Myocardial Infarct Size and Ventricular Function in Rats

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SUMMARY To define the relationship between infarct size and ventricular performance, we performed hemodynamic studies in rats 21 days after left coronary artery occlusion. Ventricular performance was assessed under ether anesthesia by measurements of baseline hemodynamics and stressed performance as determined by the peak cardiac output and stroke volume obtained during intravenous volume loading and by the peak left ventricular developed pressure obtained during occlusion of the ascending aorta. Infarct size was determined by planimetry of the endocardial circumference of each of four histological slices of the left ventricle. Rats with small (4–30%) myocardial infarctions had no discernible impairment in either baseline hemodynamics or peak indices of pumping and pressure-generating ability when compared to the sham-operated, noninfarcted rats. Rats with moderate (31–46%) infarctions had normal baseline hemodynamics but reduced peak flow indices and developed pressure. Rats with infarctions greater than 46% had congestive heart failure, with elevated filling pressures, reduced cardiac output, and a minimal capacity to respond to pre- and afterload stresses. The entire spectrum of postinfarction ventricular function was observed, from no detectable impairment to congestive failure. In this model of histologically healed myocardial infarction, the impairment of left ventricular function was directly related to the loss of myocardium. Circ Res 44: 503–512, 1979

THE OCCURRENCE of left ventricular dysfunction shortly following the onset of a myocardial infarction is well established (Swan et al., 1972; Hood et al., 1970; Page et al., 1971). After this acute insult, with the passage of time there is some improvement of global ventricular performance (Kupper et al., 1977; Rahimtoola et al., 1972; Kumar et al., 1970). Indeed, in studies of ventricular performance in dogs with healed myocardial infarctions, recovery is so complete that the hemodynamic measurements are either entirely normal (Hood, 1970) or demonstrate only a minor elevation of left ventricular end-diastolic pressure (Weisse et al., 1970; Hood et al., 1967). This lack of overt heart failure in experimental models of healed myocardial infarction certainly does not reflect the entire spectrum of dysfunction observed in man, in whom varying degrees of left ventricular dysfunction are common. The reason for this discrepancy is not...
clear, but it is possible that the absence of postinfarction heart failure may be related to the relatively narrow range of infarct sizes in surviving dogs.

Left coronary artery occlusion in rats can readily provide left ventricular free wall infarctions of varying sizes. Within 21 days of the infarction, the necrotic myocardial tissue is completely replaced by connective tissue (Fishbein et al., 1978a). The present study was undertaken to define the relationship between the size of the healed myocardial infarction and left ventricular performance. Specifically, the ability of the left ventricle to pump blood and generate pressure was related to the extent of connective tissue replacement resulting from a myocardial infarction.

**Methods**

**Operative Procedure**

Studies were performed on male and female normotensive Wistar rats (West Jersey Biological Supply) ranging in age from 11 to 41 weeks. Myocardial infarctions were produced by a method similar to that previously described (Johns and Olson, 1954; Selye et al., 1960) and modified in this department (Maclean et al., 1976, 1978). Briefly, each rat was anesthetized with ether, and a left thoracotomy was performed to exteriorize the heart rapidly by gentle pressure on the right side of the thorax. The left coronary artery was either ligated or heat-cauterized between the pulmonary artery outflow tract and the left atrium. The heart was then returned to its normal position and the thorax immediately closed. Using this method, there is 40-50% mortality within the first 24 hours following occlusion. Surviving rats were maintained on standard rat chow and water ad libitum. Control rats were those in which the operative procedure did not produce a detectable myocardial infarction, as a result of failure to occlude the coronary artery. These rats were not classified as control, or noninfarcted, until the histological determination had been made.

**Hemodynamic Studies**

Rats were anesthetized with ether 21 (19-23) days following coronary artery ligation. The right carotid artery was cannulated with a polyethylene catheter (Pfeffer and Frohlich, 1972), which was connected to a Millar micromanometer via a 17-gauge blunted needle. This fluid-filled catheter transducer system has a natural resonant frequency of 100 Hz and a damping coefficient of 0.6. The right jugular vein was cannulated and the catheter advanced into the right atrium. In most rats the catheter was then temporarily advanced into the right ventricle to record intraventricular pressure before the tip was withdrawn into the right atrium. After tracheal intubation each rat was placed on a constant volume ventilator with the minute volume adjusted according to weight. A thoracotomy through the sternoclavicular and first four sterno-costal articulations provided exposure of the ascending aorta for placement of an electromagnetic flow probe (Statham Instruments) with an i.d. of either 2.0 or 2.5 mm. Recordings of phasic and mean arterial and venous pressures and ascending aortic flow (cardiac output excluding coronary flow) were continuously displayed on a multichannel recorder (Hewlett Packard). The first derivative of aortic flow velocity, i.e., acceleration of flow, was obtained electronically.

Heart rate and other phasic values were measured as an average of 10 consecutive beats. Ejection time was measured as the interval from the initial rise in arterial pressure until the nadir of the dicrotic notch. From the measurements of arterial and venous pressures and ascending aortic flow (cardiac output), we calculated cardiac index (cardiac output/body weight), stroke volume index (cardiac index/heart rate), stroke work index (the product of stroke volume index and the difference between mean arterial and right atrial pressure converted to gram-meters by multiplying by 0.0136), minute work index (stroke work index times heart rate) and total peripheral resistance index (the quotient of the difference between mean arterial and right atrial pressure and the cardiac index).

**Preload Stress**

Warmed Tyrode's solution was infused into a femoral vein at a rate of 40 ml/min per kg for 45 seconds. This infusion produces a rise and then a plateau in cardiac output within 30-45 seconds despite further elevations in right atrial pressure (Pfeffer et al., 1976). Cardiac output and stroke volume were measured at each increment of 0.5 mm Hg in atrial pressure to ascertain their peak values.

**Afterload Stress**

Fifteen minutes after the volume load, when all hemodynamic variables, including right atrial pressure, had returned to baseline levels, the flow probe was removed and the arterial catheter was advanced into the left ventricle. Left ventricular pressure and its first derivative, dP/dt, were recorded continuously. An additional channel was used to display left ventricular pressure at a high sensitivity for determination of left ventricular end-diastolic pressure (Fig. 1). The ascending aorta was then occluded for 3 seconds with a suture, which previously had been placed around it. This maneuver produces reproducible isovolumic (except for coronary flow) contractions. Measurements of left ventricular peak systolic pressure, end-diastolic pressure, maximal dP/dt, and calculations of developed pressure (peak systolic minus end-diastolic pressure) were obtained during each of the 3 seconds of aortic occlusion.

**Determination of Infarct Size**

At the completion of the physiological study, the heart was arrested with potassium. The right and left ventricles (including the interventricular sep-
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LV Pressure (mmHg)

dP/dt (mmHg/sec)

LV Pressure (mmHg)

FIGURE 1 Left ventricular pressure tracing and the first derivative of pressure during ascending aortic occlusion from a rat with a large myocardial infarction. Note the abrupt rise in systolic pressure, reaching a plateau of only 175 mm Hg, and the progressive elevation in end-diastolic pressure to approximately 55 mm Hg by 3 seconds.

control groups occurred, infarcted groups were compared with appropriate sex controls. Rats with myocardial infarctions were arbitrarily divided into three groups according to infarct size (percent of

tum) were dissected, separated, and weighed. The hearts were fixed in 10% buffered formalin for histological study. Specimens were coded so that determinations of infarct size were made without knowledge of hemodynamic data. The left ventricles were cut from apex to base into four transverse slices, which were processed in a routine manner for histological study. Sections 10 μm thick were cut, stained with Masson's trichrome stain, and mounted (Fishbein et al., 1978a). The histological sections of all four slices of left ventricle were projected on a small screen. A planimeter (Numonics Corporation) was used to obtain the length of the entire endocardial circumference and that segment of the endocardial circumference made up by the infarcted portion from each of the four slices of the left ventricle. The fraction of the left ventricle that was infarcted was calculated from these measurements. The extent of myocardial necrosis of these well-healed infarctions was determined from the circumference rather than from the volume of the infarct, because the latter underestimates the original loss of myocardium. Other observations in our laboratory have shown that during the histological evolution of a myocardial infarction there is a marked reduction in the volume of infarcted myocardium due to thinning of the infarcted wall, whereas the surface area of the infarct is minimally altered (Fishbein et al., 1978b).

Statistical Analyses

Because sex differences in flow-related variables have been reported in rats (Pfeffer et al., 1977), control data from males and females were compared by unpaired Student's t-test. When no significant difference (P < 0.05) occurred between sexes, the data were pooled for comparison with infarcted groups. However, when a sex difference between control groups occurred, infarcted groups were compared with appropriate sex controls. Rats with myocardial infarctions were arbitrarily divided into three groups according to infarct size (percent of

FIGURE 2 Histological sections (trichrome stain, 9X) through the midwall of the left ventricle. Panel A is from a noninfarcted ventricle. Panel B is a section from a ventricle with an infarction (i between broken lines) of 20% of left ventricle. Panel C is a section from a ventricle with an infarct of 50%. Note thinning of infarcted wall.
left ventricular endocardial circumference): small, 4-30%; moderate, 31-46%; and large, 47-59%. When variances were similar in each group, a one-way analysis of variance was performed for each variable to estimate a pooled error mean square and to test the significance of differences between the four groups. When there was a significant difference between groups by Fisher's variance ratio ($P < 0.05$), Student's $t$-test by the pooled error mean square was used to assess the significance of differences between each infarct group and the control group. When the variances within groups were different (e.g., right ventricular end-diastolic pressure and right atrial pressure) each infarct group was compared directly with the control group by use of the modified $t$-test described by Snedecor and Cochran (1967).

Results

Hemodynamic studies were performed on 90 rats 3 weeks following coronary artery occlusion. Forty-six (20 males, 26 females) of these rats did not have histological evidence of a myocardial infarction and are termed control rats. The 44 infarcted rats (19 males, 25 females) demonstrated well-healed areas of infarction ranging from 4-59% of the left ventricular endocardial circumference (Fig. 2). Infarcted rats were not readily discernible by general appearance, since ascites, peripheral edema, apparent respiratory distress, and failure to groom were not noted. Body weights of control and infarcted rats were similar.

Despite marked thinning of the wall, left ventricular weight was not altered in the infarcted groups (Table 1). The right ventricular weight of both male and female rats with large myocardial infarctions (> 46% of left ventricular surface area) was markedly increased (Table 1). This right ventricular hypertrophy was associated with elevations of left ventricular end-diastolic and right ventricular systolic pressures (Fig. 3). Right ventricular end-diastolic pressure also was increased in this group of rats (control vs. > 46% infarct: $2.8 \pm 0.2$ vs. $7.9 \pm 1.6$ mm Hg, $P < 0.05$) as was right atrial pressure (Table 2).

Arterial pressure was reduced in rats with myocardial infarctions. Systolic and mean arterial pressures decreased progressively with increasing infarct size, with significant differences from control rats occurring in the groups with moderate and large infarctions (Table 2). Heart rate of each of the infarcted groups was similar to that of the control rats. However, the ejection time of the groups with moderate and extensive infarctions was prolonged (Table 2).

Baseline cardiac index was not reduced in rats with infarcts of small or moderate size (Fig. 4) but was reduced to 82% of control in rats with large infarcts (control vs. large infarcts for females: $282 \pm 16$ vs. $228 \pm 17$ ml/min per kg; for males: $232 \pm 10$ vs. $186 \pm 27$, ml/min per kg). Because of the concomitant reduction in mean arterial pressure, the total peripheral resistance index was elevated, but not significantly so, in the group with reduced cardiac index. Baseline values for stroke volume, stroke work, and minute work of both female and male rats with infarcts of small and moderate size were similar to values obtained in respective sex-matched control groups. However, stroke volume index and calculated external cardiac work indices were reduced to approximately 78% of controls ($P < 0.05$) in rats with large infarcts (control vs. large infarcts, stroke volume index, in ml/kg: females, $0.77 \pm 0.05$ vs. $0.62 \pm 0.04$, and males, $0.64 \pm 0.02$ vs. $0.48 \pm 0.06$; stroke work index in gram-meters/kg: females, $0.98 \pm 0.07$ vs. $0.80 \pm 0.07$, and males, $0.85 \pm 0.03$ vs. $0.58 \pm 0.08$; minute work index, in gram-meters/min per kg: females, $345 \pm 24$ vs. $280 \pm 22$, and males, $308 \pm 15$ vs. $225 \pm 36$). Thus, in

### Table 1

| Body and Ventricular Weight Ratios of Control Rats and Rats with Myocardial Infarcts |
|---------------------------------|----------------|----------------|----------------|----------------|
|                                 | Control        | ≤ 30%          | 31-46%         | 47-59%         |
| Males                           |                |                |                |
| BW (g)                          | 386 ± 15       | 402 ± 38       | 361 ± 15       | 380 ± 24       |
| LV/BW (mg/g)                    | 1.90 ± 0.04    | 1.91 ± 0.05    | 2.03 ± 0.08    | 1.74 ± 0.06    |
| RV/BW (mg/g)                    | 0.63 ± 0.02    | 0.66 ± 0.03    | 0.67 ± 0.05    | 0.85 ± 0.09†   |
| Kidneys/BW (mg/g)               | 7.54 ± 0.22    | 7.52 ± 0.25    | 7.51 ± 0.15    | 7.44 ± 0.34    |
| n                               | 7              | 7              | 7              | 5              |
| Females                         |                |                |                |
| BW (mg/g)                       | 274 ± 10       | 328 ± 21*      | 296 ± 16       | 247 ± 14       |
| LV/BW (mg/g)                    | 2.18 ± 0.03    | 2.19 ± 0.05    | 2.15 ± 0.09    | 2.07 ± 0.09†   |
| RV/BW (mg/g)                    | 0.71 ± 0.02    | 0.61 ± 0.05    | 0.76 ± 0.05    | 1.17 ± 0.09†   |
| Kidneys/BW (mg/g)               | 6.72 ± 0.14    | 6.29 ± 0.07    | 6.29 ± 0.22    | 6.22 ± 0.15    |
| n                               | 7              | 9              | 9              |

Results are expressed as mean ± SEM. BW = body weight; LV = left ventricular weight, RV = right ventricular weight.

* $P < 0.05$, control vs. infarct group.
† $P < 0.001$, control vs. infarct group.
in the unstressed condition, rats with myocardial infarctions involving 4—46% of the left ventricle had normal right and left ventricular filling pressures and cardiac output. In contrast, rats with large myocardial infarctions had overt congestive heart failure with elevated right and left ventricular filling pressures and reduced cardiac output, stroke volume, and external stroke and minute work.

**Preload Stress**

Control (noninfarcted) rats demonstrated a prompt rise in cardiac output and stroke volume during volume loading (Fig. 5A). The female control rats developed a peak cardiac index of 456 ± 23 ml/min per kg and peak stroke volume index of 1.31 ± 0.06 ml/kg. These indices were lower in male rats (peak cardiac index, 339 ± 17 ml/min per kg; peak stroke volume index, 0.99 ± 0.04 ml/kg). Rats with small infarcts had no significant impairment of peak

**Figure 3** Relationship of left ventricular end-diastolic (LVEDP) and right ventricular systolic pressure (RVSP) to infarct size. Open and closed circles denote females and males, respectively. Note the abrupt onset of elevated pressures with infarcts greater than 46% (broken line).

**Figure 4** Baseline cardiac index (top) and total peripheral resistance index (bottom) for control and infarct groups. Values are expressed as percent control because of the significant sex difference in cardiac index. The baseline cardiac index for the noninfarcted female rats was (in ml/min per kg) 282 ± 16, and for the male rats, 232 ± 10. The total peripheral resistance index of the control females was (in mm Hg/ml per min per kg) 0.35 ± 0.02, and that of the control males, 0.44 ± 0.03.

**Table 2** Prethoracotomy Systemic Pressures and Heart Rate of Control and Infarcted Rats

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|---------------------------------|-----------------|-----------------|-----------------|
| Arterial pressure (mm Hg)       |                 |                 |                 |
| Systolic                        | 142 ± 3         | 134 ± 4         | 128 ± 4*        |
| Diastolic                       | 99 ± 3          | 91 ± 5          | 88 ± 5          |
| Mean                            | 121 ± 3         | 114 ± 4         | 108 ± 5*        |
| Right atrial pressure (mm Hg)   | 0.4 ± 0.2       | 0.2 ± 0.4       | 1.0 ± 0.5       |
| Heart rate (beats/min)          | 368 ± 8         | 399 ± 13        | 365 ± 13        |
| Ejection time (msec)            | 72 ± 1          | 74 ± 2          | 81 ± 2*         |
| n                               | 45              | 14              | 16              |

Results are expressed as mean ± SEM.
* P < 0.05 control vs. infarct group.
† P < 0.01 control vs. infarct group.
pumping ability when compared with appropriate sex-matched control rats. Although the baseline cardiac index of rats with moderate infarcts was normal, their peak pumping ability was reduced compared to control rats \((P < 0.05)\) (peak cardiac index, in ml/min per kg: females, 384 ± 9, and males, 283 ± 20; peak stroke volume index, in ml/kg: females, 1.13 ± 0.04, and males, 0.86 ± 0.05) Rats with large infarcts had minimal increases in flow with volume loading (Fig. 5B). Thus, volume loading made manifest previously undetectable impairments in pumping ability in the group with moderate infarctions and underscored the reduced pumping ability of the group with extensive infarctions (Fig. 6).

**Afterload Stress**

The ability of the left ventricle to generate pressure during an occlusion of the ascending aorta was not sex-dependent (developed pressure during the 1st second of occlusion in control rats: males, 217 ± 4; females, 218 ± 4 mm Hg). Developed pressure is greatest during the 1st second of occlusion and then decreases progressively due to continued elevation of end-diastolic pressure. Analysis of developed pressure during the 1st second of aortic occlusion is representative of the relationship of pressure-generating capacity to infarct size observed throughout the 3-second period of occlusion. The association between infarct size and developed pressure illustrated in a scatter diagram (Fig. 7) demonstrates the progressive reduction in pressure-generating ability with increasing infarct size. On using a least-squares linear regression, the relationship is characterized by the equation: developed pressure (in mm Hg) = 219 - 1.31 × percent of infarcted left ventricular circumference, \(r = 0.80\) \((P < 0.001)\). Although the coefficient of correlation of this linear equation indicates a relatively strong relation between infarct size and developed pressure, the data are fit more closely by a complex polynomial, indicating a progressively greater reduction in pressure-generating ability with larger infarcts.

The interpretation of indices of global ventricular
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The function of a ventricle with a healed myocardial infarction represents a complex interaction between multiple factors, including the status of the nonoccluded coronary arteries, the underlying performance of the viable myocardium, the integrity of the conducting system, the location of the infarct (Corr et al., 1976), alterations in ventricular compliance, neurohumoral influences acting on the heart, the extent of compensatory hypertrophy of the noninfarcted myocardium, and the effects of preload and afterload, as well as the size of the infarct itself. Despite this multiplicity of factors contributing to ventricular performance after a myocardial infarct, studies in man have suggested a gross relationship between infarct size and ventricular performance. Mathey et al. (1974) divided patients with acute myocardial infarctions into three groups based on pulmonary artery diastolic pressure. They reported a direct relationship between filling pressure and enzymatically derived determinations of infarct size. The larger infarcts were associated with higher pulmonary artery diastolic pressure and greater mortality. The functional exercise capacity of survivors of myocardial infarcts has recently been shown to be inversely related to serum creatine phosphokinase (CPK) estimates of infarct size (Carter and Amundsen, 1977). Thus, despite the multiplicity of interacting factors, infarct size may be an important determinant of postmyocardial infarction morbidity and mortality.

The rat model of left coronary artery occlusion provided animals with histologically well-healed infarctions for determining the relation between infarct size and ventricular performance. Although coronary artery ligation in the rat is not analogous to the pathogenesis of coronary artery disease and ultimate infarction in man, the resultant histological evolution and scar formation are comparable to the experimental setting.

**Discussion**

The function of a ventricle with a healed myocardial infarction represents a complex interaction between multiple factors, including the status of the nonoccluded coronary arteries, the underlying performance of the viable myocardium, the integrity of the conducting system, the location of the infarct (Corr et al., 1976), alterations in ventricular compliance, neurohumoral influences acting on the heart, the extent of compensatory hypertrophy of the noninfarcted myocardium, and the effects of preload and afterload, as well as the size of the infarct itself. Despite this multiplicity of factors contributing to ventricular performance after a myocardial infarct, studies in man have suggested a gross relationship between infarct size and ventricular performance. Mathey et al. (1974) divided patients with acute myocardial infarctions into three groups based on pulmonary artery diastolic pressure. They reported a direct relationship between filling pressure and enzymatically derived determinations of infarct size. The larger infarcts were associated with higher pulmonary artery diastolic pressure and greater mortality. The functional exercise capacity of survivors of myocardial infarcts has recently been shown to be inversely related to serum creatine phosphokinase (CPK) estimates of infarct size (Carter and Amundsen, 1977). Thus, despite the multiplicity of interacting factors, infarct size may be an important determinant of postmyocardial infarction morbidity and mortality.

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**Figure 6** Peak cardiac (top) and stroke (bottom) indices obtained during intravenous volume load for control and infarct groups. The peak cardiac index of the noninfarcted rats was (in ml/min per kg) 456 ± 23 for females and 339 ± 17 for males. The peak stroke index for the noninfarcted rats was 1.31 ± 0.06 ml/kg for females and 0.99 ± 0.04 ml/kg for males.

**Figure 7** Relationship of developed pressure during the 1st second of aortic occlusion and infarct size. The solid line is the mean value for 45 noninfarcted rats, with the hatched area indicating plus and minus two standard deviations from the mean. The solid circles represent male rats and open circles female rats.
(Fishbein et al., 1978b). Since our objective was to study the consequences of the loss of myocardium, with infarct size used as an independent variable, it was advantageous to limit other variables by studying rats with otherwise normal myocardium and coronary arteries.

Although chronic postinfarction heart failure is a well-recognized clinical entity (Baxley et al., 1971), studies of ventricular function in animals with healed myocardial infarctions produced experimentally have not demonstrated congestive failure (Kumar et al., 1970; Weisse et al., 1970; Hood, 1970; Hood et al., 1967). In the present study, normal baseline ventricular filling pressures and cardiac output were observed in rats with myocardial infarctions constituting less than 47% of the left ventricle. More extensive infarcts, however, were associated with overt depression of left ventricular performance as manifested by elevated left ventricular filling pressures and reduced mean arterial pressure and cardiac output. This finding probably is related to the ability of rats with large infarctions to survive. In studies on ventricular performance in dogs with healed experimental infarctions (Kumar et al., 1970; Hood, 1970), a large infarction was classified as one constituting greater than 20% of left ventricular mass. Infarcts constituting more than 30% of the left ventricle almost uniformly produce fatal arrhythmias in dogs. Thus, the rat model of coronary artery ligation provides an entire range of postinfarction function from an absence of detectable impairment to gross failure.

It is well established that baseline left ventricular function may be normal in hearts whose performance during a more demanding stress reveals moderate degrees of functional impairment (Ross and Braunwald, 1964). Preload stress with rapid intravenous volume loading did indeed unmask the inability of rats with infarctions involving 31-46% of the left ventricle to produce the same levels of peak flow (cardiac index and stroke index) as did noninfarcted rats. Since the baseline filling pressures of rats with larger infarctions, i.e., involving more than 46% of the left ventricle, already were elevated markedly, it is not surprising that further increases with volume loading produced only minimal increments in flow.

Temporary aortic occlusion was used as a means to stimulate the ventricle to generate maximal isometric ventricular pressure (Goodyer et al., 1962). The developed left ventricular pressure during this maneuver has been used to demonstrate an impairment in ventricular function of dogs with myocardial infarcts (Kumar et al., 1970; Hood et al., 1967, 1969). In the present study, peak developed left ventricular pressure was closely related to infarct size over the whole range examined. This measurement appears to be very sensitive to the extent of loss of contractile tissue.

Despite the graded reduction in peak developed
pressure with increasing infarct size, the development of impaired left ventricular function in the basal state, as reflected in an elevated left ventricular end-diastolic pressure, was abrupt. Left ventricular end-diastolic pressures of rats with infarcts involving less than 47% of the left ventricle were not elevated, whereas 12 of 14 rats with larger infarcts had end-diastolic pressures exceeding 20 mm Hg. Hori et al. (1977) recently have related the extent of myocardial infarction in patients, as estimated by total CPK release, to the hemodynamic findings 1–5 months after myocardial infarction. The relationship they found between CPK release and left ventricular end-diastolic pressure resembles the relationship we observed. The abrupt increase in filling pressure of left ventricles with larger, noncontractile segments may reflect a critical loss of contractile tissue combined with dyskinetic stretching of the infarcted segment (Klein et al., 1967) as well as changes of left ventricular compliance resulting form a scar constituting a large fraction of the chamber.

When left ventricular filling pressure is elevated, right ventricular systolic pressure increases to maintain the pressure gradient across the pulmonary bed. Hence, the elevation of left ventricular end-diastolic pressure produced by extensive infarction appears to result in the right ventricular hypertrophy previously noted in this model (Norman and Coers, 1969).

In conclusion, the occlusion of the left coronary artery in rats produced well-healed myocardial infarctions. Ventricular performance was directly related to the extent of loss of myocardium. Infarcts involving less than 30% of the left ventricle were associated with no detectable impairment of left ventricular function, whereas infarcts of between 31–46% had normal baseline levels but reduced values of peak flow and developed pressure. Infarcts involving more than 46% of the left ventricle resulted in impaired left ventricular function in the basal state. The present study, documenting the dependence of left ventricular performance on infarct size, underscores the importance of salvaging potentially viable myocardium to the functional status of the ventricle following recovery from myocardial infarction.

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DIFFERENTIAL RESPONSE OF HAMSTER CHEEK POUCH MICROVESSELS TO VASOACTIVE STIMULI DURING THE EARLY DEVELOPMENT OF HYPERTENSION

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SUMMARY Arteriolar responses in the hamster cheek pouch to direct microapplications of norepinephrine (NE), angiotensin II (A II), and potassium chloride (KCl) were investigated during the early developmental phase of hypertension. After determination of arterial pressure in 12 hamsters, control luminal and wall diameters and the response of arterioles (second order branching, 28-60 μm diameters) to microapplications of NE (0.5, 1.0, 5.0 ng), A II (0.5 ng), KCl (22.2 mM) and the vehicle (Tris-buffered Ringer's solution) were determined. Then using a figure-eight ligature around each kidney hypertension was induced in nine animals, and three were sham-operated. Measurements were repeated on the same hamsters 4, 8, and 13 days later. Four of the nine animals developed a sustained hypertension (HT-S) and the remaining five developed a transient hypertension (HT-T), only on day 4. The sham-operated hamsters remained normotensive. The arteriolar response to KCl was increased significantly in the HT-S group on days 4 and 8 whereas the arteriolar response to NE and A II was increased significantly on days 8 and 13. There were no significant differences in the arteriolar responses of either the HT-T or normotensive group to any agent at any time. Furthermore, there were no significant changes in arteriolar wall/lumen ratios for any group at any time. Thus, the transient nature of the arteriolar response to potassium combined with the delayed increase in the arteriolar response to NE and A II implies that there are two vascular phases associated with the early development of hypertension in this model. The first phase may be an ionic alteration which in tum may initiate the second or humoral phase.

ALTERATIONS that can result in an increased peripheral resistance in hypertension may involve various components: (1) neurogenic, an altered autonomic output to the peripheral circulation, (2) hormonal, increased levels of vasoconstrictor or decreased levels of vasodilator substances, (3) local, changes in the vascular smooth muscle-receptor complex which lead to increased sensitivity of the blood vessels, and (4) structural, hypertrophy of the vascular smooth muscle concomitant with a decrease in luminal diameter of the arterioles. All of these factors may contribute to an increase in peripheral resistance, but the local and structural components have gained the strongest emphasis (Brody and Zimmerman, 1976).

Until recently, most conclusions about the microcirculation during hypertension have been limited to the use of whole organ (Collis and Alps, 1975; Finch and Haeusler, 1974; Lais et al., 1974), isolated vascular segment (Folkow et al., 1970; McQueen, 1956; Redleaf and Tobian, 1958), and whole animal (Finch, 1971; Okamoto et al., 1966) preparations. Thus, changes which may have taken place at the microcirculatory level to alter peripheral vascular resistance were determined indirectly. More recently, various laboratories using spontaneously hypertensive rats (SHR) (Bohlen et al., 1977; Hutchins and Darnell, 1974) or renovascular models of hypertension (Click et al., 1977; Harris et al., 1975) have demonstrated that the structural characteristics (wall/lumen ratios) of the microvessels were not altered in the early stages of hypertension. However, arterioles (40-60 μm) of the hamster cheek pouch were shown to be more sensitive to norepinephrine in a renovascular model (Click et
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