Role of Angiotensin II in the Altered Renal Function of Congestive Heart Failure

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SUMMARY. Glomerular and tubule functions were assessed by micropuncture in rats with extensive myocardial infarction produced by ligation of the left coronary artery 4 weeks prior to study. When compared to sham-operated control rats, rats with myocardial infarction involving 40 ± 4% of the left ventricular circumference had lower mean arterial pressure (96 ± 5 vs. 122 ± 4 mm Hg, P < 0.005), and higher left ventricular end-diastolic pressure (24 ± 3 vs. 5 ± 0 mm Hg, P < 0.001). Renal cortical microcirculatory dynamics of rats with myocardial infarction were characterized by reduced glomerular plasma flow rate (75 ± 8 vs. 165 ± 17 nl/min, P < 0.005), but a proportionately lesser decline in single nephron glomerular filtration rate (28.0 ± 2.8 vs. 41.7 ± 3.1 nl/min, P < 0.025), accounting for the observed rise in single nephron filtration fraction (0.38 ± 0.02 vs. 0.25 ± 0.02, P < 0.005). These renal hemodynamic alterations in myocardial-infarcted rats were accompanied by a striking elevation in efferent arteriolar resistance (3.03 ± 0.31 vs. 0.95 ± 0.16 x 10^10 dyn•sec•cm^-5, P < 0.001). In addition, fractional proximal fluid reabsorption, assessed by end-proximal tubule fluid-to-plasma inulin concentration ratio, was elevated (2.21 ± 0.12 vs. 1.64 ± 0.09, P < 0.025). The intravenous infusion of teprotide, an angiotensin I-converting enzyme inhibitor, led to the return of glomerular plasma flow rate, single nephron filtration fraction, single nephron glomerular filtration rate, efferent arteriolar resistance, and fractional proximal fluid reabsorption in myocardial-infarcted rats to, or toward, the levels found in control rats. In contrast, teprotide exerted little or no effect in control rats. Thus, the renal cortical microcirculatory and proximal tubule functions of rats with congestive heart failure are profoundly influenced by the vasoconstrictor properties of angiotensin II. (Circ Res 55: 669-675, 1984)

AS with blood flow to many other organs, renal blood flow (RBF) is often depressed in patients with congestive heart failure (Mokotoff et al., 1948; Merrill, 1949). Whereas the depressed RBF per se is hardly surprising, given the reduced cardiac output, glomerular filtration rate (GFR) is usually minimally affected, and patients usually fail to develop azotemia unless cardiac function is severely compromised (Briggs et al., 1948; Heller and Jacobson, 1950). Since the resulting high level of filtration fraction (Vander et al., 1958) favors changes in the postglomerular circulation which promote avid proximal fluid reabsorption (i.e., via elevated peritubular capillary oncotic pressure), the altered glomerular hemodynamics have been thought to be responsible for the common occurrence of sodium and fluid retention, features which also characterize this disorder (Humes et al., 1978). Since the renin-angiotensin system is known to be an important modulator of glomerular circulatory dynamics in a variety of physiological and pathophysiological conditions (Ichikawa and Brenner, 1984), and since this system has been reported to be activated in patients with congestive heart failure, as determined by an increased plasma renin concentration (Merrill et al., 1946; Watkins et al., 1976), it is likely that the acquired alterations in glomerular hemodynamics are due, at least in part, to the enhanced intrarenal action of angiotensin II. Therefore, by employing an angiotensin-converting enzyme inhibitor in a recently developed rat model of myocardial infarction (MI) (MacClean et al., 1978; Pfeffer et al., 1979), we examined the role of angiotensin II in the altered glomerular and proximal tubule function in this form of experimental congestive heart failure.

Methods

Production of Myocardial Infarction

Approximately 4 weeks prior to study, 30 adult male Munich-Wistar rats were subjected to myocardial infarction by a method similar to that originally described by MacClean et al. (1978) and recently modified by Pfeffer et al. (1979). In brief, each rat was anesthetized with ether, and a left thoracotomy was performed to exteriorize the heart rapidly. The left coronary artery was ligated between the pulmonary artery outflow tract and the left atrium, the heart was returned to its normal position, and the thorax closed. Another group of rats underwent a sham operation, involving only thoracotomy and exteriorization of the heart without ligation of the coronary artery. All animals were allowed free access to a regular pellet diet and water both before and after these procedures. Of
those rats that underwent coronary artery ligation, approxi-
mately 50% survived the 4-week postoperative peri-
period and were subjected to the following study protocol.

**Micropuncture Study**

Rats were anesthetized with Inactin (70 mg/kg, ip) and
placed on a temperature-regulated micropuncture table.
Immediately after induction of anesthesia, the left femoral
artery was cannulated with a PE-50 polyethylene catheter
for subsequent periodic blood sampling and measurement
of systemic mean arterial pressure (MAP) with an electronic
transducer (model 7754A, Hewlett-Packard Co.). A base-
line collection of 70 μl of arterial blood was then obtained.
The right carotid artery was cannulated with a polyethy-
lene catheter (PE-50) connected to a Millar micromanome-
ter for measurement of left ventricular pressure. Of the
11 rats with myocardial infarction (MI), only those 7 rats
that were shown to have left ventricular end-diastolic
pressures (LVEDP) higher than 15 mm Hg were subjected
to subsequent micropuncture study. Rats with these ele-
vations in LVEDP exhibit the characteristic features of
congestive heart failure, such as elevated left and right
ventricular filling pressures and a reduced cardiac output
(MacClean et al., 1978; Heffer et al., 1979; Hostetter et
al., 1983). Polyethylene catheters were also inserted into
the left and right jugular veins for infusion of inulin and
an angiotensin I-converting enzyme inhibitor (or vehicle)
and into the left femoral vein for infusion of isoncotic rat
plasma. Ten percent inulin solution in 0.9% NaCl was
started at the rate of 1.2 ml/hr. After a tracheostomy, the
left kidney was exposed by a subcostal incision and sep-
parated from the adrenal gland and the surrounding peri-
renal fat. The kidney was suspended on a Lucite holder
and its surface illuminated with a fiber-optic light source
and bathed with isotonic NaCl heated to 35-37°C. The
left ureter was cannulated with a polyethylene (PE-10)
catheter.

Since the plasma volume of rats prepared for micro-
puncture is reduced by approximately 20% relative to the
conscious animal (Ichikawa et al., 1978) the following
protocol for maintaining the euolemic state was em-
ployed. Soon after collection of the baseline arterial blood
sample, isoncotic rat plasma was infused for 60 minutes
at the rate of 7-10 ml/kg per hr, followed by a reduction
in this infusion rate to 1.5 ml/kg per hr for the remainder
of the experiment. In a previous study, this protocol was
found to be effective in maintaining plasma volume at a
level essentially equal to that prior to the induction of
anesthesia (Ichikawa et al., 1978).

In all experiments, the initial micropuncture measure-
ments were carried out as follows: timed (1- to 2-minute)
samples of tubule fluid were collected from late proximal
surface convolutions of two or three nephrons for the
determination of flow rate and inulin concentrations. Late
proximal convolutions were identified by observing the
passage of Lissamine green dye injected intravenously.
These measurements permit the calculation of single
nephron glomerular filtration rate (SNGFR) and absolute
proximal fluid reabsorption rate (APR). Coincident with
these tubule fluid collections, two or three samples of
femoral arterial blood were obtained in each period for
the determination of hematocrit and plasma concentra-
tions of protein and inulin. In addition, two or three
samples of urine from the experimental kidney were col-
lected for determination of flow rate, inulin concentration,
and calculation of total kidney glomerular filtration rate
(GFR). Time-averaged hydraulic pressures were measured
in surface glomerular capillaries (P_{Gc}), proximal tubules
(P_{t}), and surface efferent arterioles (P_{sa}) with a continu-
ous recording, servo-nulling micropipette transducer system
(model 3, Instrumentation for Physiology and Medicine).
Micropipettes with outer tip diameters of 2 to 3 μm and
containing 2.0 M sodium chloride were used. Hydraulic
output from the servo system was coupled electronically
to a third channel of the Hewlett-Packard recorder by
means of a pressure transducer.

The colloid osmotic pressure (π) of plasma entering
and leaving the glomerular capillaries was estimated from
values for protein concentration in femoral arterial (C_{fa})
and surface efferent arteriolar (C_{se}) plasma samples using
the equation derived by Deen et al. (1973a). Values for
C_{fa} and thus π_{fa} for femoral arterial plasma are taken as
representative of values for protein concentration and
colloid osmotic pressure for the afferent end of the glo-
merular capillary network. These estimates of prglomer-
ular and postglomerular plasma protein concentrations
permit calculation of single nephron filtration fraction
(SNFF) and glomerular capillary ultrafiltration coefficient
(K_{u}) as well as the resistance of single afferent (R_{a}) and
efferent (R_{e}) arterioles and initial glomerular capillary
plasma flow rate (Q_{p}), using equations given elsewhere
(Deen et al., 1973a).

Upon completion of these initial measurements, both
infarcted and noninfarcted control rats were given a con-
tinuous intravenous infusion of teprotide (SQ20881,
Squibb Laboratories), 6 mg/kg per hr. After a 40-minute
equilibration period, all measurements and collections de-
scribed above were repeated.

**Chemical Analyses**

The volume of fluid collected from individual end-
proximal tubules was estimated from the length of the fluid
column in a constant bore capillary tube of known
internal diameter. The concentration of inulin in tubule
fluid was measured, in duplicate, by the fluorometric
method of Vurek and Pegram (1966). Inulin concentra-
tions in plasma and urine were determined by the mo-
croanthrone method of Führ et al. (1955). Plasma protein
concentrations in efferent arteriolar and femoral arterial
blood were determined, in duplicate, by the fluorometric
method of Viets et al. (1978).

**Quantification of Infarct Size**

Upon completion of the micropuncture study, the heart
was arrested with potassium chloride and fixed by im-
mersion in 10% buffered formalin. The left ventricle was
imbedded in paraffin and 50-μm-thick sections were cut
from apex to base. Every 20th section (representing every
1 mm of length) was stained with Masson's trichrome,
from which hematoxylin was omitted, and mounted (Fish-
bein et al., 1978). These histological sections were pro-
jected onto a screen with a magnification of 12X. The
length of the entire endocardial and epicardial circumfer-
ences and the segments of these circumferences made up
by the infarcted portion from each of the sections of left
ventricle were obtained by planimetry (Numronics Corp.).
The fraction of the left ventricular circumference that was
infarcted was calculated as the sum of the infarct lengths
divided by the sum of the circumferences for each of the
endocardial and epicardial surfaces, then expressed as a
percentage by multiplying by 100. Infarct size was ex-
pressed as the average of the percent fibrous scar of the
diendocardial and epicardial surfaces.
Results are expressed as mean ± 1 SE. MI rats, myocardial-infarcted rats; SHAM rats, sham-operated rats.

* t-Tests were performed between infarcted and sham-operated rats. NS denotes P > 0.05.

** Summary of Single Glomerular Function in Infarcted and Noninfarcted Rats **

| TABLE 2 | Summary of Single Glomerular Function in Infarcted and Noninfarcted Rats |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| SNGFR (nl/min) | \( P_{GC} \) (mm Hg) | \( P_T \) (mm Hg) | \( \Delta P \) (mm Hg) | \( \mu \) (nl/min) | \( Q_A \) (nl/min) | \( R_{A} \) (x10\(^{10}\) dyn s cm\(^{-2}\)) | \( R_{E} \) (nl/s/mm Hg) | \( K_i \) (nl/s/mm Hg) |
| MI rats | | | | | | | | |
| Initial period | 28.0 | 59.4 | 13.1 | 46.3 | 19.6 | 75 | 0.38 | 2.28 | 3.03 | 0.038 |
| Second period | ±2.8 | ±1.8 | ±1.0 | ±1.9 | ±0.4 | ±8 | ±0.02 | ±0.38 | ±0.31 | ±0.010 |
| | ±3.2 | ±1.9 | ±1.2 | ±1.5 | ±0.5 | ±11 | ±0.02 | ±0.13 | ±0.17 | ±0.018 |
| SHAM rats | | | | | | | | |
| Initial period | 41.7 | 50.8 | 14.4 | 36.4 | 20.8 | 165 | 0.25 | 1.91 | 0.95 | 0.087 |
| Second period | ±3.1 | ±1.0 | ±1.6 | ±1.1 | ±0.5 | ±17 | ±0.02 | ±0.14 | ±0.16 | ±0.017 |
| | 42.8 | 49.3 | 14.6 | 34.7 | 19.4 | 172 | 0.26 | 1.57 | 0.94 | 0.095 |
| | ±4.7 | ±1.2 | ±1.4 | ±1.1 | ±0.8 | ±27 | ±0.02 | ±0.43 | ±0.18 | ±0.020 |
| \( P^* \) | <0.025 | <0.005 | NS | <0.005 | NS | <0.005 | <0.005 | NS | <0.001 | NS |
| \( P_{T} \) | <0.05 | <0.001 | NS | <0.005 | <0.005 | <0.005 | <0.001 | NS | <0.005 | <0.002 |
| \( P_{T} \) | NS | NS | NS | <0.01 | NS | NS | NS | NS | NS | NS |
| \( P_{A} \) | NS | NS | NS | <0.025 | NS | <0.05 | <0.05 | NS | NS |

Results are expressed as mean ± 1 se. MI rats, myocardial-infarcted rats; SHAM rats, sham-operated rats.

* t-Tests were performed for the initial study period between infarcted and noninfarcted rats, and for the transition from initial to second study period in MI rats (\( P^* \)) and SHAM rats (\( P_{T} \)); and between initial study period of SHAM rats vs. second study period of MI rats (\( P_{A} \)). NS denotes P > 0.05.

\( K_i \) To calculate these average values, unique \( K_i \) values (five rats during initial period and four rats during second period in MI rats, and four rats during initial and two rats during second period in SHAM rats) and minimum \( K_i \) values were pooled.
which were a consequence of the extremely high $R_E$ that prevailed in rats with MI. Values for $P_{TR}$, $\pi_A$, and $R_A$ in rats with MI were similar to those in control rats, whereas values for $K_f$ tended to be lower in rats with MI compared to control rats. Since filtration pressure equilibrium (i.e., $\pi_E = \Delta P$) was achieved in many of the infarcted and noninfarcted rats, rigorous statistical comparison of $K_f$ values between the two groups was not possible. However, in the MI rats which attained filtration pressure disequilibrium, unique values for $K_f$ were uniformly below 0.035 nl/sec/mm Hg whereas values were uniformly greater than 0.040 nl/sec/mm Hg in sham-operated control rats. Thus, $K_f$ appears to be depressed in MI rats, contributing to the low level of SNGFR observed in many of these animals.

Proximal Tubule Function

Table 3 summarizes the behavior of superficial proximal tubules of rats with and without MI during the initial study period. As can be seen, values for APR were similar in infarcted and noninfarcted rats. Since SNGFR was significantly depressed in MI rats (Table 2) compared to controls, there was a significant elevation in fractional proximal reabsorption in rats with MI as $(TF/P)_n$ determined at the end-proximal sites of MI rats averaged 2.21 ± 0.12 compared to 1.64 ± 0.09 for controls. Moreover, due to the comparable levels of APR measured in infarcted and noninfarcted rats despite a depressed SNGFR in the former group, the rate of fluid delivered out of the proximal tubules to more distal sites was significantly lower in MI rats than in sham-operated controls (13.0 ± 1.5 vs. 25.9 ± 2.3 nl/min, $P < 0.025$). In these initial experiments, two of the important variables determining the rate of fluid uptake by the peritubular capillary were assessed. Thus, although the intracapillary hydraulic pressure ($P_E$) of MI rats (19.9 ± 1.0 mm Hg) was comparable to that of controls (19.9 ± 1.6 mm Hg), significantly higher levels of effenter arteriolar oncotic pressure $\pi(t)$ were noted in rats with infarcts (42.0 ± 2.7 vs. 33.1 ± 1.3 mm Hg in noninfarcted rats).

**Effects of Angiotensin I-Converting Enzyme Inhibition**

**General**

Values for $\overline{AP}$ and LVEDP remained essentially unchanged during SQ20881 infusion in control rats ($\overline{AP}$: 122 ± 4 vs. 119 ± 4 mm Hg, and LVEDP: 5 ± 0 vs. 5 ± 1 mm Hg, before and during infusion, respectively), whereas SQ20881 led to a mild but significant fall in AP (from 96 ± 5 to 84 ± 7 mm Hg, $P < 0.005$) and LVEDP (from 24 ± 3 to 21 ± 3 mm Hg, $P < 0.05$) in MI rats. Whole kidney GFR measured in five MI rats during SQ20881 infusion tended to increase (from 0.67 ± 0.09 to 0.93 ± 0.20 ml/min) although the change did not achieve statistical significance.

**Glomerular Dynamics**

A summary of the effects of SQ20881 infusion on renal cortical microcirculatory function in infarcted and noninfarcted rats is given in Table 2 and in Figure 1. Values in Figure 1 are expressed as percentage changes from initial baseline values. The acute infusion of SQ20881 failed to bring about a significant change in any of the indices measured in sham-operated control rats. In MI rats, teprotide led to a significant rise in SNGFR, on average by 7.0 ± 2.7 ml/min, or 22%. This increase in SNGFR was associated with a proportionately greater increase in $Q_A$, averaging 38 ± 11 ml/min, or 60%. Thus, SNFF tended to increase (from 0.67 ± 0.09 to 0.93 ± 0.20 ml/min) although the change did not achieve statistical significance.

### Table 3

<table>
<thead>
<tr>
<th>APR (nl/min)</th>
<th>$(TF/P)_n$</th>
<th>$P_E$ (mm Hg)</th>
<th>$R_E$ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI rats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial period</td>
<td>15.9 ± 1.8</td>
<td>2.21 ± 0.12</td>
<td>19.9 ± 1.0</td>
</tr>
<tr>
<td>Second period</td>
<td>12.9 ± 1.5</td>
<td>1.64 ± 0.09</td>
<td>17.2 ± 1.1</td>
</tr>
<tr>
<td>SHAM rats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial period</td>
<td>15.8 ± 2.0</td>
<td>1.64 ± 0.09</td>
<td>19.9 ± 1.6</td>
</tr>
<tr>
<td>Second period</td>
<td>14.5 ± 2.6</td>
<td>1.53 ± 0.07</td>
<td>19.9 ± 1.4</td>
</tr>
<tr>
<td>$P^*$</td>
<td>NS</td>
<td>&lt;0.005</td>
<td>NS</td>
</tr>
<tr>
<td>$P^+$</td>
<td>NS</td>
<td>&lt;0.005</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>$P^\dagger$</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>$P^\ddagger$</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>$P \parallel$</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± 1 se. MI rats, myocardial-infarcted rats; SHAM rats, sham-operated rats.

$^*$ t-tests were performed between infarcted and noninfarcted rats for the initial period, and between initial and second periods in the same infarcted (†) and noninfarcted (‡) rats. Statistical comparison was also made for the changes in MI rats vs. those in SHAM rats ($) and the difference between second period of MI rats and initial period of SHAM rats (∥).

Proximal Tubule Function

Proximal tubule function was also evaluated during SQ20881 infusion in the same infarcted and noninfarcted rats. As shown in Table 3 and Figure 2, APR remained essentially unchanged during SQ20881 infusion in both groups of rats. In con-
junction with the significant increase in SNGFR seen in MI rats with teprotide, however, there was a significant decrease in fractional proximal reabsorption, as assessed by \((TF/P)_{\text{in}}\) at end-proximal tubule.

so that fluid delivery to distal sites increased (from \(13.0 \pm 1.5\) to \(22.0 \pm 2.9\) nl/min, \(P < 0.025\)). In contrast, SNGFR, \((TF/P)_{\text{in}}\) and distal fluid delivery were not affected by teprotide in sham-operated controls. Although no important changes were seen in APR, efferent arteriolar colloid osmotic pressure, \(\pi_E\) fell significantly in MI rats, but not in control rats, while peritubular capillary hydraulic pressure tended to fall slightly in infarcted but not in sham-operated rats (Table 3).

**Discussion**

The rat model of extensive myocardial infarction employed in the present study enabled us to define the systemic and renal circulatory derangements of congestive heart failure. It has previously been established that rats with large infarcts tend to be mildly hypotensive and to have low cardiac outputs despite high left ventricular filling pressures (Pfeffer et al., 1979). The renal cortical microcirculatory dynamics assessed in euvoletic rats in the present study showed several features previously predicted to prevail in congestive heart failure (Humes et al., 1978). Thus, low values of glomerular plasma flow rate and high values of filtration fraction were demonstrated at the single nephron level. The measurement of preglomerular, glomerular, and postglomerular pressures and flows revealed that these reductions in glomerular plasma flow rate and elevations in filtration fraction were the consequence primarily of the profound constriction of the efferent arterioles. The effect of the latter was to sustain glomerular capillary hydraulic pressure at relatively high levels, thereby preventing a marked fall in GFR. Although not measured in our study, elevated venous pressure, which frequently prevails in congestive heart failure, may also contribute to the high \(P_{GC}\).

There is ample reason to implicate a role for alterations in the renin-angiotensin system in
congestive heart failure. Previous studies have documented high levels of plasma renin and aldosterone in humans and experimental animals with various forms of heart failure (Merrill et al., 1946; Watkins et al., 1976). Several factors are thought to be involved in the activation of the renin-angiotensin system in congestive heart failure. Hypotension and renal hypoperfusion are potentially capable of stimulating renal renin release (Davis and Freeman, 1976). Alterations in cardiac function that produce chronic atrial distension and blunting of atrial receptor sensitivity may decrease vagal tone, thereby increasing sympathetic neural current to the juxtaglomerular apparatus, the site of renal renin synthesis (Vander, 1965; Ganong, 1973; Davis and Freeman, 1976). In the present study, we evaluated the contribution of the renin-angiotensin system to the alterations of renal cortical microcirculatory dynamics in MI rats by administration of the angiotensin I-converting enzyme inhibitor, teprotide (SQ20881). Whereas teprotide infusion failed to change any of the microcirculatory indices measured in sham-operated control rats, significant alterations in each of these variables were seen in rats with myocardial infarction and congestive heart failure. Thus, only in rats with MI did teprotide lead to a marked increase in glomerular plasma flow rate, a modest rise in SNGFR, and a fall in single nephron filtration fraction. As discussed in detail in the Results, these changes were due to dilation of the renal arterioles, especially the efferent arteriole, and the rise in the glomerular capillary ultrafiltration coefficient.* These observed changes in glomerular dynamics to or toward normal control levels during inhibition of angiotensin II synthesis strongly suggest that the altered glomerular dynamics in congestive heart failure are due primarily to the enhanced intrarenal action of angiotensin II.

As discussed earlier, SNGFR was significantly depressed in rats with MI under baseline conditions. However, the absolute proximal fluid reabsorption rate, APR, in rats with MI was essentially identical to that in sham-operated rats so that fractional proximal reabsorption was elevated. Due to this alteration in proximal tubule function, fluid delivery out of the proximal tubules was depressed markedly in MI rats, to approximately 50% of control values. We also measured two important variables that determine peritubular capillary uptake of proximal reabsorbate, $P_E$ and $\pi_E$. Whereas $P_E$ of MI rats was similar to that of sham-operated controls, $\pi_E$ was increased significantly. Since this change in the intracapillary uptake force would otherwise predict an enhanced absolute proximal reabsorption in MI rats, the observed near-normal APR values in MI rats requires a concurrent offsetting change in one or more of the other determinants of peritubular capillary uptake which were not assessed in the present study. Of these remaining determinants, high interstitial oncotic pressure or abnormally low interstitial hydrostatic pressure could account for the observed level of APR in MI rats (Deen et al., 1973b).

A second possibility to account for the observed value for APR in MI rats relates to the decline in peritubular capillary plasma flow rate also measured in MI rats. In a recent series of experiments (Kon et al., 1983), the peritubular capillary reabsorption coefficient (an index of peritubular capillary surface area) was shown to be dependent upon the rate of blood entering the peritubular capillary network. Thus, the observed near-normal level of APR in MI rats may have been a consequence of the opposing influences of a high intracapillary colloid osmotic pressure and a low blood flow-induced reduction in reabsorptive surface area in the peritubular capillary network.

Of interest, the return of glomerular dynamics to or toward the normal control pattern seen during teprotide infusion in MI rats was accompanied by a return of proximal tubule fluid reabsorption toward normal control levels also. Teprotide led to a significant reduction in fractional proximal reabsorption and a nearly 2-fold increase in distal fluid delivery. In sham-operated control rats, however, no such changes were observed in glomerular and proximal tubule functions. The observed near-constancy in absolute proximal fluid reabsorption during teprotide infusion despite a marked reduction in peritubular capillary colloid osmotic pressure in rats with myocardial infarction again is consistent with the notion that the peritubular capillary surface area is dependent on the rate of blood entering this capillary network.

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* SNGFR was predicted to fall to 20.9 nl/min according to the mathematical model of Deen et al. (1973a), when a fall in $F_{EG}$ (from 98.6 to 43.0 mm Hg) and rise in $Q_{G}$ (from 75 to 113 nl/min) (i.e., consequences of arteriolar dilation) are assumed to occur, but $K_{G}$ remains constant with all inhibition in MI rats. This indicates that the effect of angiotensin II inhibition to elevate $K_{G}$ was more profound than its simultaneous action to lower $R_{C}$, thus resulting in a rise in SNGFR.

INDEX TERMS: Heart failure • Myocardial infarction • Renal hemodynamics • Glomerular ultrafiltration • Angiotensin II
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