The Effect of Acute Salt Loads on the Urinary Sodium Output of Normotensive and Hypertensive Patients before and after Surgery

By Jesse E. Thompson, M.D., Thomas F. Silva, M.D., Dera Kinsey, M.D., and Reginald H. Smithwick, M.D.

Under the stress of acute hypertonic salt loading, hypertensives excrete sodium at a much greater rate than normotensives. Immediately following splanchnicectomy, sodium excretion is markedly reduced in the hypertensive, but after several months it returns toward preoperative levels. There appears to be a rough correlation between maximum rate of sodium excretion and mean blood pressure. Normotensives by contrast exhibit insignificant differences pre- and postoperatively.

Evidence from various sources indicates that the metabolism of sodium in patients with essential hypertension is probably different from that of normotensive patients. Perera and Blood\(^1\) found that sodium restriction in normotensive control subjects was followed by a significant weight loss and increased urinary volume output, but these effects were not evident in hypertensive patients subjected to the same degree of sodium restriction. The sodium values in the urine, however, decreased to the same extent in both the normotensive and the hypertensive subjects. It is well known that hypertensives tolerate sodium restriction without difficulty and occasionally will exhibit a lowering of blood pressure. This is in marked contrast to the normotensive subject, who tolerates very poorly rigid sodium restriction. Our interest in this problem arises out of a long-term study of the effects of thoracolumbar splanchnicectomy on hypertensive cardiovascular disease in more than 2400 patients.\(^2\) We have observed patients who fail to respond to a preoperative diet containing 200 mg. of sodium daily, who, following splanchnicectomy, respond with a lowering of blood pressure when a diet containing 1 Gm. of sodium daily is added to the postoperative regime. We have also observed in many instances that hypertensive patients postoperatively are unable to tolerate the strict regime of 200 mg. of sodium daily. The postsplanchnicectomy hypertensive patient thus appears to be more sensitive to sodium restriction than the unoperated one. We have numerous cases in which neither splanchnicectomy nor low-sodium diet alone was satisfactory in lowering blood pressure, but the combination of splanchnicectomy and moderate sodium restriction effected the desired result. Furthermore, there is some recent experimental evidence\(^2\) which suggests that the sympathetic nerves may actually affect the handling of sodium by the kidney. On this background, therefore, we have studied the urinary output of sodium in normotensive and hypertensive patients subjected to acute sodium loads.

Subjects and Methods

Acute salt loading tests were performed on eight hypertensive and five normotensive patients. Six of the hypertensives and four of the normotensives were tested before and immediately after surgery (one to two weeks). Three of the hypertensive patients were retested several months later. The hypertensives had bilateral splanchnicectomy performed, in which sympathetic ganglia D-8 to L-1 inclusive and the splanchnic nerves were removed. The normotensives had operations of comparable magnitude. All patients had normal renal and cardiac function. Salt and water intake was unrestricted in the days prior to the study except for the eight hours immediately prior to testing when the patients were thirsting and fasting. All tests were
done with subjects in the horizontal position. A catheter was placed in the bladder and urine collected during two 20-minute control periods. Approximately 500 cc. of 5 per cent sodium chloride was then infused intravenously over the course of one hour. Urine was collected at the end of the infusion and every 30 minutes thereafter for two additional hours. Blood samples for plasma sodium,

### Table 1.—Normotensives

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Sex</th>
<th>Age</th>
<th>Operation</th>
<th>Time Relation to Operation</th>
<th>B.P.</th>
<th>Total Urine Volume (cc.)</th>
<th>Max. Urine Flow (cc./min.)</th>
<th>Total Urine Na % Load*</th>
<th>Max. Rate Na Excretion (mEq./min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F.S.</td>
<td>43</td>
<td>Abdominal hysterec-</td>
<td>Pre</td>
<td>120/70</td>
<td>263</td>
<td>2.30</td>
<td>15.53</td>
<td>.568</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>tomy</td>
<td>Post-7 d.</td>
<td>204</td>
<td>2.10</td>
<td>12.60</td>
<td>.535</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M.D.C.</td>
<td>31</td>
<td>Gastrectomy plus de-</td>
<td>Pre</td>
<td>130/85</td>
<td>458</td>
<td>3.76</td>
<td>21.66</td>
<td>.825</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>hiscence</td>
<td>Post-16 d.</td>
<td>124/75</td>
<td>346</td>
<td>2.55</td>
<td>23.73</td>
<td>.756</td>
</tr>
<tr>
<td>3</td>
<td>L.S.</td>
<td>47</td>
<td>Complicated recurrent</td>
<td>Pre</td>
<td>110/80</td>
<td>504</td>
<td>4.97</td>
<td>33.40</td>
<td>1.127</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>herniorrhaphy</td>
<td>Post-7 d.</td>
<td>452</td>
<td>3.56</td>
<td>28.01</td>
<td>.892</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>R.I.</td>
<td>29</td>
<td>Inguinal herniorrhaphy</td>
<td>Pre</td>
<td>100/60</td>
<td>458</td>
<td>4.50</td>
<td>22.51</td>
<td>.905</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-7 d.</td>
<td>102/50</td>
<td>648</td>
<td>5.00</td>
<td>32.25</td>
<td>1.050</td>
</tr>
<tr>
<td>5</td>
<td>A.D.V.</td>
<td>30</td>
<td>Vaginal hysterectomy</td>
<td>Pre</td>
<td>126/72</td>
<td>433</td>
<td>3.30</td>
<td>19.65</td>
<td>.716</td>
</tr>
</tbody>
</table>

*The total urine sodium is calculated as the cumulative sodium output in mEq. from the beginning of loading to the end of the test, expressed as per cent of the total sodium load infused. (See figs. 1–4.)

### Table 2.—Hypertensives

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Sex</th>
<th>Age</th>
<th>Operation</th>
<th>Time Relation to Operation</th>
<th>B.P.</th>
<th>Total Urine Volume (cc.)</th>
<th>Max. Urine Flow (cc./min.)</th>
<th>Total Urine Na % Load*</th>
<th>Max. Rate Na Excretion (mEq./min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>G.A.</td>
<td>45</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>176/98</td>
<td>1692</td>
<td>15.83</td>
<td>66.56</td>
<td>2.404</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-13 d.</td>
<td>142/76</td>
<td>573</td>
<td>4.00</td>
<td>34.68</td>
<td>1.086</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-3 mo.</td>
<td>140/77</td>
<td>1247</td>
<td>11.60</td>
<td>60.50</td>
<td>2.152</td>
</tr>
<tr>
<td>2</td>
<td>K.W.</td>
<td>35</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>100/120</td>
<td>1135</td>
<td>8.87</td>
<td>55.00</td>
<td>1.743</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-12 d.</td>
<td>150/110</td>
<td>511</td>
<td>3.30</td>
<td>24.56</td>
<td>.735</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-9 mo.</td>
<td>140/95</td>
<td>726</td>
<td>6.76</td>
<td>33.00</td>
<td>1.394</td>
</tr>
<tr>
<td>3</td>
<td>B.G.</td>
<td>50</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>165/105</td>
<td>852</td>
<td>6.47</td>
<td>44.86</td>
<td>1.300</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-14 d.</td>
<td>150/90</td>
<td>355</td>
<td>2.26</td>
<td>17.64</td>
<td>.501</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-3½ mo.</td>
<td>165/107</td>
<td>774</td>
<td>6.10</td>
<td>46.67</td>
<td>1.430</td>
</tr>
<tr>
<td>4</td>
<td>L.D.</td>
<td>39</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>165/105</td>
<td>2036</td>
<td>17.25</td>
<td>82.23</td>
<td>3.107</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-13 d.</td>
<td>160/110</td>
<td>670</td>
<td>4.56</td>
<td>32.01</td>
<td>1.035</td>
</tr>
<tr>
<td>5</td>
<td>B.D.</td>
<td>37</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>190/115</td>
<td>498</td>
<td>3.46</td>
<td>30.81</td>
<td>.893</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-14 d.</td>
<td>150/100</td>
<td>253</td>
<td>2.15</td>
<td>5.37</td>
<td>.256</td>
</tr>
<tr>
<td>6</td>
<td>J.B.</td>
<td>37</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>186/124</td>
<td>1493</td>
<td>15.60</td>
<td>51.46</td>
<td>2.350</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Post-28 d.</td>
<td>176/117</td>
<td>888</td>
<td>7.83</td>
<td>38.69</td>
<td>1.620</td>
</tr>
<tr>
<td>7</td>
<td>P.C.</td>
<td>42</td>
<td>Splanchnicectomy</td>
<td>Pre</td>
<td>230/130</td>
<td>1302</td>
<td>10.74</td>
<td>66.20</td>
<td>2.177</td>
</tr>
<tr>
<td>8</td>
<td>C.L.</td>
<td>39</td>
<td>None</td>
<td>Pre</td>
<td>250/160</td>
<td>1530</td>
<td>13.83</td>
<td>62.48</td>
<td>2.530</td>
</tr>
</tbody>
</table>
hemoglobin and hematocrit determinations were taken before the test, at the end of the infusion and at the end of the test. Urine volumes were recorded. The exact volume of the infusing solution was measured. Urine, plasma and infused sodium determinations were done on the flame photometer. All blood pressure readings were taken in the horizontal position with a sphygmomanometer.

**Results**

Table 1 lists the results obtained on the normotensive patients and table 2 the data on the hypertensives. Table 3 is a summary of the mean values. The average preoperative cumulative sodium output in the normotensives was 22.55 per cent of the infused load compared with 57.45 per cent in the preoperative hypertensives. The average maximum rate of sodium excretion in the preoperative normotensives was 0.846 mEq. per minute compared with 2.063 mEq. per minute in the preoperative hypertensives. Figure 1 compares normotensive patient A.D. with hypertensive patient P.C. in the unoperated state. The average postoperative cumulative sodium output in the normotensives was 24.16 per cent and the maximum rate of sodium excretion was 0.809 mEq. per minute. These are not materially different from the preoperative values. Figure 2 shows the pre- and postoperative data in normotensive patient F.S.

**Table 3.** Mean Values

<table>
<thead>
<tr>
<th></th>
<th>Total Urine Vol. (cc)</th>
<th>Max. Urine Flow (cc/min)</th>
<th>Total Urinary Na (% of infused load)</th>
<th>Max. Rate of Na Excretion (mEq/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive—preop.</td>
<td>441.0</td>
<td>3.77</td>
<td>22.55</td>
<td>0.846</td>
</tr>
<tr>
<td>Normotensive-postop.</td>
<td>412.5</td>
<td>3.30</td>
<td>24.16</td>
<td>0.809</td>
</tr>
<tr>
<td>Hypertensive—preop.</td>
<td>1317.0</td>
<td>11.51</td>
<td>57.45</td>
<td>2.063</td>
</tr>
<tr>
<td>Hypertensive—immed.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>postop.</td>
<td>542.0</td>
<td>4.02</td>
<td>25.49</td>
<td>0.874</td>
</tr>
<tr>
<td>Hypertensive—long-term postop.</td>
<td>916.0</td>
<td>8.15</td>
<td>46.72</td>
<td>1.650</td>
</tr>
</tbody>
</table>

Fig. 1. Acute sodium loading in normotensive versus hypertensive subjects (unoperated). Note the greatly increased sodium excretion in the hypertensive under conditions of loading. The solid and the cross-hatched lower portions of the vertical bars represent the preloading control rates of sodium excretion. At basal rates the marked difference between normotensive and hypertensive was not apparent.

Fig. 2. Acute sodium loading in a normotensive subject (F. S.), pre- and postoperatively (hysterectomy). There was no significant difference in sodium excretion in this normotensive patient before and after total abdominal hysterectomy.

Fig. 3. Acute sodium loading in a hypertensive subject (L. D.), pre- and postoperatively (splanchnicectomy). Note the high level of sodium excretion in this hypertensive patient before operation and the marked depression 13 days following operation.
of sodium excretion was 0.874 mEq. per minute. This is a marked decrease from the preoperative levels in these patients. Figure 3 demonstrates the preoperative and the immediate postoperative data in hypertensive patient L.D. The average long-term postoperative cumulative sodium output in the hypertensives tested was 46.72 per cent, and the average maximum rate of sodium excretion was 1.659 mEq. per minute. These figures are considerably higher than those of the immediate postoperative period and approach the preoperative figures. Figure 4 shows these data plotted for hypertensive patient G. A. Also shown are the blood pressure data at the different levels of cumulative sodium excretion.

The average preoperative total urinary volume for the normotensives was 441 cc. for the test period and the maximum rate of urine flow was 3.77 cc. per minute, compared with an average for the hypertensives of 1317 cc. total volume and a maximum rate of 11.51 cc. per minute. The average postoperative urinary volume of the normotensives was 412.5 cc. and the average maximum rate 3.30 cc. per minute, values not appreciably different from the preoperative ones. The average urinary volume for the hypertensive patients immediately postoperative was 542 cc., and the average maximum rate was 4.02 cc. per minute. The average long-term postoperative volume for the hypertensives was 916 cc. and the maximum rate was 8.15 cc. per minute.

Figure 5 shows mean blood pressures plotted against maximum rates of sodium excretion.

Fig. 4. Acute sodium loading in a hypertensive subject (G. A.), pre- and postoperatively (splenectomy). At 3 months postoperative the sodium excretion was approaching the preoperative level and was considerably higher than the output at 13 days postoperative in spite of the fact that the blood pressure levels were the same at the two postoperative tests.

Fig. 5. Mean blood pressures plotted against maximum rates of sodium excretion. The mean blood pressure is calculated as half the sum of the systolic and diastolic levels. There is a rough correlation between the level of blood pressure and sodium excretion, except in the immediately postoperative hypertensive patients. These subjects exhibited lower rates of sodium output for a given blood pressure level.

Fig. 6. Maximum rates of sodium excretion plotted against maximum rates of urine flow. Note the direct linear relationship regardless of the operative status of the patients.
EFFECT OF ACUTE SALT LOADS ON URINARY SODIUM OUTPUT

There is a rough correlation between the level of blood pressure and sodium excretion, except in the immediately postoperative hypertensive patients. The latter subjects exhibited lower rates of sodium output for a given pressure level. Figure 6 is a graph of the maximum rates of sodium excretion plotted against the maximum rates of urine flow for all the subjects tested. The relationship is a direct linear one.

Increases in the plasma sodium concentration upon infusion of hypertonic saline were of the same order of magnitude in both the normotensive and hypertensive patients. The average peak value was in the vicinity of 150 mEq. per liter.

**Discussion**

**A. Comparison of Hypertensives and Normotensives Unoperated.** The studies reported here show that preoperative hypertensive patients reject a much higher proportion of infused sodium than do preoperative normotensives and excrete sodium at a greater rate under the stress of hypertonic salt loading. Our observations are in agreement with those of Farnsworth and Barker, Weston and co-workers and Birchall and associates. The latter group also noted that a salt load was necessary to bring out the differences between normotensives and hypertensives, since they could not be distinguished on the basis of sodium excretion under reasonably basal conditions. Using mannitol diuresis, Brodsky and Graubarth demonstrated the minute losses of sodium and chloride in the hypertensive to be two to two and one-half times greater than in the normal individual.

The reasons for the differences in sodium excretion in normotensives and hypertensives are not yet evident. Our own data are insufficient to determine whether the hypertensive filters more sodium or reabsorbs less of that presented to the tubules or both.

**B. Comparison of Normotensives before and after Operation.** The normotensive patient appears to have a very slightly but insignificantly lower rate of sodium excretion immediately following major surgery. One of the patients, however, actually had a slightly increased rate of sodium excretion postoperatively. The differences here are very small and are what one might expect on the basis of the metabolic response to the stress imposed by surgery. The important point is that under the conditions of this study there was no appreciable difference in the pre- and postoperative rates of sodium output in the normotensives tested.

**C. Comparison of Hypertensives before and after Splanchnicectomy.** Our studies show that the hypertensive patient excretes a greatly reduced proportion of infused sodium at a greatly reduced rate two weeks following splanchnicectomy. When tested several months after splanchnicectomy the hypertensive excretes sodium at a slightly reduced rate or at the same rate when compared with the preoperative values.

The influence of splanchnicectomy, an operation which effects renal denervation, upon renal function and renal hemodynamics in man has not been completely elucidated. Pfeiffer and Wolff have shown that renal hemodynamics may be altered in the direction of less vasoconstriction following operation. Wilkins and his collaborators, however, have failed to demonstrate any change in the renal salt and water responses to venous congestion of the limbs after splanchnicectomy.

Freis and Smithwick have noted an increase in the thiocyanate space of hypertensives in the second week after operation. They did not consider these changes a specific consequence of sympathectomy. If one reanalyzes the data of Freis and his co-workers, a very interesting fact is brought out. The average increase in “available fluid” volume of 12 hypertensives after splanchnicectomy was 17 per cent, with a range from +3 per cent to +28 per cent. By contrast, the average increase among eight normotensives after other operations was 3.6 per cent, with a range from −6 per cent to +8.5 per cent. This is further evidence that the hypertensive responds to the stress of surgery in a different fashion from the normotensive. Further investigations along these general lines might
be very rewarding. Whether splanchnicectomy has a specific effect or whether hypertensive patients subjected to an operation of comparable magnitude other than splanchnicectomy would show similar salt and water responses must still be determined.

There are in the literature several recent reports on the effects of splanchnic nerve resection upon renal electrolyte excretion. It has been reported in acute experiments on anesthetized normotensive dogs that renal denervation may result in an increased elimination of sodium, chloride, and water, with and without increases in the glomerular filtration rate. In the unanesthetized, chronically denervated dog, Surtshin and associates have demonstrated equal excretion of water and sodium from the denervated and control kidneys. Ether and pentobarbital anesthesia, however, produced falls in water and sodium excretion in the normal kidney but not in the denervated one. Similar results, when autonomic blocking drugs are used, have also been reported. It is entirely possible that the effects of splanchnicectomy on the kidney are brought out only under specific conditions of stimulation. This may be the state of affairs in the human, where splanchnicectomy is known to abolish certain normally active splanchnic bed vasoconstrictor reflexes.

D. Comparison of Blood Pressure Levels with Rates of Sodium Excretion. Figure 5 is a graph of mean blood pressure plotted against maximum rate of sodium excretion. In a general way the rate of sodium excretion is proportional to the mean blood pressure level. The correlation is not too strict and may be representative of the variability which blood pressure is known to exhibit. Green and coworkers have reported a fairly strict correlation between the level of the mean blood pressure and the rate of sodium excretion.

It is of interest to note that the immediately postoperative hypertensive patients tend to fall above the others on the graph; that is, at the same level of blood pressure the rate of sodium excretion is lower. All of this lends further support to the primary thesis that the metabolism of sodium is somehow involved in the basic mechanism of hypertensive disease.

E. Comparison of Rates of Urine Output and Rates of Sodium Excretion during Salt Loads. Figure 6 depicts a graph of rate of urine flow plotted against maximum rate of sodium excretion. It is evident that this is a direct linear function and confirms the finding of Weston and colleagues that there is a direct proportionality between the urine volume and the rate of electrolyte excretion in hypertensive patients. This curve is characteristic of an osmotic diuresis. Our normotensive data appear to fall along the same line as the hypertensive. Also, the immediately postoperative and the long-term postoperative data appear to fall along the same line. It appears, therefore, that whatever mechanism is responsible for the marked decrease in sodium excretion in the hypertensive patient immediately after operation is equally effective in reducing the water output by the kidneys, under the conditions of these studies. In our experiments splanchnicectomy appears to have no differential influence upon the rate of sodium excretion when compared with the rate of urine flow. From the data we can make no statement relative to the long-term effects of splanchnicectomy upon the rate of sodium excretion which might explain the apparent sensitivity to salt restriction which the postoperative patients exhibit. Further investigations are necessary.

Summary

1. In acute salt-loading tests it has been observed that preoperative hypertensive patients reject a much higher proportion of infused sodium than do preoperative normotensive patients.

2. The normotensives have an insignificantly lower rate of sodium excretion immediately following major surgery. The hypertensives excrete a greatly reduced proportion of infused sodium at a greatly reduced rate immediately following splanchnicectomy.

3. The hypertensive patients tested several months after splanchnicectomy excrete sodium
EFFECT OF ACUTE SALT LOADS ON URINARY SODIUM OUTPUT

at a slightly reduced rate or at the same rate as before operation.

4. There is a direct relationship between the rate of sodium excretion and the rate of urine flow during the stress of acute salt loading in both normotensives and hypertensives before and after operation.

5. There appears to be a rough correlation between the maximum rates of sodium excretion and the levels of mean blood pressure in both normotensives and hypertensives, except in the immediate period after splanchnicectomy in the hypertensive group when the rate of sodium excretion is reduced even at high blood pressure levels.

**Sumario Español**

1. En pruebas de recarga aguda con sal se ha observado que los pacientes preoperatorios hipertensos rechazan una proporción mucho mayor del sodio instilado que los pacientes preoperatorios normotensos.

2. Los normotensos tienen un promedio insignificativamente más bajo de excreción de sodio inmediatamente después de cirugía mayor. Los hipertensos eliminan una proporción, grandemente reducida del sodio instilado a una velocidad grandemente reducida inmediatamente después de la espláncnicocolecotomía.

3. Los pacientes hipertensos probados algunos meses después de la espláncnicocolecotomía eliminan sodio a una velocidad ligeramente reducida o a la misma velocidad que antes de la operación.

4. Hay una relación directa entre la velocidad de excreción del sodio y la velocidad de producción de orina durante el esfuerzo de la recarga aguda con sal en ambos normotensos e hipertensos antes y después de la operación.

5. Aparenta haber una correlación tosca entre la velocidad máxima de excreción de sodio y los niveles de presión arterial promedio en ambos normotensos e hipertensos, excepto en el período inmediato después de la espláncnicocolecotomía en el grupo hipertenso cuando la velocidad de excreción del sodio se reduce, aún a niveles altos de presión arterial.

**References**


THOMPSON, SILVA, KINSEY, AND SMITHWICK


The Effect of Acute Salt Loads on the Urinary Sodium Output of Normotensive and Hypertensive Patients before and after Surgery

JESSE E. THOMPSON, THOMAS F. SILVA, DERA KINSEY and REGINALD H. SMITHWICK

_Circulation_. 1954;10:912-919
doi: 10.1161/01.CIR.10.6.912

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1954 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/10/6/912

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/