The Distribution of Intrarenal Blood Flow in Normal and Hypertensive Man

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SUMMARY

Observations were made on eight normotensive subjects and on 12 patients with essential hypertension to determine whether the intrarenal distribution of blood flow is altered in essential hypertension. Dye-dilution curves were recorded across the renal vascular bed and a set of integral transformations, developed by Gomez, was used to determine distribution of blood flow per unit renal blood volume across the renal vascular bed from dye-dilution curves. Observations also were made on two hypertensives and two normotensives during administration of norepinephrine. The distribution of specific blood flow and the functional renal blood volume in the right kidney of patients with essential hypertension were comparable to those in normal subjects, but the mean specific blood flow was reduced in essential hypertension. Failure to demonstrate altered distribution of specific blood flow in essential hypertension indicated an absence of focal reductions in renal blood flow and that blood flow is reduced uniformly throughout the renal vascular bed in essential hypertension. This reduction in specific renal blood flow is attributed to arteriolar vasoconstriction.

Additional Indexing Words:
Nephrosclerosis
Indicator-dilution technique
Norepinephrine

RENAL blood flow is reduced relative to functional tubular mass in essential hypertension, but whether this represents a primary alteration in renal hemodynamics rather than a manifestation of the kidney's participation in the generalized vasoconstriction which characterizes essential hypertension is not known. Reasoning from the experimental production of hypertension by partial clamping of the renal artery and from its clinical counterpart, renal artery stenosis, it has been postulated that renal ischemia secondary to arteriolar sclerosis might play a role in the pathogenesis of essential hypertension. That renal ischemia in essential hypertension might be focal in nature is suggested by certain anatomic and functional features of the kidney in this disease. Renal arteriolar sclerosis is patchy in distribution, and tubular atrophy, which has been attributed to ischemia, is irregularly distributed throughout the renal parenchyma. Further, our previous demonstration of disparities in renal hemodynamics and in excretion of salt and water between the separate kidneys suggests that the hemodynamic alterations within the kidney might not be uniform in essential hypertension.

In the present study an attempt has been made to determine whether there is an al-
teration in the intrarenal distribution of blood flow in essential hypertension. Since clearance techniques describe the blood flow of the kidney as a whole and do not provide information regarding blood flow through individual nephrons, we have utilized dye-dilution curves recorded across the renal vascular bed in order to compare the distribution of intrarenal blood flow in normotensive subjects and patients with essential hypertension. The distribution of blood flow per unit renal blood volume across the renal vascular bed has been inferred from the frequency distribution of transit times which make up the dye-dilution curve by applying a set of integral transformations developed by Gomez.

**Methods**

Observations have been made in eight normotensive subjects and in 12 patients with essential hypertension selected from the wards of the New York University Medical Division of Bellevue Hospital. The normotensive subjects ranged in age from 29 to 39 years; all had blood pressures below 140/90 mm Hg and were considered to be free of cardiovascular or renal disease. Nine patients with essential hypertension had glomerular filtration rates in excess of 90 ml/min and were free of proteinuria; they ranged in age from 25 to 53 years (table 1). Three hypertensive patients with advanced nephrosclerosis (J.C., B.J., and C.L.) and decreased filtration rate and $T_{mPAH}$ are considered separately (table 2).

All subjects were maintained on a regular ward diet. Studies were performed in the fasting state with moderate hydration. An infusion of 5% mannitol was administered at 2 ml/min to ensure adequate flow of urine. Ureteral catheterization was performed, and the glomerular filtration rate (GFR) and renal plasma flow (RPF) of the individual kidneys were measured throughout the study according to techniques and methods described previously. Odman-Ledin green catheters were then introduced into the common femoral artery and vein according to the method of Seldinger, manipulated into the right renal artery and vein, and their position confirmed by the injection of a small amount of diatrizoate (Hypaque). The right kidney was chosen for study in order to avoid mixture of the renal venous sampling with blood from the spermatic (or ovarian) and adrenal or anomalous veins.

Indocyanine green was injected into the renal artery, and the concentration of the dye in the renal vein was measured with a Gilford continuous recording densitometer. The volume of the injectate was 0.6 ml and the injection time approximately 0.2 second. The volume of blood contained by the venous sampling catheter was 0.7 ml; a constant flow of 0.5 ml/sec through this catheter and the densitometer was maintained using a Harvard withdrawal pump. The output of the densitometer was corrected for the time constant of the photocell by inserting a resistance-capacitance combination between two DC amplifiers of the recording polygraph. The curves were corrected for catheter distortion as described previously.

In four subjects, two hypertensives and two normotensives, an additional series of observations was made during the administration of nor-adrenaline via the antecubital vein at rates of 6 to 20 mg/min. In one subject indicator-dilution curves were recorded immediately after the administration of acetylcholine, 230 mg/min, into a branch of the renal artery via a subselective catheter advanced beyond the renal artery catheter.

Inulin and p-aminohippurate (PAH) concentrations in serum and urine were determined by methods given previously. In the determination of the extraction ratio of PAH ($E_{PAH}$), the concentration of PAH in renal venous blood was measured using a 1:6 rather than 1:15 dilution of plasma with an appropriate set of standards. All clearance values were corrected to 1.73 m² body surface area.

Renal blood flow, $Q_{PAH}$, of the right kidney was calculated from the plasma clearance and extraction ratio of PAH and the hematocrit.

$$Q_{PAH} (\text{ml/sec}) = \frac{C_{PAH} (\text{ml/min})}{E_{PAH} \times (1 - \text{hematocrit}) \times 60 (\text{sec/min})}.$$

In a separate calculation, a value for renal blood flow, $Q_{dyne}$, was derived from the area of the dye-dilution curve.

GFR of the right kidney in the normotensive subjects averaged $53 \pm 9$ ml/min and in the hypertensives without advanced nephrosclerosis $49 \pm 9$ ml/min (table 1). RPF averaged $260 \pm 9$ ml/min.
Table 1
Renal Hemodynamics, Functional Blood Volume, and Distribution of Specific Blood Flow

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)</th>
<th>GFR (ml/min)</th>
<th>RPF (ml/min)</th>
<th>Filtration fraction</th>
<th>$E_{PAH}$ (ml/sec)</th>
<th>$Q_{PAH}$ (ml/sec)</th>
<th>$Q_{PAH}$ (ml/sec)</th>
<th>Renal blood volume (ml)</th>
<th>Mean specific blood flow (sec^-1)</th>
<th>$\Delta T$</th>
<th>$T_1$</th>
<th>$T_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.C.</td>
<td>26</td>
<td>73</td>
<td>349</td>
<td>0.21</td>
<td>0.81</td>
<td>11.1</td>
<td>14.8</td>
<td>46.2</td>
<td>0.240</td>
<td>0.617</td>
<td>0.317</td>
<td>1.98</td>
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<tr>
<td>A.J.</td>
<td>34</td>
<td>61</td>
<td>329</td>
<td>0.18</td>
<td>0.89</td>
<td>10.3</td>
<td>13.8</td>
<td>28.7</td>
<td>0.359</td>
<td>0.650</td>
<td>0.325</td>
<td>2.44</td>
</tr>
<tr>
<td>J.F.†</td>
<td>29</td>
<td>59</td>
<td>306</td>
<td>0.19</td>
<td>0.73</td>
<td>10.9</td>
<td>10.5</td>
<td>47.6</td>
<td>0.229</td>
<td>0.575</td>
<td>0.418</td>
<td>2.45</td>
</tr>
<tr>
<td>E.M.</td>
<td>39</td>
<td>58</td>
<td>314</td>
<td>0.18</td>
<td>0.86</td>
<td>9.9</td>
<td>13.5</td>
<td>56.0</td>
<td>0.178</td>
<td>0.685</td>
<td>0.303</td>
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<td>W.W.</td>
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<td>49</td>
<td>230</td>
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<td>0.89</td>
<td>6.5</td>
<td></td>
<td>33.7</td>
<td>0.193</td>
<td>0.612</td>
<td>0.330</td>
<td>2.13</td>
</tr>
<tr>
<td>W.M.†</td>
<td>34</td>
<td>46</td>
<td>158</td>
<td>0.29</td>
<td>0.86</td>
<td>5.5</td>
<td>5.9</td>
<td>28.9</td>
<td>0.190</td>
<td>0.663</td>
<td>0.301</td>
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<td>C.H.†</td>
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<td>43</td>
<td>223</td>
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<td>6.6</td>
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<td>0.233</td>
<td>0.653</td>
<td>0.326</td>
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<tr>
<td>C.S.</td>
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<td>40</td>
<td>170</td>
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<td>0.92</td>
<td>5.0</td>
<td>5.7</td>
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<td>0.216</td>
<td>0.749</td>
<td>0.249</td>
<td>2.46</td>
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<tr>
<td>Mean</td>
<td>53</td>
<td>260</td>
<td>±9</td>
<td>±0.04</td>
<td>±0.04</td>
<td>±0.06</td>
<td>±10.9</td>
<td>±0.053</td>
<td>±0.044</td>
<td>±0.28</td>
<td>±0.28</td>
<td>±0.28</td>
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</table>

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)</th>
<th>GFR (ml/min)</th>
<th>RPF (ml/min)</th>
<th>Filtration fraction</th>
<th>$E_{PAH}$ (ml/sec)</th>
<th>$Q_{PAH}$ (ml/sec)</th>
<th>$Q_{PAH}$ (ml/sec)</th>
<th>Renal blood volume (ml)</th>
<th>Mean specific blood flow (sec^-1)</th>
<th>$\Delta T$</th>
<th>$T_1$</th>
<th>$T_2$</th>
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<td>0.91</td>
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<td>0.628</td>
<td>0.359</td>
<td>2.54</td>
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<td>J.B.</td>
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<td>54</td>
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<td>5.9</td>
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<td>0.570</td>
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<tr>
<td>E.F.†</td>
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<td>53</td>
<td>238</td>
<td>0.22</td>
<td>0.87</td>
<td>7.8</td>
<td>7.5</td>
<td>39.0</td>
<td>0.200</td>
<td>0.613</td>
<td>0.328</td>
<td>2.18</td>
</tr>
<tr>
<td>R.W.</td>
<td>53</td>
<td>50</td>
<td>223</td>
<td>0.22</td>
<td>0.75</td>
<td>7.5</td>
<td>7.5</td>
<td>41.2</td>
<td>0.182</td>
<td>0.660</td>
<td>0.243</td>
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</tr>
<tr>
<td>H.W.</td>
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<td>49</td>
<td>200</td>
<td>0.25</td>
<td>0.86</td>
<td>7.8</td>
<td>6.5</td>
<td>33.6</td>
<td>0.232</td>
<td>0.612</td>
<td>0.336</td>
<td>2.21</td>
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<tr>
<td>E.S.</td>
<td>39</td>
<td>48</td>
<td>174</td>
<td>0.28</td>
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<td>4.8</td>
<td>5.9</td>
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<td>0.564</td>
<td>0.378</td>
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<td>180</td>
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<td>7.4</td>
<td>34.1</td>
<td>0.173</td>
<td>0.586</td>
<td>0.345</td>
<td>1.98</td>
</tr>
<tr>
<td>F.B.</td>
<td>49</td>
<td>36</td>
<td>150</td>
<td>0.24</td>
<td>0.73</td>
<td>5.8</td>
<td></td>
<td>32.9</td>
<td>0.176</td>
<td>0.724</td>
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</tr>
<tr>
<td>Mean</td>
<td>49</td>
<td>207</td>
<td>±9</td>
<td>±0.03</td>
<td>±0.03</td>
<td>±0.05</td>
<td>±6.9</td>
<td>±0.028</td>
<td>±0.063</td>
<td>±0.097</td>
<td>±0.25</td>
<td>±0.25</td>
</tr>
</tbody>
</table>

*Values are those for the right kidney. Clearance values shown were obtained during the recording of the dye-dilution curves.
†Bladder collection. Clearances for right kidney assumed to equal total $/2$.
‡Bladder collection. Clearances for right kidney calculated as total $/1.8$ based on previous determination of separate function.
DISTRIBUTION OF INTRARENAL BLOOD FLOW

Table 2
Renal Hemodynamics, Functional Blood Volume, and Distribution of Specific Blood Flow in Patients with Advanced Nephrosclerosis*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)</th>
<th>GFR (ml/min)</th>
<th>RPF (ml/min)</th>
<th>Filtration fraction</th>
<th>$E_{PAH}$</th>
<th>$T_{PAH}$ (mg/min)</th>
<th>Renal blood volume (ml)</th>
<th>Mean specific blood flow (sec$^{-1}$)</th>
<th>$\Delta t/\bar{t}$</th>
<th>$\bar{z}/\bar{t}$</th>
<th>$\bar{z}_{max}/\bar{t}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>J.C.</td>
<td>46</td>
<td>37</td>
<td>96</td>
<td>0.39</td>
<td>0.75</td>
<td>14</td>
<td>30.3</td>
<td>0.127</td>
<td>0.698</td>
<td>0.284</td>
<td>2.40</td>
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<tr>
<td>B.J.</td>
<td>57</td>
<td>28</td>
<td>111</td>
<td>0.25</td>
<td>0.83</td>
<td>36</td>
<td>26.9</td>
<td>0.190</td>
<td>0.715</td>
<td>0.278</td>
<td>2.65</td>
</tr>
<tr>
<td>C.L.</td>
<td>40</td>
<td>15</td>
<td>47</td>
<td>0.33</td>
<td>0.33</td>
<td>12</td>
<td>16.8</td>
<td>0.095</td>
<td>0.734</td>
<td>0.277</td>
<td>2.84</td>
</tr>
</tbody>
</table>

*Values are those for the right kidney.

69 ml/min in the normotensives and was significantly lower in the patients with essential hypertension, 207 ± 35 ml ($P < 0.05$). The mean filtration fraction was 0.21 in the normotensives, 0.24 in the hypertensives. The values for GFR and RPF in the normotensive subjects do not differ significantly from those reported previously in the separate kidneys in a larger group of normotensive subjects who were examined during ureteral catheterization.8

From mathematical treatment of the dye-dilution curve a representation of the range and relative frequency of blood flow per unit blood volume through the kidney is obtained. The renal vascular bed is considered to be composed of an infinite number of channels of unit blood volume and the blood flows are expressed relative to these units. This ratio of flow per unit blood volume (or per "channel") is designated as specific blood flow ($\zeta$). Transformation of the dye-dilution curve as described in previous publications9,7 yields the distribution curve of specific blood flow.

A representative dye-dilution curve and the frequency distribution curve derived from it are shown in figures 1 and 2.

From the distribution of specific blood flow, $\zeta$, the mean specific blood flow, $\bar{\zeta}$, (which is numerically equal to the reciprocal of the mean transit time) is determined. In addition $\bar{\zeta}_{2}$, the highest specific blood flow (numerically equal to the reciprocal of the appearance time), $\bar{\zeta}_{1}$, the specific blood flow at which the ordinate is 1% of the maximal amplitude of the distribution curve, and $\Delta \zeta$, the width of the curve at one half the ordinate value of the peak are identified.

Renal blood volume was calculated from the renal blood flow ($Q_{PAH}$) and the mean specific blood flow as defined by the distribution function, that is:

Renal blood volume (ml/1.73 m² body surface area) = $Q_{PAH}/\bar{\zeta}$.

**Results**

In both normotensive and hypertensive subjects the distribution curve of specific blood

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**Figure 1**
Dye-dilution curve from renal vein (normotensive subject). The two upper curves are electronically corrected for the time constant of the densitometer; the lowest curve is not. The arrow indicates the time of injection. Time intervals: 0.2 sec.

**Figure 2**
Distribution curve of specific blood flow (normotensive subject). On the abscissa, specific blood flow (flow per unit volume); on the ordinate, relative number of units $h(\zeta)$.

*Circulation, Volume XXXV, February 1967*
flow was, in every instance, unimodal. Representative distribution curves for all normotensive subjects and the nine patients with essential hypertension are shown in figure 3. The mean specific blood flow, \( \bar{Q} \), was significantly reduced in the patients with essential hypertension, \( 0.188 \pm 0.028 \text{ sec}^{-1} \) as compared to the value of \( 0.230 \pm 0.053 \text{ sec}^{-1} \) in the normotensive group (\( P < 0.05 \); table 1). The ratio of the lowest specific blood flow to the mean specific blood flow, \( \xi_1/\bar{Q} \), averaged 0.32, and the ratio of the highest specific blood flow to the mean, \( \xi_2/\bar{Q} \), averaged 2.44 in the normotensives. While the mean specific blood flow

Figure 3

Distribution curves of specific blood flow. (Upper panel) Normotensive subjects. All curves have been normalized to the same area. The heavier line represents a mean distribution curve obtained utilizing, in the transformation equation, mean values from the dye curves of individual patients. (Lower panel) Hypertensive subjects. Curves of individual subjects and a mean distribution curve are shown. The mean curve demonstrates displacement in the direction of lower specific blood flow.
was lower in the patients with essential hypertension, the range of specific blood flows about the mean was the same as in the normotensives ($\zeta_1/\bar{z} = 0.33, \zeta_2/\bar{z} = 2.25$; table 1). No significant difference in the shape of the distribution curve was found when the curves in the two groups were compared in respect to $\Delta \zeta/\bar{z}$, the ratio of the half width of the distribution to the mean.

A further comparison of the distribution of specific blood flow in normotensive and hypertensive subjects was carried out by determining the skewness and kurtosis of the distribution curves in each subject. In the normotensive subjects skewness averaged $0.372 \pm 0.217$ and kurtosis $3.045 \pm 0.264$, while in the hypertensives the average values for skewness and kurtosis were $0.223 \pm 0.156$ and $2.838 \pm 0.150$. There was no significant difference in the skewness or kurtosis of the distribution of specific blood flow in the normotensive and hypertensive groups ($P < 0.05$). This is seen graphically in figure 4 where the curves representing the means of the normotensives and the hypertensive subjects are replotted with equal half width and coincident maximal amplitude.

The functional renal blood volume was comparable in the two groups; in normotensives, $36.7 \pm 10.9$ ml and in hypertensives, $37.7 \pm 6.9$ ml. The average renal blood volume in a group of 12 hypertensives reported by Cohen and Gombos was $47.4 \pm 3.6$ ml. Assuming an average kidney weight of 150 grams, the ratio of functional renal volume to kidney mass in our subjects would calculate to be approximately 24 ml/100 g kidney, a value which is comparable to that published by Chinard and Lillienfeld and their associates concerning the dog.

Each of the three patients with advanced nephrosclerosis was found to have reduction in mean specific blood flow; in two, these values were different from the mean value of the patients with essential hypertension by more than 2 standard deviations. Despite the marked reduction in specific blood flow, the distribution of specific blood flows in these patients did not differ from that found in normotensive subjects (table 2).

Administration of norepinephrine to two normotensive and two hypertensive subjects decreased the mean specific blood flow to values ranging from 55% to 83% of control values. No significant change occurred in the form of the distribution curve of $\zeta$, or in renal blood volume (table 3).

In order to determine how the form of the indicator-dilution curve and the frequency distribution of specific blood flow would be affected by a known alteration in the distribution of intrarenal blood flow, acetylcholine was infused into a branch of the renal artery to induce increased perfusion of a portion of the kidney. In studies carried out in our laboratory, acetylcholine has resulted in increased renal blood flow and specific blood flow, an effect which persists for 10 to 20 minutes after perfusion is terminated. The perfusion of a segment of the kidney was reflected by a modest increase in renal plasma flow as determined from PAH clearance for the whole kidney (from 205 ml/min to 262 ml/min). A distinct alteration in the indicator-dilution curve recorded across the renal vascular bed was observed (fig. 5); the distribution of specific blood was skewed to the right and a bimodal distribution of intrarenal specific blood flows resulted.

The variation in renal blood flow, $Q_{dye}$, as determined from successive dye-dilution curves recorded serially during a 5 minute

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**Figure 4**

Mean curves in normotensive and hypertensive subjects replotted with coincident maximum and equal half width. (Heavy line) Normotensives; (dashed line) hypertensives. The two curves do not differ significantly when compared for skewness and kurtosis.
Table 3

**Effect of Norepinephrine on Functional Renal Blood Volume and Distribution of Specific Blood Flow**

<table>
<thead>
<tr>
<th>Subject and diagnosis</th>
<th>Norepinephrine</th>
<th>Mean blood pressure (mm Hg)</th>
<th>( Q_{PAH} ) (ml/sec)</th>
<th>( E_{PAH} )</th>
<th>Renal blood volume (ml)</th>
<th>( \bar{t} )</th>
<th>( \Delta t/\bar{t} )</th>
<th>( t_r/\bar{t} )</th>
<th>( t_v/\bar{t} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>W.M., Control, normotension</td>
<td>Control</td>
<td>81</td>
<td>5.9</td>
<td>0.86</td>
<td>29.1</td>
<td>0.190</td>
<td>0.663</td>
<td>0.301</td>
<td>2.80</td>
</tr>
<tr>
<td></td>
<td>7 ( \mu g/min )</td>
<td>129</td>
<td>4.4</td>
<td>0.86</td>
<td>25.6</td>
<td>0.129</td>
<td>0.627</td>
<td>0.314</td>
<td>3.54</td>
</tr>
<tr>
<td>J.B., Control, normotension</td>
<td>Control</td>
<td>101</td>
<td>4.1</td>
<td>0.88</td>
<td>31.0</td>
<td>0.165</td>
<td>0.693</td>
<td>0.281</td>
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</tr>
<tr>
<td></td>
<td>10 ( \mu g/min )</td>
<td>120</td>
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<td>34.5</td>
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<td>0.615</td>
<td>0.351</td>
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<tr>
<td>S.Z., Control, essential hypertension</td>
<td>Control</td>
<td>119</td>
<td>7.8</td>
<td>0.91</td>
<td>44.6</td>
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<td>0.628</td>
<td>0.359</td>
<td>2.54</td>
</tr>
<tr>
<td></td>
<td>20 ( \mu g/min )</td>
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<td>0.097</td>
<td>0.638</td>
<td>0.331</td>
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<td>E.F., Control, essential hypertension</td>
<td>Control</td>
<td>131</td>
<td>7.5( \dagger )</td>
<td>0.87</td>
<td>37.5</td>
<td>0.200</td>
<td>0.613</td>
<td>0.328</td>
<td>2.18</td>
</tr>
<tr>
<td></td>
<td>6 ( \mu g/min )</td>
<td>180</td>
<td>6.2( \dagger )</td>
<td>0.87</td>
<td>37.5</td>
<td>0.165</td>
<td>0.623</td>
<td>0.312</td>
<td>2.05</td>
</tr>
</tbody>
</table>

*Values are those for the right kidney.

\( \dagger \)Renal blood flow measured by dye dilution (\( Q_{dy} \)).

Period was examined in 12 patients. Five to thirteen curves were obtained in each patient; the average deviation for the group was found to be 7.7%. This variability may reflect minute-to-minute fluctuations in renal blood flow, as well as errors inherent in the dye-dilution method, such as variable loss of dye during rapid injection, inadequate mixing of blood in the renal vein, or admixture of vena caval blood during aspiration from the renal vein.

A comparison of the values for renal blood flow as measured by the indicator-dilution technique (\( Q_{dy} \)) and the clearance technique

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**ACETYLCHOLINE**

<table>
<thead>
<tr>
<th>Renal Blood Flow (ml/min)</th>
<th>Dye Dilution Curve</th>
<th>Distribution Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>360</td>
<td><img src="example.png" alt="Dye Dilution Curve" /></td>
<td><img src="example.png" alt="Distribution Curve" /></td>
</tr>
<tr>
<td>473</td>
<td><img src="example.png" alt="Dye Dilution Curve" /></td>
<td><img src="example.png" alt="Distribution Curve" /></td>
</tr>
</tbody>
</table>

**Figure 5**

Altered distribution of specific blood flow. (Upper panel) Control measurements. (Lower panel) Measurements after segmental perfusion with acetylcholine. All curves were recorded following injection of dye into the main renal artery.
Discussion

We have found that the distribution of specific blood flow in the kidney of patients with essential hypertension is comparable to that in normal subjects despite a reduction in mean specific blood flow. Failure to demonstrate alteration in the distribution of specific blood flow in the patients with essential hypertension indicates that focal reductions in renal blood flow were not present. Focal ischemia, that is, reduced blood flow through some vascular channels would be expected to produce skewing of the distribution curve in the direction of lower specific blood flow.

The presence of completely obliterated channels in a random distribution would yield an unaltered distribution curve of specific blood flow in the remaining nephrons, but would not be consistent with our finding of essentially normal glomerular filtration rates and renal blood volumes in the hypertensive subjects. Loss of vascular channels with preponderantly higher or lower specific blood flow would result in distortion of the distribution curve as well as reduction in functional renal blood volume. Our present finding is in accord with the studies of Smith and co-workers in which the distribution of blood flows per unit of tubular excretory capacity was unaltered in a group of hypertensive subjects in whom the intrarenal distribution of blood flow was inferred from consideration of the titration curve of excretion of iodopyracet (Diodrast).

Although the pathological abnormalities in the kidney would suggest focal ischemia, our data indicate that the distribution of blood flow is not altered in essential hypertension. While the present technique would have revealed an alteration in the distribution of specific blood flow if the reduced renal blood flow were attributable in toto to focal ischemia, it is possible that there might be some abnormality in intrarenal blood flow beyond the resolution of the present technique. Alteration in the distribution of specific blood flow, albeit of physiological significance, might not be detected if flow were reduced focally in sufficiently small numbers of channels. Further, it is possible that focal reduction in specific blood flow resulting from structural alterations within the renal vascular bed which might be detectable by our present method was masked by the predominant effect of superimposed arteriolar constriction.

Significant reduction in mean specific blood flow was observed in the subjects with essential hypertension. The hemodynamic pattern of reduction in mean specific blood flow, unaltered distribution of specific blood flow,
and unchanged functional renal blood volume suggest the presence of uniform reduction in blood flow in the renal vascular bed. Previous observations provided evidence that renal arteriolar resistance is increased in essential hypertension.⁶ Although post-glo- 

merular hemodynamics also contribute to overall renal resistance, the major component is arteriolar⁶ and we attribute the reduction in specific blood flow to arteriolar vasoconstriction. It is not possible, however, to conclude that the uniformity of reduction in specific blood flow is due to strictly uniform arteriolar vasoconstriction since changes in postglomerular hemodynamics may contribute to the maintenance of unaltered distribution of specific blood flow. Reduction in renal blood flow resulting from arteriolar constriction would not be expected to result in significant alteration in renal blood volume since the peritubular capillaries comprise, by far, the largest component of the renal vascular bed.⁸ The hypothesis that uniform decrease in specific blood flow in the presence of unchanged renal blood volume in essential hypertension results from renal arteriolar vasoconstriction is supported by our additional observation that vasoconstriction as induced by norepinephrine reproduced the hemodynamic pattern of the hypertensive patients in two normotensive subjects, and further decreased specific blood flow without changing renal blood volume in two patients with essential hypertension.* No change in the shape of the distribution curve of specific blood flow occurred during norepinephrine-induced vasoconstriction. Observations made after reduc-

*The finding that $E_{PAH}$ was unchanged during administration of norepinephrine confirms previous observations¹⁷ and is in agreement with the conclusion, based on the observation that epinephrine does not affect transport maxima for glucose and Diodrast,¹⁵ that vasoconstriction does not exclude from perfusion any substantial quantity of tubular mass. The observation that the renal blood volume is unchanged despite reduction in renal blood flow stands in contrast to the behavior of other vascular beds, such as that of muscle, in which reduction of blood flow is accompanied by a decrease in vascular volume attributed to closure of precapillary sphincters.

Conclusions

The distribution of specific blood flow through the kidney was compared in eight normotensive subjects and in 12 patients with essential hypertension. From the demonstration of reduced specific blood flow, unaltered distribution of specific blood flow, and normal functional renal blood volume, it is concluded that blood flow is reduced uniformly throughout the renal vascular bed in essential hypertension.

Although we attribute the reduction in specific blood flow to arteriolar vasoconstriction, it cannot be concluded that arteriolar resistance is necessarily increased uniformly, since postglomerular hemodynamics may also affect renal resistance and the distribution of intrarenal blood flow.

Acknowledgment

We are grateful to Mr. Robert Bloom for assistance in data programming and to Misses Susan Baron, Francine Reff, Eileen McIntosh, and Iris Hollingsworth for technical assistance.

References


Circulation, Volume XXXV, February 1967

A Centennial Note—Canadian Medical Association

Among the various associations which are the least tinctured with selfishness, and therefore tend to elevate our nature and benefit mankind, are those having such objects in view as I have just detailed. Whatever tends to raise and dignify our profession, tends also to the comfort and well being of society. Whatever tends to make individual members of that profession better men and better physicians, contributes most materially to the advantage of the public at large. There is nothing selfish, then, in this or similar conventions which are annually taking place throughout the world. We are not seeking our own aggrandisement, nor our own individual advantages; we desire to promote the general welfare of our fellow-men, and shall rest content to benefit the mass.—James A. Sewell: The Organizing Meeting at Quebec, October 9, 1867. In H. E. MacDermot: History of the Canadian Medical Association, 1867-1921. Toronto, Murray Printing Co., Ltd., 1935, p. 29.
The Distribution of Intrarenal Blood Flow in Normal and Hypertensive Man

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Circulation. 1967;35:250-259
doi: 10.1161/01.CIR.35.2.250

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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