“Peripheral Resistance” in Hypertension Following the Abolition of Local Sympathetic Tone

By Francis S. Caliva, M.D., Jay F. Harris, M.D., and Richard H. Lyons, M.D.

Blood flows of the toe were studied before and after nerve block in normotensive and hypertensive patients, and an estimate of peripheral resistance was made. It was found that in all hypertensive patients there was an increased “peripheral resistance” at rest in the skin of the toe. Following abolition of sympathetic tone, the “resistance” in some individuals fell to a normal level, in others the “resistance” dropped less. The possible significance of these facts is discussed in the light of the etiologic factors responsible for the vasomotor tone.

The role of the sympathetic nervous system in producing the increased peripheral resistance of hypertension remains unsettled. The problem has been investigated by a number of workers using a variety of technics and approaches, but results have been conflicting. Recent work has tended to minimize a neural factor and to ascribe the increased resistance to some type of change in the arterial wall itself.

It occurred to us that the technic of toe plethysmography might lend itself well to the further study of this problem. The tissue studied is mainly of one type, i.e., skin, and the vascular bed is restricted to small vessels. In this way, the varying reactivity of different-sized vessels or vasculature in various tissues is not a complicating factor.

Abolition of sympathetic tone in the toe is easily accomplished by posterior tibial nerve block, a method which leaves little doubt that the vasoconstrictor impulses have been interrupted and interrupted only locally. Also the entire procedure is a simple one and can be done without much discomfort or anxiety on the part of the patient.

Materials and Methods

Blood flows of the toe were measured according to the method of Simeone et al. in 22 normotensive and 43 hypertensive patients. The hypertensive patients had blood pressure readings on the ward regularly at 140/90 or above, and were not receiving antihypertensive medication at the time of study. They ranged in age from 19 to 62, with a mean of 38. The ages of the normal patients were from 18 to 47, with a mean of 32.

In both groups an attempt was made to study patients who clinically exhibited no heart failure or peripheral vascular disease. In a further effort to exclude peripheral vascular disease, no patient whose blood flow following posterior tibial block did not reach a maximum of 6 ml./100 ml. of tissue/min. (minimal normal in our laboratory) was included in either group.

Twenty-five of the patients with elevated blood pressures were diagnosed as “benign essential hypertension.” Diagnoses in the others were chronic nephritis in 11 (2 of these with unilateral kidney disease), post-toxemia of pregnancy in 3, malignant hypertension in 2, and pheochromocytoma and thyrotoxicosis, 1 each. The normal persons were, in general, patients without significant disease.

All patients were lightly clad, supine, and lying comfortably on a stretcher in a constant-temperature room (21 C. ± 2 C.). The occlusion cuff was placed at the ankle and no correction was made for this factor in calculating blood flows that were expressed as ml./100 ml. of tissue/min. In each instance the occlusion pressure (usually 40 to 60 mm. Hg) which resulted in the maximum inflow slope was utilized. Brachial artery blood pressures were obtained by auscultation at frequent intervals during the period of observation. The mean blood pressure was calculated as the average of systolic and diastolic readings. The level at which the pressure “stabilized” was used in the calculations for “peripheral resistances.”

During the nerve block 4 normotensive patients underwent blood pressure changes that placed their mean pressures at hypertensive levels. However, since these rises were mainly in the systolic pressure, and since the ward determinations had been consistently normal, they were classified in

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From the Department of Medicine, Upstate Medical Center, State University of New York and Veterans Administration Hospital, Syracuse, N.Y.
HYPERTENSION AND LOCAL SYMPATHETIC TONE

TABLE 1.—Hemodynamic Changes after Nerve Block

<table>
<thead>
<tr>
<th>No.</th>
<th>Mean blood pressure and standard deviation (mm. Hg)</th>
<th>Mean blood flow and standard deviation (ml./100 ml./min.)</th>
<th>Mean &quot;peripheral resistance&quot; and standard deviation (mm. Hg)</th>
<th>Mean blood pressure and standard deviation (mm. Hg)</th>
<th>Mean blood flow and standard deviation (ml./100 ml./min.)</th>
<th>Mean &quot;peripheral resistance&quot; and standard deviation (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>30</td>
<td>98 ± 10.8</td>
<td>.9 ± .64</td>
<td>143 ± 73.2</td>
<td>97 ± 9.9</td>
<td>14.5 ± 5.5</td>
</tr>
<tr>
<td>Group 1</td>
<td>30</td>
<td>147 ± 27</td>
<td>.7 ± .15</td>
<td>331 ± 274</td>
<td>142 ± 24</td>
<td>18.4 ± 6.2</td>
</tr>
<tr>
<td>Group 2</td>
<td>13</td>
<td>176 ± 29.9</td>
<td>.6 ± .26</td>
<td>333 ± 128.2</td>
<td>171 ± 27.4</td>
<td>8.2 ± 7.8</td>
</tr>
</tbody>
</table>

Fig. 1 Left. Changes that occurred in the 3 groups of patients before and after posterior tibial nerve block. Center point represents mean values for both “peripheral resistance” and blood flows. Length and thickness of lines extending from the center represent the standard error of the mean of the “peripheral resistance” and blood flows respectively. Mean blood pressures before and after block are plotted separately on right side of graph.

Fig. 2 Right. Scattergraph of all “peripheral resistances” after block plotted against mean blood pressure, also after block. Group 1 patients are those with “peripheral resistances” of less than 14.6 and group 2 those with higher values.

RESULTS

Table 1 and figure 1 summarize the results obtained in these studies.

In the control period, the range of blood flows was not significantly different in either normotensive (.9 ± .64) or hypertensive (.7 ± .15 and .6 ± .26) patients, indicating a difference in peripheral resistance in the 2 types of patients. After nerve block in the normal patients, the flow values increased many times, and the calculated “resistance” fell to low levels (8 ± 3.3).

All the hypertensive patients, however, did not react in the same way to the abolition of local sympathetic tone. While certain of them did demonstrate large increases in flow and

the normotensive group. In addition, when 2 known hypertensive subjects were studied, their mean blood pressures were in the normotensive range. Because of their history and previous pressure readings, they were included in the group with high blood pressure.

After fairly constant blood flows had been obtained, a posterior tibial nerve block was performed with 5 ml. of 2 per cent procaine with added hyaluronidase. Completeness of block was tested by loss of sensation over the cutaneous distribution of the nerve. If sensory loss was incomplete, more procaine was injected until the desired result was obtained. An estimation of peripheral resistance was made by dividing the mean blood pressure by the average blood flow before the block and the average of the highest set of readings after the block.5,17,18 No attempt was made to measure venule pressure.
falls in "peripheral resistance," others exhibited comparatively small increases in flow. In this latter group, the calculated "peripheral resistance" was much higher.

Hypertensive patients were, therefore, subdivided as follows: Group 1, those in whom the "peripheral resistance" following block fell to within 2 standard deviations of the normal subjects, i.e., 14.6, and group 2, the patients whose "resistances" after block were over 14.6.

It can be seen from the table that the control "peripheral resistances" in the hypertensive groups 1 and 2 differed significantly from the normal group (p<.01), but not from each other. Following nerve anesthesia, the relatively low mean flows achieved in group 2 were markedly different from those of either group 1 (p = .01) or of the individuals with normal pressures (p = .01).

Since groups 1 and 2 varied so in their responses, the clinical records of these patients were reviewed and analyzed. These data are summarized in tables 2 and 3.

Group 1 was composed of 16 males and 14 females. Twenty-four were diagnosed as essential hypertension. There were 2 patients with chronic nephritis, 2 with post-toxemia of pregnancy, and 1 each with acute nephritis and thyrotoxicosis. Twenty-six patients in this group had either normal or grade-I eye-ground (Keith-Wagener) changes. There were 4 with grade-III changes. Of the renal function tests performed (urinalysis, NPN, PSP, Mosenthal, IVP) only 9 had abnormalities. In 4 of these more than 1 test was abnormal: 3 of these patients had nephritis and the other one had had toxemia of pregnancy.

Group 2 was made up of 13 patients, 5 women and 8 men. Six of the 9 nephritic patients in the series fell into this group as did the 2 individuals with malignant hypertension. The patient with the pheochromocytoma preoperatively had a calculated "peripheral resistance" of 29.5 units and was listed in group 2. About 6 months after surgery, even though he was still hypertensive, his "peripheral resistance" had fallen to 7.6 units and he was now clearly in group 1.

Seven patients in group 2 had eye-ground changes classified as grade IV. The other 6 had typical findings of grades I and II. Only 3 patients had no detectable abnormality of renal function.

Both patients with unilateral renal disease were included in group 2. One of these subsequently underwent nephrectomy with no change in blood pressure, but with some fall in "peripheral resistance" (25-15 units). The other patient with unilateral renal disease had been diagnosed ante mortem as malignant hypertension. At autopsy, he was found to have thrombosis of the renal artery with a "Goldblatt-type" kidney.

Two nephritic patients in group 2 and 1 in group 1 were markedly anemic. Otherwise,
blood viscosity as judged by hematocrits and total protein was within normal limits in all other patients.

It is interesting that all the patients with grade-IV eyeground changes fell into group 2, and there were no patients in this group in whom eyegrounds were normal.

Several of the hypertensive subjects in both groups were studied on more than one occasion in an effort to determine the reproducibility of the method and also to assess more definitely the role of the level of blood pressure in our calculations. Table 4 summarizes these studies and illustrates that, with the exception of the patients who had undergone surgery, the results of repeated testing are quite similar in spite of varying blood pressure levels.

**Discussion**

It is fully recognized that the term "peripheral resistance," as we have used it, can refer to only a very crude estimate of the actual physiologic resistance. To obtain a more precise figure would have required measurements of both toe artery and vein pressures.

Further accuracy could have been obtained in control blood flows if the occluding cuff had been placed closer to the toe cup than the ankle. However, the large flows after block might not have been correctly measured by this method. Since we were primarily interested in blood flows after block and only incidentally in the controls, we chose to keep the cuff at the ankle.

Each of the aforementioned, though recognized, are constant errors which do not interfere with a comparison between the various groups. One possible exception is the measurement of small vein pressures. There is some evidence, accumulated in our laboratory, that the small-vein pressure in the toe rises following posterior tibial nerve block. Since this is presumably due to the opening of arteriovenous shunts and a direct passage of high pressure arterial blood into the veins, the vein pressure might rise in proportion to the level of the existing arterial pressure. This, then, would not be a constant, but would vary from patient to patient according to the systemic blood pressure. On the other hand, even were this true, the new figures certainly would not be great enough to effect the large and definite differences that have been demonstrated between the groups.

Since there was considerable variation in mean blood pressure among the patients, a scattergraph was made of all resistances after block plotted against mean blood pressure (fig. 2). It is obvious from this graph that the group variation in "resistance" is not merely a reflection of differences in blood pressure.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Diastolic (mm Hg)</th>
<th>Mean blood pressure (mm Hg)</th>
<th>&quot;Peripheral resistance&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z.B.</td>
<td>Unilateral renal disease</td>
<td>8/26/56</td>
<td>186</td>
<td>25</td>
</tr>
<tr>
<td>J.B.</td>
<td>Malignant hypertension</td>
<td>3/20/57</td>
<td>175</td>
<td>35</td>
</tr>
<tr>
<td>T.C.</td>
<td>Essential hypertension</td>
<td>2/14/57</td>
<td>179</td>
<td>37</td>
</tr>
<tr>
<td>N.R.</td>
<td>Essential hypertension</td>
<td>2/2/54</td>
<td>137</td>
<td>12</td>
</tr>
<tr>
<td>W.S.</td>
<td>Essential hypertension</td>
<td>7/8/53</td>
<td>120</td>
<td>7</td>
</tr>
<tr>
<td>C.U.</td>
<td>Essential hypertension</td>
<td>11/30/54</td>
<td>168</td>
<td>12</td>
</tr>
<tr>
<td>A.S.</td>
<td>Post-toxemia</td>
<td>3/21/54</td>
<td>170</td>
<td>30</td>
</tr>
<tr>
<td>M.M.</td>
<td>Essential hypertension</td>
<td>4/7/57</td>
<td>155</td>
<td>7</td>
</tr>
<tr>
<td>H.G.</td>
<td>Essential hypertension</td>
<td>4/18/52</td>
<td>127</td>
<td>10</td>
</tr>
<tr>
<td>R.C.</td>
<td>Pheochromocytoma</td>
<td>5/16/56</td>
<td>185</td>
<td>30</td>
</tr>
<tr>
<td>R.M.</td>
<td>Essential hypertension</td>
<td>2/19/54</td>
<td>136</td>
<td>7</td>
</tr>
<tr>
<td>N.V.</td>
<td>Acute nephritis</td>
<td>7/20/53</td>
<td>145</td>
<td>10</td>
</tr>
</tbody>
</table>

*After surgery.
†Dibenzyline therapy.
‡Recovered.
Our figures are in agreement with those of many other workers with respect to resting blood flows. There can be little question that in hypertension, blood flow of the skin is within normal limits. The skin, and the toe in particular, therefore, participate in the increased vascular resistance in the patients with elevated blood pressure.

On the other hand, our data do differ from work showing that peripheral resistance in hypertensive patients cannot be reduced to normal levels. The patients included in group 1, after abolition of local sympathetic tone, all had calculated "resistances" that fell within the same range as that of the normotensive subjects. These were individuals who, in general, had fewer evidences of involvement elsewhere, viz., eye-ground and kidney. Two patients in this group have died in a 3-year period.

This group stands in contrast to group 2 with "high resistances." Structural vessel changes as suggested by Conway, Mendlowitz, and others may well have been present in these patients. Their blood flows were low, their eye-ground changes were advanced, and a large proportion showed definite impairment of renal function. Half of these patients have died in 3 years.

We think, then, that our data suggest a basic difference between various types and stages of hypertension. At least patients would seem to vary with respect to arterial circulation to the toe following abolition of sympathetic tone. There are some hypertensive patients with little or no renal or eye-ground changes in whom the increased peripheral resistance in the toe is primarily on a neurogenic basis. This confirms some of the earlier work of Mendlowitz done on fingers and employing another technic to abolish sympathetic tone.

The high "resistances" in group 2 may have been due to either of the following possibilities: (1) structural vascular changes which may or may not be reversible, and (2) pressor activity other than neurogenic. We are unable to say which of these possibilities is the more likely.

**Summary**

The vessels of the toe participate in the increased peripheral resistance found in hypertension.

Following sympathetic block, hypertensive subjects can be divided into 2 groups: (1) those in whom resistance falls into normal levels and (2) those in whom it does not.

Patients in group 2 in this series were those in whom the hypertensive process was obviously more severe as evidenced by eye-ground and renal changes and prognosis for life.

It is suggested that changes in the wall of the blood vessel may well have been present in group 2, but were probably absent in group 1, where neurogenic vasospasm seemed to play a dominant role.

**Acknowledgment**

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**Summario in Interlingua**

Le vasos del digitos del pede partecipara in le augmentate resistentia peripheric que es trovate in hypertension.

Post bloco sympathic, hypertensivos forma 2 gruppos: (1) Subjectos in qui le resistentia descende a nivellos normal e (2) subjectos in qui iste evento non occurre.

In le serie de patientes del presente reporto, gruppo 2 consisteva del subjectos in qui le processo hypertensive esseva obviamente plus sever, a judicar per alterationes del fundo ocular e del renes e per le prognose del curso futur.

Es suggerite que alterationes in le pariete vascular esseva probabilmente presente in gruppo 2 sed absent in gruppo 1, ubi vaso-spasmo neurogene pareva haber un rolo dominante.

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