock. Such intense vasoconstriction in the presence of a reduced stroke volume may be followed by a fluid retention syndrome which, in the presence of a defective myocardium, results in congestive heart failure as well as the shock-like state. These compensatory reactions to a reduced stroke volume appear beneficial in that by raising aortic pressure they aid in the maintenance of coronary blood flow, but they also seem detrimental in that they add in various ways to the work load of an already damaged heart.

CASE SUMMARIES

H. B.—A 60 year old white male dentist developed increasing substernal oppression seven hours prior to admission to the hospital. This was associated with profuse sweating but there was no dyspnea. The lungs were clear and the heart sounds were of good quality. The electrocardiogram was within normal limits on the day of admission but the next day disclosed changes consistent with a recent posterior myocardial infarction. Recovery was uneventful.

L. B.—A 56 year old colored male was admitted to the hospital complaining of substernal pain of three hours duration. He had been hospitalized two years previously for a "heart attack." The lungs were clear and there was no dyspnea or orthopnea. The electrocardiogram was consistent with a recent posterior myocardial infarction. Recovery was uneventful.

J. W.—This 45 year old white male had experienced angina intermittently for two months. On the day of admission while pushing his car he developed substernal pain lasting for six hours. Aside from apprehension the physical examination was not remarkable. The electrocardiogram disclosed the pattern of fresh anterolateral myocardial infarction. He made an uneventful recovery.

J. S.—A 37 year old male developed severe squeezing pain in the substernal area 11 hours before admission to the hospital. For the two months preceding this episode there had been angina on exertion. The patient was pale but the heart sounds were of good quality and the lungs were clear. The electrocardiogram indicated a recent anteroseptal infarction. Recovery was uneventful.

J. V.—This 54 year old male with diabetes mellitus, dyspnea and angina on effort, all of one year's duration, began to have intermittent and then continuous substernal pain radiating to both arms on the day preceding admission to the hospital. His early clinical course was characterized by marked dyspnea and orthopnea with moist rales at the lung bases, but no hepatomegaly or peripheral edema. Serial electrocardiograms were consistent with a diagnosis of recent, subendocardial, anterolateral infarction as well as old anterolateral infarction. The patient began to improve after the third hospital day and thenceforth made an uneventful recovery.

T. P.—A 63 year old male, who had suffered with asthma for six years, developed paraesthesias of the left arm and hand for three weeks and severe continuous substernal pain without radiation for one day prior to admission to the hospital. The patient was dyspneic, mentally dulled and exhibited crackling rales at both lung bases. The electrocardiogram indicated anteroseptal infarction. Several days following admission the patient developed a hemiparesis, which, however, gradually cleared and the further course was uneventful.

D. S.—This 64 year old male developed diabetes mellitus one year ago at which time the electrocardiogram was interpreted as indicating "coronary insufficiency." Two days prior to admission to the hospital he developed crushing substernal pain radiating to the left shoulder. There was slight dyspnea but the lungs were clear. The electrocardiogram indicated recent posterior infarction and AV block with 2 to 1 conduction. On the second hospital day he developed hypotension, bradycardia and oliguria and died on the following day. Autopsy was not obtained.

R. E.—This 56 year old male, who had mild essential hypertension and diabetes mellitus for many years, suffered a posterior myocardial infarction three years ago. He was admitted to the hospital because of an attack of pulmonary edema. Response to therapy was slow and while convalescing he developed typical anginal pain and a recurrence of congestive heart failure. The electrocardiogram indicated a recent anteroseptal infarction. The hemodynamic studies were carried out on the second day of this attack. The patient appeared to recover from this episode but died suddenly five weeks later during a third attack of angina and acute pulmonary edema.

F. McC.—This 58 year old male had experienced angina on effort for the past six months. On the evening of admission to the hospital he developed squeezing substernal pain accompanied by sweating and dyspnea. There were fine moist rales at both bases and a pleuropericardial friction rub was heard. The electrocardiogram disclosed posterior and lateral subendocardial infarction. Three days after admission he developed hypotension, extreme prostration, cyanosis, increased pulmonary rales,

hepatomegaly and oliguria but no orthopnea. He remained in this state for an additional 10 days, the blood non-protein nitrogen rising gradually during this period to a level of 210 mg. per cent two days before death. No autopsy was performed.

P. C.—A 57 year old male suffered a cerebrovascular accident two years ago and an acute myocardial infarction one year ago. Since the latter he had frequent bouts of angina particularly at night. On the day of admission he developed mild but continuous pain in the parasternal area. On admission he appeared pale with cold hands and feet and was dyspneic and orthopneic. The heart was enlarged, the lungs moderately congested and the liver edge was palpated 4 cm. below the costal margin. The electrocardiogram revealed the pattern of fresh anterolateral infarction. The blood pressure remained low, the congestive heart failure increased and the patient died after one week in the hospital. Permission for autopsy was refused.

G. McK.—A 54 year old male who previously had been in excellent health developed transient substernal pain two months before admission to the hospital. On the morning of admission he was awakened with severe substernal pain radiating to the left arm accompanied by profuse sweating but no dyspnea. On admission he appeared to be in shock with distant heart sounds and fine moist rales at the lung bases. The electrocardiographic changes indicated acute anteroseptal infarction, intraventricular block (R.B.B.B. type) and frequent interpolated ventricular beats. The clinical course was characterized by increasing shock with mental confusion and later delirium. The signs of congestive heart failure, except for dyspnea, never were prominent and there was no orthopnea. The blood nonprotein nitrogen rose gradually to 137 mg. per cent and he died six days after admission. Autopsy revealed coronary thrombosis left and infarction of the entire wall of the left ventricle extending into the interventricular septum. There was also chronic passive congestion of the lungs, liver, spleen and gastrointestinal tract.

ACKNOWLEDGMENT

The authors wish to acknowledge the valuable assistance given by Dr. Robert Kelley and Mr. Victor R. Landi.

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