Serial Hemodynamics after Renal Allotransplantation in Man

By SAMUEL L. KOUNTZ, M.D., GARY TRUEX, M.D.,
LAURENCE E. EARLEY, M.D., AND FOLKERT O. BELZER, M.D.

SUMMARY
Serial measurements of glomerular filtration rate (GFR), independent and simultaneous clearances and extractions of para-aminohippurate (PAH), radiohippuran, and iodopyracet (Diodrast) were made in 11 adults and one child who received renal transplants from living donors. Measurements were made within 3 hours and repeated two to four times during the following 14 days. Immediately after transplantation, PAH clearance averaged 385 ml/min (range, 218 to 510), GFR averaged 54 ml/min (range, 22 to 87), renal plasma flow (RPF) averaged 672 ml/min (range, 309 to 1424), and marked vasodilatation was present with an average renal blood flow (RBF) of 979 ml/min (range, 435 to 2,114). As observed in other studies, immediate diuresis and natriuresis but no glycosuria occurred. Extraction ratios for PAH (EPAH) were below normal, ranging from 0.59 to 0.94, and those for $^{125}$ (or $^{131}$)I-hippuran, and $^{131}$I-Diodrast were even lower. Extraction ratio for PAH to radiohippuran averaged 1.43 in 17 simultaneous studies. However, RPF measured simultaneously with these agents was the same, indicating a true difference in transport of these substances. The low extraction ratio for PAH, $^{131}$ (or $^{125}$)I-hippuran and $^{131}$I-Diodrast was not related to depression of the maximal tubular transport of PAH and may have been a consequence of vasodilatation and increased RBF. Another observation made on these kidneys was a low filtration fraction which averaged 0.089. These hemodynamic changes did not appear to relate to circulating factors in the anephric recipient since they persisted throughout the 13-day study period in eight patients. In four patients showing transient rejection, GFR and the clearance of PAH and $^{131}$I-hippuran decreased proportionately more than RBF. It is concluded that marked vasodilatation and a low filtration fraction are characteristic of uncomplicated renal allotransplantation in man, and that early rejection is expressed by measurable decreases in the clearances of PAH and insulin despite maintenance of RBF. These changes were present prior to clinical evidence of rejection.

Additional Indexing Words:
Renal hemodynamics Extraction ratios Renal vasodilatation

ALTHOUGH changes in renal blood flow are thought to be an early expression of the rejection reaction, which has been detected by independent changes in the renogram,1 glomerular filtration rate (GFR),2-4 intrarenal distribution of blood flow,5,6 pulsatile and total blood flow,7-9 and the single-injection $^{131}$I-hippuran

---

From the Departments of Surgery and Medicine, University of California School of Medicine, San Francisco, California.
Supported in part by Grant FR-79 (GCRC), Divisions of Research Facilities and Resources and Grant AM11290 from the U. S. Public Health Service; Grant C-67-21 from the Life Insurance Medical Research Foundation; and a grant from the San Francisco Heart Association.
Address for reprints: Dr. Samuel L. Kountz, Department of Surgery, University of California, San Francisco Medical Center, San Francisco, California 94122.
Received April 18, 1969; accepted for publication October 8, 1969.

Circulation, Volume XXI, February 1970

217
clearance, the patterns of renal hemodynamics following transplantation in man have not been reported.

The purpose of this study was to measure the renal hemodynamic changes repeatedly during the early postoperative period in a series of patients who received kidneys from living donors. This offered the opportunity to observe the course of renal hemodynamics in patients with and without the complication of transient rejection. In addition, the effect of transplantation on normal kidneys in an altered physiologic state of the recipient was observed almost immediately after operation. Although the clearance of PAH has been reported to be within the normal range immediately after transplantation, the present data demonstrate that this measurement grossly underestimates true renal plasma flow in the transplanted kidney. The extraction ratios for PAH and related substances were strikingly depressed immediately after transplantation and remained low throughout the 14-day period of observation. The data demonstrate that marked vasodilatation is characteristic of uncomplicated renal transplantation and may persist to a relative degree during transient rejection when there has been a severe depression of the clearances of inulin and PAH.

Methods

Twelve consecutive patients who received renal allografts from living donors (eight related and four unrelated) were studied. The kidneys were transplanted by the standard technic. At the time of transplantation, catheters were placed in the transplanted renal artery and vein and were exteriorized onto the anterior abdominal wall (fig. 1). The arterial catheter was used for intrarenal administration of immunosuppressive and pharmacologic agents. The venous catheter was used for collection of renal venous blood. The sampling tip was placed 4 to 6 cm from the iliac-renal vein anastomosis to make sure the samples of renal vein blood were not contaminated with systemic blood. At the end of each study period, the position of the renal venous catheter was confirmed radiologically (fig. 2).

Initial measurements of renal hemodynamics were begun within 3 hours after transplantation. Following operation, the patients received 5% dextrose and water for 24 to 48 hours at

Figure 1
Technic of inserting renal venous catheter.

Figure 2
Venogram 14 days after transplantation showing tip of catheter high up in the renal vein. A = artery; V = vein.

approximately 1 ml/min and then were allowed a regular house diet.

Hemodynamic Studies

The glomerular filtration rate (GFR) was estimated by independent or simultaneous clearances of inulin and 125I-iothalamate. In 26 simultaneous clearance determinations of inulin and 125I-iothalamate, the GFR was 58.4 and 60.8 ml/min, re-
HEMODYNAMICS AFTER RENAL TRANSPLANT

respectively. Student's t-test showed no significant difference. Independent and simultaneous clearances (C) and extraction ratios (E) of paraaminohippurate (PAH), 131I (or 125I)-hippuran, and 131I-iodopyracet (Diodrast) were calculated from the following formulae: 

\[ C = \frac{UV}{A} \]

where U is the urine concentration of these substances, V is the rate of urine flow (ml/min), and A, the arterial concentration of the substances; and

\[ E = \frac{A - R}{A} \]

where, in addition, R is the renal venous concentration of these substances. Renal plasma flow (RPF) was calculated by the formula of Wolf \(^{15}\) as

\[ \text{RPF} = \frac{V}{(U - R)} \]

renal blood flow was calculated as 

\[ \text{RBF} = \frac{\text{RPF}}{1 - \text{hematocrit}} \]

and filtration fraction was calculated as GFR/RPF. Maximal tubular transport (TmPAH) was determined during infusion of PAH sufficient to increase plasma concentrations to levels greater than 53 mg/100 ml. At the beginning of each study, priming injections of inulin or 125I-iothalamate, or both were given; then PAH and 131I-hippuran or PAH, I-hippuran and 131I-iodopyracet were given, followed by constant intravenous infusion of these substances in amounts sufficient to permit measurements of clearance. Analyses in plasma and urine were performed by previously described technics.\(^{10,16}\) After a 45 to 60-min equilibration period, three to four consecutive 15 to 29-min urinary collection periods were performed. At the mid-point of each urinary collection period, peripheral arterial and renal venous blood samples were collected. Values were expressed as an average of the three or four collection periods. All studies were performed in the fasting state, and fluids were frequently given by mouth to achieve an adequate output of urine.

**Results**

Clinical and hemodynamic data on all 12 patients are summarized in table 1. Eight patients had an uncomplicated course and four exhibited hemodynamic evidence of transient rejection. Immediately following transplantation, GFR averaged 54 ml/min (range, 22 to 87), PAH clearance averaged 385 ml/min (range, 218 to 510), clearance of 131I-hippuran, 366 ml/min (range, 198 to 999), and RBF, 979 ml/min (range, 435 to 2,114). Two patients had minimal glycosuria (Clinistix) during the initial studies. These two patients (patients HS and BG, table 1) had the longest warm ischemic times. In the eight patients without complication (patients JH through BC, table 1), marked vasodilatation, low extraction, and low filtration fraction persisted during repeated measurements (up to 13 days, table 1). In four patients (WH through BP), evidence of transient rejection occurred initially as manifested by only a decline in GFR and the clearance of 131I-hippuran, both changes being out of proportion to RBF. This fall in clearance of hippuran without a proportional fall in RBF related to a decrease in the renal extraction of this substance. These hemodynamic changes were the only expressions of the apparent rejection process which would not have become evident from observations of the serum creatinine alone (JD and KC, table 1). In all four subjects, reversal of the rejection process was evidenced by a return of GFR and the clearance of 131I-hippuran toward normal.

The consistent finding of a low extraction of PAH and 131I-hippuran suggested the possibility of a defect in tubular transport. This was investigated by measurements of TmPAH. The results of repeated measurements in three patients are shown in table 2. In patient BP, in whom TmPAH was determined during an episode of apparent rejection, TmPAH was unaltered despite a significant decline in GFR and the clearance of 131I-hippuran. Simultaneous extraction ratios for PAH and 131I-hippuran in these six studies were significantly different. \(^{15}\)PAH was greater than \(^{15}\)I-hippuran on every test in the three cases except during an episode of transient rejection (patient BP, table 2) when it was lower. Furthermore, extraction ratios of hippuran were depressed in studies employing only isotopic tracer amounts, which could not exceed transport maxima. It is possible that the low extraction ratios for these transported substances were related in some way to their molecular sizes and the high rates of blood flow.\(^{17}\) The possibility that the differences in extraction ratios were related to the molecular size of the substances was investigated further by simultaneously measuring the extraction of PAH, \(^{125}\)I-hippuran, and \(^{131}\)I-iodopyracet in three patients on five separate occasions. The
Table 1
Clinical Data and Serial Hemodynamics after Renal Allotransplantation in Twelve Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Donor relationship</th>
<th>Day</th>
<th>Ischemic time (min)</th>
<th>BP</th>
<th>P</th>
<th>Serum creatinine (mg %)</th>
<th>GFR (ml/min)</th>
<th>RBF (ml/min)</th>
<th>C (ml/min)</th>
<th>E</th>
<th>GFR/RPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>JH</td>
<td>Mother</td>
<td>0</td>
<td>17</td>
<td>150/100</td>
<td>96</td>
<td>7.6</td>
<td>46</td>
<td>826</td>
<td>296</td>
<td>0.55</td>
<td>0.086</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>180/100</td>
<td>92</td>
<td>1.6</td>
<td>49</td>
<td>1156</td>
<td>352</td>
<td>0.50</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td>100/80</td>
<td>88</td>
<td>1.4</td>
<td>62</td>
<td>852</td>
<td>320</td>
<td>0.57</td>
<td>0.110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td></td>
<td>155/90</td>
<td>90</td>
<td>1.4</td>
<td>64</td>
<td>1088</td>
<td>399</td>
<td>0.52</td>
<td>0.083</td>
</tr>
<tr>
<td>HS</td>
<td>Unrelated (friend)</td>
<td>0</td>
<td>26</td>
<td>170/100</td>
<td>84</td>
<td>8.4</td>
<td>39</td>
<td>939</td>
<td>253</td>
<td>0.38</td>
<td>0.058</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>160/100</td>
<td>76</td>
<td>1.2</td>
<td>71</td>
<td>2716</td>
<td>918</td>
<td>0.47</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td>140/90</td>
<td>78</td>
<td>1.1</td>
<td>67</td>
<td>1796</td>
<td>502</td>
<td>0.37</td>
<td>0.049</td>
</tr>
<tr>
<td>WW</td>
<td>Brother</td>
<td>0</td>
<td>20</td>
<td>210/118</td>
<td>98</td>
<td>12.0</td>
<td>32</td>
<td>908</td>
<td>296</td>
<td>0.47</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>160/100</td>
<td>86</td>
<td>1.1</td>
<td>65</td>
<td>1115</td>
<td>408</td>
<td>0.48</td>
<td>0.076</td>
</tr>
<tr>
<td>EB</td>
<td>Mother</td>
<td>0</td>
<td>16</td>
<td>140/100</td>
<td>102</td>
<td>9.6</td>
<td>41</td>
<td>435</td>
<td>198</td>
<td>0.64</td>
<td>0.135</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td>135/80</td>
<td>94</td>
<td>0.8</td>
<td>78</td>
<td>987</td>
<td>416</td>
<td>0.56</td>
<td>0.105</td>
</tr>
<tr>
<td>BG</td>
<td>Sister</td>
<td>0</td>
<td>30</td>
<td>190/110</td>
<td>100</td>
<td>10.4</td>
<td>55</td>
<td>912</td>
<td>314</td>
<td>0.58</td>
<td>0.102</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td>150/100</td>
<td>86</td>
<td>0.6</td>
<td>62</td>
<td>1576</td>
<td>490</td>
<td>0.40</td>
<td>0.051</td>
</tr>
<tr>
<td>JJ</td>
<td>Brother</td>
<td>0</td>
<td>20</td>
<td>140/85</td>
<td>88</td>
<td>6.4</td>
<td>87</td>
<td>503</td>
<td>230</td>
<td>0.64</td>
<td>0.242</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td></td>
<td>140/80</td>
<td>92</td>
<td>1.2</td>
<td>54</td>
<td>542</td>
<td>203</td>
<td>0.53</td>
<td>0.138</td>
</tr>
<tr>
<td>LL</td>
<td>Unrelated (friend)</td>
<td>2</td>
<td>20</td>
<td>170/90</td>
<td>88</td>
<td>1.3</td>
<td>60</td>
<td>1195</td>
<td>460</td>
<td>0.54</td>
<td>0.071</td>
</tr>
<tr>
<td>BC</td>
<td>Mother</td>
<td>0</td>
<td>17</td>
<td>160/90</td>
<td>98</td>
<td>6.6</td>
<td>79</td>
<td>2114</td>
<td>999</td>
<td>0.70</td>
<td>0.055</td>
</tr>
<tr>
<td></td>
<td>(child)</td>
<td>2</td>
<td></td>
<td>130/90</td>
<td>90</td>
<td>0.7</td>
<td>81</td>
<td>929</td>
<td>481</td>
<td>0.66</td>
<td>0.111</td>
</tr>
<tr>
<td>WH</td>
<td>Unrelated (friend)</td>
<td>0</td>
<td>21</td>
<td>180/100</td>
<td>88</td>
<td>9.9</td>
<td>86</td>
<td>1400</td>
<td>436</td>
<td>0.47</td>
<td>0.093</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>190/90</td>
<td>94</td>
<td>1.0</td>
<td>61</td>
<td>1245</td>
<td>355</td>
<td>0.41</td>
<td>0.070</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>180/100</td>
<td>84</td>
<td>2.0</td>
<td>9</td>
<td>704</td>
<td>81</td>
<td>0.16</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8</td>
<td></td>
<td>170/100</td>
<td>96</td>
<td>2.8</td>
<td>6</td>
<td>1289</td>
<td>88</td>
<td>0.09</td>
<td>0.006</td>
</tr>
<tr>
<td>JD</td>
<td>Unrelated (father-in-law)</td>
<td>0</td>
<td>16</td>
<td>200/110</td>
<td>94</td>
<td>9.8</td>
<td>35</td>
<td>666</td>
<td>281</td>
<td>0.55</td>
<td>0.068</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td>190/100</td>
<td>88</td>
<td>3.4</td>
<td>27</td>
<td>679</td>
<td>265</td>
<td>0.47</td>
<td>0.048</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td></td>
<td>180/100</td>
<td>80</td>
<td>2.0</td>
<td>34</td>
<td>643</td>
<td>283</td>
<td>0.58</td>
<td>0.070</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14</td>
<td></td>
<td>180/90</td>
<td>90</td>
<td>1.5</td>
<td>22</td>
<td>545</td>
<td>167</td>
<td>0.44</td>
<td>0.058</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23</td>
<td></td>
<td>174/92</td>
<td>82</td>
<td>1.0</td>
<td>66*</td>
<td>433*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KC</td>
<td>Sister</td>
<td>0</td>
<td>17</td>
<td>150/85</td>
<td>90</td>
<td>9.2</td>
<td>22</td>
<td>867</td>
<td>211</td>
<td>0.35</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>180/110</td>
<td>96</td>
<td>6.8</td>
<td>4</td>
<td>367</td>
<td>26</td>
<td>0.09</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td></td>
<td>170/110</td>
<td>88</td>
<td>4.4</td>
<td>9</td>
<td>421</td>
<td>71</td>
<td>0.22</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16</td>
<td></td>
<td>180/105</td>
<td>94</td>
<td>1.9</td>
<td>33</td>
<td>634</td>
<td>198</td>
<td>0.41</td>
<td>0.068</td>
</tr>
<tr>
<td>BP</td>
<td>Brother</td>
<td>0</td>
<td>19</td>
<td>170/80</td>
<td>94</td>
<td>6.0</td>
<td>50</td>
<td>986</td>
<td>376</td>
<td>0.53</td>
<td>0.071</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9</td>
<td></td>
<td>220/100</td>
<td>90</td>
<td>1.4</td>
<td>24</td>
<td>669</td>
<td>226</td>
<td>0.47</td>
<td>0.050</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18</td>
<td></td>
<td>160/90</td>
<td>96</td>
<td>1.1</td>
<td>69*</td>
<td>448*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 24-hour creatinine clearance.
† Determined by single injection of 131I-hippuran.
Table 2

Serial Hemodynamics and PAH Transport in Renal Allografts

<table>
<thead>
<tr>
<th>Patient</th>
<th>Donor relationship</th>
<th>Day</th>
<th>GFR (ml/min)</th>
<th>Extraction ratio</th>
<th>Renal plasma flow (ml/min)</th>
<th>TmPAH (mg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EB</td>
<td>Mother</td>
<td>0</td>
<td>41</td>
<td>0.64</td>
<td>0.72</td>
<td>309</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>78</td>
<td>0.56</td>
<td>0.78</td>
<td>743</td>
</tr>
<tr>
<td>BG</td>
<td>Sister</td>
<td>0</td>
<td>55</td>
<td>0.58</td>
<td>0.70</td>
<td>541</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>62</td>
<td>0.40</td>
<td>0.86</td>
<td>1225</td>
</tr>
<tr>
<td>BP</td>
<td>Brother</td>
<td>0</td>
<td>50</td>
<td>0.53</td>
<td>0.59</td>
<td>709</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9</td>
<td>24</td>
<td>0.47</td>
<td>0.27</td>
<td>480</td>
</tr>
</tbody>
</table>

Table 3

Simultaneous Extraction Ratios for PAH, 125I-Hippuran, and 131I-Iodopyracet

<table>
<thead>
<tr>
<th>Patient</th>
<th>Day</th>
<th>PAH</th>
<th>125I-Hippuran</th>
<th>131I-Iodopyracet</th>
</tr>
</thead>
<tbody>
<tr>
<td>JJ</td>
<td>0</td>
<td>0.75</td>
<td>0.64</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.72</td>
<td>0.53</td>
<td>0.36</td>
</tr>
<tr>
<td>LL</td>
<td>2</td>
<td>0.82</td>
<td>0.54</td>
<td>0.43</td>
</tr>
<tr>
<td>BC</td>
<td>0</td>
<td>0.94</td>
<td>0.70</td>
<td>0.49</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.86</td>
<td>0.66</td>
<td>0.35</td>
</tr>
</tbody>
</table>

results of these studies are summarized in table 3. In each study, the extraction ratio for PAH was greater than that for 125I-hippuran which in turn was greater than that for 131I-iodopyracet. These observations indicate an inverse relationship between molecular size and extraction ratio and are consistent with the view that the extent of extraction may be limited by diffusion of the species from plasma at these high rates of blood flow. However, further studies would be necessary to delineate the exact mechanism. These differences in extraction ratios were reflected by a similar difference in the clearance of the three substances (fig. 3). However, RPF calculated from the simultaneous measurements of clearances and extractions was the same for each substance (fig. 4).

Discussion

Two unexpected findings emerged from this study—the marked and persistent vasodilation and the varying degrees of depression of the extraction ratios for PAH, radiohippuran, and iodopyracet. The extraction ratios were inversely related to molecular size of the species. In these patients, therefore, clearances of these substances grossly underestimated true RPF and during rejection when extraction ratios were further decreased, this error was even greater. Under these conditions and in the absence of a rejection episode, PAH, which has the lowest molecular weight, would most closely approximate RPF. The finding of relative maintenance of total renal blood flow during the rejection in the face of marked depression of the clearances of inulin, PAH, and radiohippuran agrees with the earlier
Eleven simultaneous RPFs for PAH and 131I-hippuran
and five simultaneous RPFs for PAH, 131I-hippuran
and 131I-Diostax are compared. There is no significant
difference.

Figure 4

Observation of Dempster, who found an
adequate total blood flow up to the oliguric
stage of rejecting canine renal allografts. This
suggests that during the rejection reaction,
blood flows more rapidly through the graft,
that is, increased transient time, which could
be the result of intrarenal vascular lesions
known to occur during allograft rejection. This
phenomenon may be enhanced by vasoconstriction,
which is also believed to be associated with the
rejection reaction. The rapid flow of blood
accompanied by the intrarenal vascular reaction
during rejection could further limit tubular contact
with transported substances in the plasma.
Therefore, declines in the clearances
of inulin and PAH, rather than a decrease in totalrenal
blood flow, are the earliest expressions of
the rejection reaction and provide a sensitive
guide for the effectiveness of immunosuppressive
drug therapy.

Ogden and co-workers observed an average
clearance of PAH of 207 and 357 ml/min
6 and 18 hours, respectively, after transplantation
in five patients. The clearance of PAH
averaged 385 ml/min in six of our patients
studied immediately after transplantation,
which is in close agreement with their
findings. However, true renal plasma flow
(RPF) in our studies averaged 672 ml/min.
This striking degree of vasodilatation would
be overlooked without measurements of
extraction ratios. However, the etiology of the
vasodilatation is obscure. Although we, like
others, observed marked initial diuresis
and natriuresis, the persistence of vasodilata-
tion after this phase makes it unlikely that this
was responsible. The possibility that a humoral
factor in end-stage renal failure may be
responsible is also unlikely, since it would be
unusual for such a substance to persist for 13
days after correction of the azotemic state.
However, it is possible that the diuresis and
natriuresis were the result of allograft
vasodilatation. Henderson and associates postulated proximal tubular malfunction as
the etiology of the post-transplant diuresis
and natriuresis. Support for their hypothesis was
the finding of glycosuria in their patients. Our
data are in contradistinction to theirs, as
minimal glycosuria was observed initially in
only two of our patients. This difference may
be related to the length of the warm ischemic
time, which was longer in their cases. It is also
possible that in our studies the degree of
initial renal ischemia was minimized and
vasodilatation was maximized from the initial
intrarenal injection of immunosuppressive
drugs. However, we believe this to be
unlikely because vasodilatation was repeatedly
observed when these substances were not
being intrarenally infused. In our studies,
further evidence against tubular malfunction
was the finding of a normal PAH which
remained normal during a transient rejection
episode.

Arteriovenous fistulae have been observed
during the rejection reaction in dogs by
Almgard and associates. They observed a
greater decline in GFR and PAH than in RBF
in allografts, but not in autografts. Also, they
demonstrated arteriovenous shunts by micro-
angiograms and suggested that these shunts
explained the observed hemodynamic
abnormalities. However, such a mechanism would
predict a shunting of more than 50% of RBF in
some cases, which appears unlikely.
HEMODYNAMICS AFTER RENAL TRANSPLANT

The low extraction ratios for PAH, radiohippuran, and iodopyracet, which were inversely related to their molecular sizes, seem best explained by the hypothesis that their diffusion from plasma to the tubules is limited by their molecular size during high rates of blood flow. The possibility that anemia or protein binding is responsible appears unlikely since the difference in extraction ratios was less pronounced in the same subject as the vasodilatation decreased and the GFR increased. It is interesting that marked increases in the GFR were not observed. The proposed hypothesis may explain the occasional failure to obtain identical clearance values of transported substances, especially when the single injection technic is simultaneously compared with the constant infusion technic, for example, PAH and radiohippuran. Therefore, simultaneous measurements of extraction ratios of transported substances having different molecular sizes are important in comparing their clearance rates. This should allow differentiation of clearance differences due to defects in tubular transport from those due to a diffusion limit at high rates of blood flow. It is theoretically possible for this to occur to some degree in the absence of vasodilatation, that is, when RBF is out of proportion to GFR.

This unique hemodynamic phenomenon of the singly transplanted human kidney (vasodilatation, varying degrees of depression of the extraction ratios of PAH, radiohippuran, and iodopyracet, and low filtration fraction) may well be the same as the response of a normal kidney either to (1) lack of renal mass in relation to body surface area, (2) severance of the renal nerves, or (3) the responsibility to regulate the internal milieu and perform the total excretory work. A similar phenomenon has been observed in the normal intact kidney under pharmalogic vasodilatation.

Acknowledgment

We thank Miss Sandra Schmitt, Miss Lisbeth Streiff, Miss Edyth Ringgold, and Miss Diana Farley for technical assistance.

References

1. FIGUEROA JE, RODRIGUEZ-ANTUNEZ A, NAKO-  
15. WOLF AV: Total renal blood flow at any urine flow or extraction fraction. Amer J Physiol 133: 496, 1941
Serial Hemodynamics after Renal Allotransplantation in Man
SAMUEL L. KOUNTZ, GARY TRUEX, LAURENCE E. EARLEY and FOLKERT O. BELZER

_Circulation_. 1970;41:217-224
doi: 10.1161/01.CIR.41.2.217

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1970 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/41/2/217

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/