Sympathetic Denervation in the Treatment of Acute Arterial Occlusion

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The effect of sympathectomy on the size of the collateral vessels in acute arterial ligation in a hind limb was measured by an angiographic angiometric technic and by noting the pressure in the ligated artery distal to the ligature. The size of the largest collateral vessel present on the sympathectomized side was the same as that on the innervated side. The blood pressure in the ligated artery distal to the ligature was quite similar on the sympathectomized and innervated sides. The usual increase in temperature on the sympathectomized side was noted. This must be due to a shift of blood from the deeper tissues of the hind limb to the arteriovenous shunts of the skin of the toes, rather than to an increase in collateral blood flow.

There is still no general agreement as to which of the therapies available for the treatment of acute arterial occlusion in man are most important for limb and patient survival.1-5 One of the major disagreements concerns the advisability of sympathetic blocks or sympathectomy in the early hours after acute occlusion.1, 6, 7, 8 It is well established that sympathetic block or denervation, and similarly body heating, can increase total blood flow through the toes in the presence of arterial occlusion.1, 9-13 Total blood flow includes the temperature-regulating arteriovenous shunt flow and the nutritional flow. It is often implied, however, that dilatation of the collateral arterial vessels in the early hours after acute arterial occlusion can be produced by sympathetic block but not by reflex heat.1, 14 If it can be substantiated, this is certainly an important difference in favor of sympathetic block.

The use of sympathetic block, however, does entail some known disadvantages. There is a slight risk of hemorrhage, since immediate heparinization is almost always advisable in acute arterial occlusion. The patients are frequently quite ill5 and do not readily tolerate the manipulation and exposure that is often involved in the usual performance of a sympathetic block. The evaluation of the degree of progression or regression of ischemia is an important factor in determining the need for embolectomy.5 The close observation of the limb required in making a decision in regard to the latter may be interfered with during the execution of the block. Also, if the sympathetic chain is not successfully blocked, further cooling of the limb often ensues. This would appear to be detrimental. If, however, it can be shown that sympathetic block or sympathectomy can dilate the collaterals to a therapeutically significant degree, and simpler therapy cannot, the drawbacks associated with sympathetic block listed above would be minor deterrents. The evidence in this regard as applied to man is controversial.5, 7, 15

It is important to recall that the collaterals apparently open up spontaneously with the passage of time after acute occlusion. While observing a limb that has just suffered an acute occlusion, one not infrequently notes—usually within several hours, and occasionally up to 24 hours or so—a more or less rapid disappearance of the signs and symptoms of tissue ischemia.5, 16, 17 In clinical experiments using alternate patients as controls, if one could show that soon after sympathetic block one obtained not only an elevation of skin temperature of the acral parts, but also a return of sensation and motion toward normal, one could conclude that sympathetic block is indeed important in the treatment, and that

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the effect was probably due to dilatation of collateral vessels. We think the latter presumption would be justified by the knowledge that any ischemia great enough to produce loss of motion and sensation of the acral parts must represent a marked impairment of inflow. Opening the "faucets" at the end of the line above that normally existing, and probably augmented by the ischemia, would probably not result in an increase of blood flow. Since such experiments in man have not as yet been done because of the inherent complexities, one might try to draw inferences from conclusions obtained from animal work.

In the dog, it is claimed that sympathectomy does increase collateral flow in acute arterial occlusion. Mulvihill and Harvey found that following external iliac artery ligation the skin temperature of the paw (normally over 90 F. in the anesthetized dog) dropped rather rapidly toward room temperature, and after several hours it spontaneously started rising toward that of the control hind paw, so that in 12 hours or so both hind paws were again at the same temperature. Sympathetic denervation of the involved limb, performed before the arterial ligation, prevented the drop in temperature, and denervation performed after the temperature drop had occurred rapidly returned the temperature of the involved paw to that of the control paw. These authors surmized that this was evidence in favor of a salutary effect of sympathectomy on the collateral vessels. This may, however, represent an effect primarily on the temperature-regulating peripheral arteriovenous shunts in the presence of a normal collateral flow and may involve a concomitant reduction in blood flow through the deeper tissues, such as the muscles.

Theis, however, has presented more direct evidence that sympathectomy can bring about dilatation of collateral vessels in acute arterial occlusion. He mentions four dogs in which he measured the pressure in the femoral artery distal to an acute occlusion (ligature)—the tip of the cannula pointing peripherally—with sympathetic denervation of one limb and without denervation of the other hind limb. He also measured the rate of blood flow through the cannulas. He found that both the blood pressure and the rate of blood flow were greater on the sympathectomized side. He intimates that he did similar or related experiments in 106 other dogs, and that similar results were obtained in them; no details are given. Such evidence strongly supports the contention that, at least in the dog, sympathectomy could dilate collaterals or relieve any spasm of the main or collateral vessels. Since no
further work bearing on the question could be found, and since we recently have devised an angiographic method for measuring the size of vessels during life, we attempted to repeat and extend the work of Theis. Preliminary work in the rat showed that after acute arterial occlusion the known changes in the size of collaterals with time could be demonstrated by our angiographic angiometric technic (fig. 1). However, both the rat and rabbit were unsatisfactory animals for this study since it was difficult to be sure one had done a unilateral lumbar sympathectomy that was thorough without having disturbed the sympathetics on the contralateral side. The smallest of the research laboratory animals that sufficed for this purpose was the cat. Since Theis' work was done in the dog, the latter animal was also used, although to a lesser extent, in this work.

**Methods**

Skin temperature was measured with thermocouples on the ventrum of the paw of the hind limbs, using a Leeds-Northrup potentiometer. Room temperature, body temperature, and forelimb temperatures were also recorded in most experiments. The room temperature was occasionally increased during the experiment, or covers were put over the animal, to help prevent the drop in body temperature (and forelimb and hindlimb temperatures) that tended to occur during and following unilateral lumbar sympathectomy in the cat.

Lumbar sympathectomy was always done on the left side, since it was easier on that side. Four or five ganglia and the intervening chain were removed: one or two ganglia lying above the left renal artery and two or three ganglia lying below the left renal artery. This represented a ganglionectomy from the diaphragm to just below the pelvic brim. The sympathectomy was done either before or after the arterial ligation, just as done by Theis.

The injection of mercury was used to visualize the vessels on the roentgenogram. The injection pressure needed to show filling of the ligated artery distal to the ligature indicated the size of the largest collateral vessel. In previous work we have shown that, given the interfacial tension of mercury against blood, at any given injection pressure the size of the vessel at the place where the front of the mercury comes to rest can be calculated from the formula:

\[ d = \frac{11,250}{p} \]

where \( d \) is the diameter in microns of the vessel at the mercury-blood interface, \( p \) is the filling pressure in millimeters of Hg, and 11,250 is the value derived from the known mercury-blood interfacial tension. The data so obtained in regard to the size of the largest arteriovenous communications in various organs appeared to check well with other methods of measurement.

Cats and dogs were utilized and intravenous or intraperitoneal pentobarbital sodium anesthesia was used. We attempted to maintain the animals in light anesthesia throughout the studies. Atropine, given subcutaneously, was also used in some of the cats.

The external iliae or femoral arteries were used. The former were ligated as they arose from the aorta, the latter were ligated below the profunda (below the inguinal ligament). The animals were heparinized before they were injected with the mercury or cannulated for the pressure studies. Various intervals of time were allowed to elapse before proceeding with these studies, so that any effects related to the duration of ischemia might also be noted.

One group of animals was used for the mercury injection study. The abdominal aorta, the renal, superior mesenteric, or the inferior mesenteric artery was cannulated. Use of a branch of the aorta permitted us to leave the circulation to the limbs undisturbed by the mercury injection procedure until just before the actual injection started. At that time the aorta just central to the cannulated portion was ligated and the mercury injection begun. Some of the abdominal vessels were also ligated so as to minimize loss of mercury into these vessels and their collaterals that would only serve to fill the aorta central to the ligature.

Another group of animals was used to study the pressure changes in the artery distal to the tie. Mean blood pressure was measured in the ligated artery about two inches distal to the ligature by cannulation with 18 or 20 gauge needles directed centrally. The artery was tied around the needle. The pressures in the arteries of the two hind limbs were measured alternately and repeatedly, rather than precisely simultaneously, with a mercury manometer. Only one of the animals so studied was also subjected to a mercury study.

**Results**

Thirty-one cats were used. Skin temperature studies were carried out in 23 of the animals that had bilateral ligation of either the femoral or external iliac arteries and lumbar sympathectomy on the left side only (tables 1, 3, and 4). All exhibited a higher paw temperature on the sympathectomized side except one which showed the same temperature (90 F.) on both hind paws. The temperature differences were greatest in those animals that were not too
deeply anesthetized or not too chilled or shocked by the surgery. Deep anesthesia tended to produce a "chemical sympathectomy" of the unoperated hind limb. A drop in body temperature tended to lower the paw temperature of the sympathectomized limb toward that of the nonsympathectomized limb. The average of the maximum temperature differences obtained in each of the animals was 6.6 F., and the range was 0 to 17.5 F. It is apparent that sympathectomy resulted in an increase of the total blood flow to the skin of the paw.

Satisfactory mercury studies were completed in 12 of 17 animals that had bilateral femoral or external iliac artery ligation and left lumbar sympathectomy. In the other five animals the ties were not placed with exact bilateral symmetry; although the results in these were quite similar to those in the other 12, they have not been included in the reported data. The hind limb arteries were ligated either immediately before the mercury studies (the least time from peripheral arterial ligation to completion of a mercury study was several minutes) or up to 402 minutes before the mercury studies. The sympathectomy was completed 30 to 325 minutes before the mercury studies. The arteries of the two hind limbs were tied approximately simultaneously (within a few minutes of each other). Usually the injection pressure was started at 50 mm. Hg and adjusted upward until the mercury just started to flow into the aorta ("zero" pressure) and then elevated by 30 mm. Hg increments every 30 to 60 seconds, a roentgenogram being taken at each pressure, until mercury was seen in both femoral arteries distal to the ties on direct vision.

In table 1 it can be seen that on the average there was no difference in the size of the largest collateral arterial vessel on the sympathectomized side as compared with the control side. That is, the pressure at which the portion of the femoral artery distal to the tie was filled (as seen on the roentgenogram) was similar in both hind limbs. The series of films in one of the cats is seen in figure 2 (cat 29).

In table 1 it can be seen that the size of the largest collateral vessel varied markedly from animal to animal, and to a lesser degree from one hind limb to the contralateral limb, even when one takes into account the differences in "zero" pressures. It was already noted that the "zero" pressure is that pressure at which the injected mercury just started to flow. Since the cannulas used and the vessels cannulated were large in size, the pressure resisting the inflow of mercury was primarily the blood pressure in the cannulated abdominal vessel after it was tied off centrally (owing to its own collateral circulation).

It can also be seen that there was no apparent correlation between the differences in paw temperature between the two hind limbs of any one animal and the size of the largest collateral vessel in each of the two limbs. It appeared, then, that the differences in skin temperature between the denervated and innervated limb were not related to the size of the largest collateral present.

As a check on the mercury method under the above experimental circumstances, mercury studies were done in eight cats where one hind limb artery was ligated several hours before the study and the artery of the contralateral limb was ligated only shortly before the study. It is known that some dilatation of the collateral vessels takes place very shortly after

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**Table 1.—The Injection Pressure (mm. Hg) at Which the Hind Limb Artery (Distal to the Ligature) Filled in Cats with Bilateral Ligature and Left Lumbar Sympathectomy. Mercury Injection Method.**

<table>
<thead>
<tr>
<th>Animal</th>
<th>Press. at which Hg flow began</th>
<th>Press. at which distal lt. limb artery filled</th>
<th>Press. at which distal rt. limb artery filled</th>
<th>Max. temp. diff. between two hind limb paws (degrees F.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>W4</td>
<td>90</td>
<td>240</td>
<td>240</td>
<td>2.5</td>
</tr>
<tr>
<td>W5</td>
<td>?</td>
<td>380</td>
<td>380</td>
<td>5.5</td>
</tr>
<tr>
<td>W11</td>
<td>?</td>
<td>60</td>
<td>60</td>
<td>13.0</td>
</tr>
<tr>
<td>W13</td>
<td>?</td>
<td>150</td>
<td>150</td>
<td>13.0</td>
</tr>
<tr>
<td>15</td>
<td>50</td>
<td>170</td>
<td>170</td>
<td>5.0</td>
</tr>
<tr>
<td>16</td>
<td>110</td>
<td>170</td>
<td>170</td>
<td>5.0</td>
</tr>
<tr>
<td>17</td>
<td>70</td>
<td>150</td>
<td>150</td>
<td>5.0</td>
</tr>
<tr>
<td>W25</td>
<td>120</td>
<td>200</td>
<td>230</td>
<td>6.0</td>
</tr>
<tr>
<td>W26</td>
<td>70</td>
<td>210</td>
<td>140</td>
<td>4.5</td>
</tr>
<tr>
<td>W27</td>
<td>50</td>
<td>220</td>
<td>220</td>
<td>2.0</td>
</tr>
<tr>
<td>28</td>
<td>90</td>
<td>300</td>
<td>210</td>
<td>10.0</td>
</tr>
<tr>
<td>29</td>
<td>90</td>
<td>240</td>
<td>210</td>
<td>0.0</td>
</tr>
</tbody>
</table>

* The temperature was greater on the denervated side in all except cat 29.
greater diameter in the limb in which the main artery was ligated about five to seven hours before the mercury study (six of eight cats). In one the reverse was found, and in one there was no difference. The greatest difference was in cat 36 where the femoral artery distal to the tie filled at 80 mm. Hg pressure on the side tied 6 hours and 27 minutes before the mercury study (right) as compared with 230 mm. Hg on the side tied just before the study (left). Using the formula cited previously, this would indicate that the largest collateral on the right was 141 μ in diameter and on the left was 48 μ. Some of the films from that study are shown in figure 3 (cat 36).

Further experiments in eight cats were conducted. The blood pressure in the femoral artery at some distance peripheral to the tie was determined. The data obtained where both external iliac arteries were ligated simultaneously (approximately) and a left lumbar sympathectomy was performed are presented in table 3 (two animals). There was no notable distal femoral artery blood pressure difference between the two hind limbs. That is, the total collateral cross-sectional flow in the denervated limb was similar to that of the other hind limb. The data obtained in six other cats where one external iliac artery was ligated five to seven hours before the study and where the other external iliac artery was ligated im-

### Table 2.—The Injection Pressure (mm. Hg) at Which the Hind Limb Artery (Distal to Ligature) Filled in Cats Where One Hind Limb Artery Was Tied Several Hours Before and the Other Just Before the Mercury Injection Study.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Lt. hind limb</th>
<th>Rt. hind limb</th>
<th>Press. at which Hg flow began</th>
</tr>
</thead>
<tbody>
<tr>
<td>W8</td>
<td>330 5 hrs., 13 min.</td>
<td>330 Several min.</td>
<td>90</td>
</tr>
<tr>
<td>23</td>
<td>330 Several min.</td>
<td>240 6 hrs.</td>
<td>70</td>
</tr>
<tr>
<td>31</td>
<td>160 Several min.</td>
<td>130 5 hrs., 20 min.</td>
<td>45</td>
</tr>
<tr>
<td>32</td>
<td>250 Several min.</td>
<td>130 6 hrs., 15 min.</td>
<td>50</td>
</tr>
<tr>
<td>33</td>
<td>320 Several min.</td>
<td>200 6 hrs., 40 min.</td>
<td>40</td>
</tr>
<tr>
<td>36</td>
<td>280 Several min.</td>
<td>130 6 hrs., 27 min.</td>
<td>50</td>
</tr>
<tr>
<td>37</td>
<td>370 Several min.</td>
<td>280 7 hrs., 35 min.</td>
<td>40</td>
</tr>
<tr>
<td>43</td>
<td>280 5 hrs., 53 min.</td>
<td>130 Several min.</td>
<td>50</td>
</tr>
</tbody>
</table>

Fig. 2. Mercury angiograms of the hind limbs of a cat, at 90 mm. Hg (a), at 120 mm. Hg (b), and at 150 mm. Hg (c) over the "zero" injection pressure. Bilateral arterial ligation and left lumbar sympathectomy. (a) There is no filling of the femoral artery distal to the ligature on either side. (b) There is filling on the right side. (c) There is also filling on the left side.
mediately before or during the blood pressure study are presented in table 4. Only one of these animals had a left lumbar sympathectomy (cat 40). It can be seen that the pressure studies were equivocal, probably because of the small number of animals used and the large chance variation in the size and number of the collaterals between the two limbs. This variability is also apparent when comparing the preligation femoral artery pressure with the postligation pressure (distal to the tie), as in the first four animals in table 4.

In one of the above six cats (cat 43), mercury studies were done following the blood pressure studies (the femoral arteries had to be ligated above and below the site of cannulation). The mercury studies indicated that the largest collateral was significantly larger on the right side. The femoral artery distal to the external iliac ties filled at 130 mm. Hg on the right and 280 mm. Hg on the left side. This corroborates the differences in distal femoral blood pressure noted in this animal in table 4.

Studies similar to those above in the cat were also carried out in the dog. Fourteen dogs were used. They all had a left lumbar sympathectomy. The external iliac arteries or the femoral arteries (distal to the profunda) were tied approximately simultaneously in the two hind limbs, either before or after the sympathectomy. Ten dogs were used for mercury studies and four were used for blood pressure studies (distal to the arterial tie). These studies were done soon after the arteries were tied or within 2 hours and 55 minutes of that time.

The temperature differences between the skin of the sympathectomized hind paws and the innervated hind paws in the 14 dogs varied from 3 to 11.5 °F., with an average of 9.1 °F. (tables 5 and 6). The size of the largest collateral after bilateral iliac artery ligation and left lumbar sympathectomy was not significantly different on the two sides as measured.

![Fig. 3. Mercury angiograms of the hind limbs of a cat, at 50 mm. Hg (a), at 80 mm. Hg (b), and at 230 mm. Hg (c) over the "zero" injection pressure. Arterial ligation on the right was performed just before and on the left 6 hours and 27 minutes before the study. (a) There is no filling of the femoral artery distal to the ligature on either side. (b) There is filling on the right. (c) There is also filling on the left side.](image-url)
by the mercury technic in 10 dogs (table 5). The blood pressure in the femoral artery distal to the ligature in four dogs similarly prepared was greater on the denervated side in three and greater on the control side in one (table 6).

One can see that there was no apparent correlation between size of the largest collateral vessel present or the total collateral cross-sectional flow (arterial blood pressure distal to the tie) and the skin temperature of the paw (tables 5 and 6).

**Discussion**

The fact that sympathectomy can increase total blood flow to the skin of the toes, as measured by skin temperature, after acute arterial occlusion has been verified in the cat. It could not be shown that this effect was due in any significant degree to an enhancement of the collateral blood flow, as indicated by the size of the largest collateral vessel present (mercury technic) or the aggregate flow in all of the involved collaterals (the blood pressure in the femoral artery distal to the ligature). In the cat, there was no apparent correlation between the differences in skin temperature of the denervated paw as compared with the control paw and the size of the largest collateral present.

Similar findings were recorded in the dog. Sympathectomy resulted in an increase in total blood flow (arteriovenous shunt flow and nutritional flow) to the skin of the paw after acute arterial occlusion. The mercury studies
and the studies of the blood pressure in the femoral artery distal to the ligature indicated that sympathetic denervation did not affect the size of the largest collateral vessel present or the blood pressure.

If an increase in total blood flow in the feet or hands is thought desirable, warming the body may be simpler than, and as effective as, sympathetic block. Without such a study it might be well to attempt to control one’s clinical observations by using sympathetic block only after other less contested therapy has not produced a good result within the first one to two hours in patients seen soon after acute arterial occlusion.5

One might argue that even if sympathectomy did not dilate normal collaterals it might well dilate those collaterals that might be in spasm in association with the acute arterial occlusion due to embolus or ligature in man.1 14 If spasm was present following arterial ligation in the cats and dogs used in our experiments, sympathectomy had no effect on it. Spasm is generally not considered a part of the picture of acute arterial occlusion due to thrombosis, so at least in the latter type of occlusion one might ask for better controls in judging the claimed benefit from sympathetic block. It should probably be stressed that although our studies were conducted under Nembutal anesthesia, the depth of anesthesia was usually not so great as to sympathectomize “chemically” the innervated hind limb, as was indicated by the difference in temperature between the two hind paws.

This work bears no evidence on the possible chronic effects of sympathectomy on the collateral vessels. It is conceivable that in days or weeks sympathectomy might increase the dilatation or the possible new formation of the collaterals. Again however, we would have to show that sympathectomy produced an increase in collateral flow greater than that which apparently occurs with time alone. We have shown in the above experiments that in a relatively short time the collaterals dilate spontaneously. It has also been shown that collaterals continue to dilate spontaneously for longer periods of time.19 22 23 25

Conclusions

Sympathectomy can prevent or erase the drop in temperature of the skin of the hind paws of the cat or dog that occurs when the main limb artery is suddenly ligated. By means of an angiographic angiometric technic it was shown that the size of the largest collateral vessel present on the sympathectomized side is the same as that present on the innervated side. Also, by means of blood pressure measurements in the ligated artery distal to the ligature it was shown that sympathectomy produced no increase in collateral blood flow. Therefore, the temperature effects of sympathectomy in acute arterial ligations in the cat and dog is probably due to a shift of blood to the arteriovenous shunts of the toes, in the face of an unchanged flow distal to the arterial ligation.

Since reflex heat and sympathectomy have been claimed to produce similar increases in total blood flow in the skin of the toes of man under most conditions, one might wonder whether reflex heat might not be used in place of sympathetic block in the treatment of acute arterial occlusion in man, if such therapy is thought to be indicated.

Controlled clinical studies are urgently needed on the effect of sympathetic block (or sympathectomy) on the state of tissue ischemia (especially as indicated by sensation and motion in the acral parts) in acute arterial occlusion, when routine therapy including heparinization and reflex heat are already in use.

Sumario Español

El efecto de la simpatectomía en el calibre de los vasos colaterales en la ligación arterial aguda en la extremidad trasera se midió por medio de técnica angiográfica y angiométrica y por determinación de la presión en la parte distal de la arteria ligada. El tamaño del vaso colateral mayor presente en el lado simpatectomizado fue igual al lado inervado. La presión arterial en la parte distal de la arteria ligada fue similar en el lado simpatectomizado y el lado inervado. El aumento usual en temperatura en el lado simpatectomizado fue observado. Esto se puede deber al desvío de sangre de los tejidos profundos de la extremidad.
trasera a los “shunts” arteriovenosos de la piel de los dedos, más que a un aumento en la circulación colateral.

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