Similarity of Blood Flow in the Normal and the Sympathectomized Dog Hind Limb during Graded Exercise

By David E. Donald, Ph.D., Derek J. Rowlands, M.B., and David A. Ferguson

ABSTRACT
The possibility of sympathetic vasoconstrictor control of blood flow to active muscles was studied in dogs during graded exercise by comparing the blood flow in the normal with that in the sympathectomized hind limb. Blood flow was measured by electromagnetic flow transducers around each external iliac artery, or inferred from the oxygen saturation of blood samples from the common iliac veins. The dogs either ran for successive periods of 3 minutes at 5.5 km/hr and grades of 0, 7, 14, 21, and 28% or ran each level of exercise separately. Unilateral lumbar sympathectomy (L-2 through L-7) was performed when the flow transducers were implanted or later by a snare technique. The latter allowed observations during exercise as early as 4 hours after sympathectomy. The magnitude of limb blood flow during exercise and the decline of exercise hyperemia were similar in the normal and the sympathectomized limb, as were the changes in the oxygen saturation of limb venous blood. However, electric stimulation of the lumbar sympathetic chain at the L-5 level in the conscious dog by a chronically implanted electrode reduced limb blood flow at all levels of exercise, the maximal flow of 1,000 ml/min was almost halved.

ADDITIONAL KEY WORDS peripheral circulation peripheral resistance vasomotor nerves

Several studies in man have shown that during exercise there is an increase in the activity of the sympathetic vasoconstrictor nerves to inactive regions such as the kidney (1), the splanchnic bed (2), the liver (3), and quiescent skeletal muscle (4). If there were a similar increase in activity in the vasoconstrictor nerves to the active muscles, the final vascular state would depend on the balance between the dilator action of the local metabolic factors and the constrictor action of the sympathetic nerves. Studies in anesthetized dogs and cats have shown that maximal electric stimulation of the sympathetic vasoconstrictor nerves to active muscles does not greatly affect the dilatation caused by the local metabolic changes (5), and causes only a minor decrease in flow during prolonged stimulation (6). More recently in man, augmentation of activity in sympathetic vasoconstrictor nerves by applying subatmospheric pressure to the lower parts of the body was shown to result in a reduction of blood flow in exercising muscles and in the postexercise hyperemia (7).

If blood flow to exercising muscles normally is curtailed by sympathetic vasoconstrictor nerve activity and if the intensity of nerve activity is proportional to the severity of the work, measurable differences should be expected in blood flow to the normal and the

From the Mayo Clinic and Mayo Foundation, Section of Physiology (Dr. Donald and Mr. Ferguson), and from the Mayo Graduate School of Medicine, University of Minnesota (Dr. Rowlands), Rochester, Minnesota 55901.

This investigation was supported in part by U. S. Public Health Service Grant HE-0143 from the National Heart Institute. Dr. Rowlands is the recipient of a British Medical Research Council Travelling Fellowship and of a grant from the Dickenson Scholarship Fund.

Received May 20, 1969. Accepted for publication December 1, 1969.

Circulation Research, Vol. XXVI, February 1970
sympathectomized limb during graded exercise. The following study was therefore undertaken in dogs in which limb blood flow was measured during exercise of continuously increasing severity by electromagnetic flow transducers chronically implanted around the external iliac arteries, and in which unilateral lumbar sympathectomy was produced by a technique that allowed observations during exercise as early as 4 hours after sympathectomy.

Methods

The basic plan of the study was the measurement of blood flow in the iliac artery of the normal and the sympathectomized limb during graded exercise. Two approaches were employed: in one, limb blood flow was inferred from measurements of the oxygen saturation of blood in each common iliac vein; in the other, limb blood flow was measured directly by electromagnetic flow transducers. Heart rate, mean systemic blood pressure, and in some dogs, cardiac output were also measured.

Female dogs weighing 10 to 16 kg were trained to run free on a power-driven treadmill. A light harness was made to carry flowmeter cables, pressure transducers, and other equipment. Each dog was exercised wearing the harness until accustomed to the experimental procedures. The treadmill speed was kept constant at 5.5 km/hour, and different intensities of work were obtained by increasing the inclination of the platform. Two types of exercise were used. In one, the work load was increased and the animal ran continuously for successive 3-minute periods at grades of 0, 7, 14, 21, and 28%, for a total exercise time of 15 minutes. The measurements were continued for the first 5 minutes of recovery. In the second type, each work level was run separately, and a 20-minute rest was allowed between the work periods. The dog ran for 1 minute at the selected grade, and recovery was followed for 1 minute. There was no consistent order of the different work levels.

Animals in the first group were prepared by removing the right or the left lumbar chain intact from the L-2 through the L-7 level. A small Silastic catheter was inserted into each right and left internal iliac vein and advanced so that the tip of each catheter lay just within the right and the left common iliac vein, respectively. The free ends of the catheters were exteriorized on either side of the midline at the level of T-10. The catheters were maintained patent by daily flushing with saline and were filled with heparin and plugged with a short steel rod between studies.

Only continuous exercise was studied. Venous samples were withdrawn simultaneously from both veins during the control and recovery periods and in the third minute of running at each exercise level. During control and recovery periods, the animal was kept walking slowly (1.7 km/hour) on the horizontal treadmill. The oxygen saturation of the venous blood samples was measured with a direct-reading oximeter, which had been calibrated with blood analyzed by the Van Slyke method. One or more spot checks by the same method were made during the study of each dog.

The second group of animals were prepared in one of two ways. The right or left lumbar chain was removed intact from the L-2 through the L-7 level. Noncannulating square-wave electromagnetic flow transducers of suitable diameter were implanted around each external iliac artery close to its origin from the aorta. Small rings of Ivalon sponge were also fitted around the artery, above and below the transducer, to help maintain it at right angles to the vessel. A pneumatic Silastic occluding cuff designed by one of us (DAF) was applied to the artery distal to each flow transducer. The transducer cable and the cuff-inflating tube of each artery were brought through a small wound in the flank region of the abdominal wall and exteriorized about 6 cm from the scapulas, one set on either side of the dorsal midline. Small Silastic buttons were attached to the cuff-inflating tubes, one just before the point of exit from the abdomen and the other just after the tube emerged through the skin. These buttons served to immobilize the tube and to prevent it from being withdrawn beneath the skin. Studies were first begun in these animals 12 to 14 days after implantation of the flow transducers and were repeated at intervals of 2 to 3 days for as long as 36 days.

The second method was designed to produce unilateral lumbar sympathectomy without immediate laparotomy and thus permit studies of exercise 4 to 5 hours later. Flow transducers and occlusion cuffs were implanted as described previously. A snare of 2-0 Deknatel suture was placed around each lumbar sympathetic ganglion from the L-2 through the L-7 level on either the right or the left side. The free ends of the snare wires were tied around a small Silastic tube under the skin in the flank region.

Studies were begun 10 to 12 days after operation, and an attempt was made to obtain four or five complete sets of observations. After this, the dogs were anesthetized with ether or with sodium thiopental (25 mg/kg), and the free

---

1American Optical Co., Buffalo, N. Y.
2Carolina Medical Electronics, King, N. C.
ends of the snares were exposed. Sympathectomy was accomplished by steadily pulling the snares until each was withdrawn unbroken. In a few animals, flow in the iliac arteries was measured at the time the lumbar sympathetic nerves were disrupted. The skin wound was closed and the first study of exercise was made 4 or 12 hours later. Studies were made daily for the first 4 days and thereafter at intervals of 2 to 3 days, for as long as 60 days after sympathectomy.

After six or seven sets of postoperative data had been obtained, the dogs were anesthetized with sodium thiopental (25 mg/kg), and the left omocervical artery was exposed at the base of the neck. A small thick-walled Silastic catheter was introduced into the vessel lumen and advanced to the aorta. The other end of the catheter was exteriorized dorsally in the midline just anterior to the scapulas. The catheter was maintained patent as described previously. To record pressure, the catheter was connected to a pressure transducer (Statham Model P23Db) mounted on the harness. Mean pressure was recorded during exercise by electric damping of the pulsatile pressure. When exposed to a square-wave pressure of 200 mm Hg, this damped pressure required 3 seconds to reach 90% of maximum. Mean aortic pressure, hind-limb blood flow, and heart rate were recorded simultaneously during graded exercise in six dogs.

In four dogs, a further operation was performed, and an electromagnetic flow transducer was installed around the ascending aorta. The cable of the transducer was exteriorized just in front of the cable from the transducer on the left iliac artery.

All surgical procedures were carried out with sterile technique, and daily care was given to the points at which the transducer cables, catheters, and cuff-inflating tubes emerged through the skin.

Testing of Sympathectomy and Calibration of Flow Transducers.—At the end of the study, the completeness of sympathectomy was tested by the methods described in part II of the preceding paper.

Before implantation, each pair of flow transducers was matched in sensitivity and calibrated with blood over the expected range of flow. The final calibration was obtained in situ in the living, anesthetized dog and was used in the analysis of the records. The deep femoral, cranial femoral, and superficial circumflex iliac arteries were exposed and ligated. Thus all of the blood flowing through the transducer on the iliac artery was delivered into the femoral artery, from which a calibrated roller pump returned the blood to the carotid arteries. A small windkessel was placed between the femoral artery and the pump. As long as the level of blood in the windkessel was unchanged, the constancy of the pump output was assured. Eight to 10 points were obtained for the purposes of calibration, and the maximal flow during calibration was equal to or within 10% of the maximal flow observed during the study.

At each of the calibration flows, the pressure gradient across the flow transducer was measured. If the pressure gradient at the maximal flow exceeded 5 mm Hg, the blood flow data from the transducer in question were eliminated from the study.

The aortic flow transducer was calibrated at each level of exercise by equating the transducer output to an estimate of cardiac output obtained by the dye-dilution technique (indocyanine green). Two indicator-dilution curves were recorded at each level of exercise, and their averaged value was used.

Recording and Analyzing Blood Flow Signals.—The outflow from each iliac and aortic flow transducer was fed into an integrating circuit which measured total forward flow during periods of 3 or 6 seconds. Blood flow, heart rate, and blood pressure was measured over 6-second intervals during the continuous exercise, and over 3-second intervals during the 1-minute periods of exercise. Also, in each dog, records were obtained of phasic blood flow both at rest and during exercise.

In the final analysis of the data obtained during the continuous runs, the 6-second measurements of blood flow, heart rate, and blood pressure were averaged for the last 2 minutes of running at each level of exercise, for each minute of recovery, and for 30 seconds before the start of exercise. Data thus obtained from individual runs were summed to give mean values for the selected periods for all the studies of exercise in each animal.

The 1-minute runs were replotted on graph paper to compare the rate of change of flow at the onset of running at the different levels of exercise.

In one dog, after the studies of exercise had been completed, the abdomen was reopened by a sterile surgical technique, and the left lumbar sympathetic chain was exposed at the L-5 level. The rami communicantes to the L-5 ganglion were severed, and the lumbar chain was crushed just caudal to the L-4 ganglion. A small, bipolar, platinum electrode was applied around the lumbar chain immediately distal to the L-5 ganglion. The electrode was shielded from the surrounding tissues by an envelope of thin Silastic rubber sheeting, and the body of the electrode was secured to the lumbar muscles. The electrode leads were brought out through a stab wound in the flank region and finally exteriorized in the midline behind the scapulas. As judged by the
Changes in oxygen saturation of blood from common iliac vein of normal (solid circles) and of sympathectomized limb (open circles) during graded exercise. Four studies were done in dogs A, C, and D. Dog B was studied once only, 5 days after left lumbar sympathectomy. In curves for dogs A, C, and D, solid line connects mean value of observations from normal limb, and interrupted line connects mean value from sympathectomized limb. During control (C) and recovery (R) periods, dog walked at 1.7 km/hour on horizontal treadmill. During exercise (E), running speed was 5.5 km/hour at gradients indicated.

Results

Oxygen Saturation of Hind-Limb Venous Blood.—The results of four successful studies are shown in Figure 1. The data were obtained between the fifth and the fifteenth postoperative day. There was considerable variation in the results from the same dog and between dogs, but on any one day, the results in an individual dog were consistent.

In each of the four dogs, the oxygen saturation of venous blood from the sympathectomized limb tended to be higher than in the normal limb, both in the control period (walking at 0 grade and 1.7 km/hour) and
TABLE 1

Hind-Limb Blood Flow during Graded Exercise 24 and 48 Hours after Sympathectomy

<table>
<thead>
<tr>
<th>State</th>
<th>Time (hr)</th>
<th>Dog 2</th>
<th>Dog 4</th>
<th>Dog 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Pre*</td>
<td>270 (66)</td>
<td>150 (18)</td>
<td>206 (43)</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>220</td>
<td>207</td>
<td>132</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>220</td>
<td>238</td>
<td>148</td>
</tr>
<tr>
<td>Treadmill gradient</td>
<td>0%</td>
<td>Pre</td>
<td>500 (34)</td>
<td>422 (41)</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>500</td>
<td>562</td>
<td>580</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>495</td>
<td>450</td>
<td>658</td>
</tr>
<tr>
<td></td>
<td>7%</td>
<td>Pre</td>
<td>650 (31)</td>
<td>579 (37)</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>630</td>
<td>660</td>
<td>646</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>651</td>
<td>586</td>
<td>746</td>
</tr>
<tr>
<td></td>
<td>14%</td>
<td>Pre</td>
<td>780 (50)</td>
<td>706 (77)</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>740</td>
<td>702</td>
<td>822</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>785</td>
<td>720</td>
<td>895</td>
</tr>
<tr>
<td></td>
<td>21%</td>
<td>Pre</td>
<td>890 (61)</td>
<td>855 (94)</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>815</td>
<td>790</td>
<td>970</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>870</td>
<td>836</td>
<td>1,020</td>
</tr>
<tr>
<td></td>
<td>28%</td>
<td>Pre</td>
<td>990 (77)</td>
<td>980 (42)</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>915</td>
<td>837</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>990</td>
<td>890</td>
<td></td>
</tr>
</tbody>
</table>

*Mean value before sympathectomy, SD in parentheses. Number of tests before sympathectomy: 6 in dog 2, 4 in dog 4, and 6 in dog 6.

During the milder grades of exercise. This was most pronounced in dog A when the mean difference in O\textsubscript{2} saturation was 9.0, 5.5, 2.8, 8.0, 5.0, and 3.3\%, respectively, during the control period and when running at grades of 0, 7, 14, 21, and 28\%. On the assumption that the oxygen uptake in each leg was identical, the ratio of blood flow in the sympathectomized limb to that in the normal limb could be calculated. The mean values for the four studies on dog A were 1.14, 1.09, 1.04, 1.11, 1.06, and 1.04, respectively, for the control period and the five consecutive grades of exercise.

The pooled data from dogs A, C, and D were analyzed by Student's t-test with paired observations (8). During the control period and when exercising at grades of 0 and 14\%, the venous blood from the sympathectomized limb had a significantly higher O\textsubscript{2} saturation than that from the normal limb. Respectively, the average differences in saturation were 4.6\% (P < 0.02), 4.0\% (P < 0.01), and 3.3\% (P < 0.05). In contrast, during the first minute of recovery, the mean value for oxygen saturation of venous blood was significantly higher in the normal than in the sympathectomized limb (P < 0.001). This difference during recovery varied from one exercise study to the next but averaged 12.5, 9.5, and 8.8\% saturation in dogs A, C, and D, respectively (Fig. 1). The corresponding calculated ratios of blood flow in the normal limb to that in the sympathectomized limb were 1.30, 1.20, and 1.21.

Hind-Limb Blood Flow during Graded Exercise.—Thrombosis or stenosis of the iliac artery and failure of flow transducers eliminated a number of dogs from the study.

TABLE 2

Hind-Limb Blood Flow as Percent of Cardiac Output

<table>
<thead>
<tr>
<th>State</th>
<th>Limb sympathectomized</th>
<th>Dog 2</th>
<th>Dog 4</th>
<th>Dog 6</th>
<th>Dog 8 (normal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.4</td>
<td>5.0</td>
<td>7.6</td>
<td>8.1</td>
<td></td>
</tr>
<tr>
<td>Treadmill gradient</td>
<td>0%</td>
<td>8.7</td>
<td>11.0</td>
<td>12.4</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td>7%</td>
<td>10.6</td>
<td>12.5</td>
<td>15.5</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td>14%</td>
<td>11.6</td>
<td>13.1</td>
<td>15.6</td>
<td>12.1</td>
</tr>
<tr>
<td></td>
<td>21%</td>
<td>12.7</td>
<td>13.5</td>
<td>16.2</td>
<td>12.5</td>
</tr>
<tr>
<td></td>
<td>28%</td>
<td>12.6</td>
<td>17.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Observations of the blood flow in the normal and the sympathectomized limb during graded exercise were obtained in eight dogs (Figs. 2-6; Tables 1 and 2). In each of these dogs, the final testing procedures failed to reveal reflex sympathetic vasoconstriction in the denervated limb. In one dog (9, Fig. 7), blood flow studies were made in the normal limb only.

A comparison of blood flow in the same leg and between legs, before and after sympathectomy, could be made in dogs 2 and 3. The data from these two dogs and from dog 8 showed that there could be differences in blood flow of 20% in limbs apparently doing the same work, and also that the normal leg might show a slight increase in flow after contralateral sympathectomy.

In the three dogs whose limb blood flow was measured at the time of withdrawal of the lumbar snares, blood flow in the sympathecto-

mized limb immediately increased two- to threefold, while flow in the contralateral limb did not change. When ether anesthesia was discontinued 1 hour later, this difference in blood flow was still present, though reduced in magnitude. However, when the conscious dogs were examined standing on the treadmill 4 hours later, no consistent difference in blood flow between the two limbs could be detected.

Limb blood flows from studies of continuous exercise at 24 and 48 hours after sympathectomy are shown in Figure 5 (dog 8) and Table 1 (dogs 2, 4, and 6), and at 4 and 24 hours after sympathectomy in Figure 6 (dogs 3 and 5). The greatest change was seen in dog 3 in which blood flow in the sympathectomized limb exceeded that recorded before sympathectomy by an average of 38% at 24 hours and of 17% at 48 hours after sympathectomy (not shown in Fig. 6). In this dog, however, blood flow in the normal limb was also increased by an average of 36% at 24 hours and 28% at 48 hours. No significant differences between blood flow in the normal and the sympathectomized limb were observed at these times in the other dogs.

Likewise, when all of the data obtained in each dog during exercise of continuously increasing severity were considered, there were no differences of any magnitude between the blood flow recorded in the normal and the sympathectomized limb. If the limb blood flow recorded during the control period was taken as 100, then the average relative blood flows (±SD) during exercise for all the normal limbs were 242 (± 49), 314 (± 55), 387 (± 74), 458 (± 93), and 508 (± 110) at grades of 0, 7, 14, 21, and 28%, respectively. The corresponding values for all the sympathectomized limbs were 264 (± 73), 337 (± 91), 410 (± 104), 474 (± 115), and 527 (± 109). Thus, in both groups, the greatest increment in flow was between the control and the first level of exercise. Thereafter the magnitude of the limb blood flow was linearly related to the severity of the exercise.

Figure 7 shows the relationships among cardiac output, heart rate, mean aortic blood
pressure, and limb blood flow in three dogs with sympathectomized limbs and one normal dog (dog 9) during exercise of continuously increasing severity. The figure was constructed by reploting, at intervals of 6 seconds, the data measured on the original record. The cardiovascular responses were similar in both groups. This similarity is also seen in Table 2, which shows limb blood flow as a percent of cardiac output during the control period and at each level of exercise.

When the different levels of exercise were studied individually, an overshoot in blood flow was observed in both the normal and the sympathectomized limbs during the first 15 to 30 seconds of running. This overshoot was seen constantly in six of the dogs, inconstantly in one dog, and not at all in two dogs. Examples of these blood flow changes, present constantly in the six dogs, are shown in Figure 8. The overshoot averaged from 50 to 350 ml/min above the average limb blood flow in the steady state. In the six dogs, the overshoot was always seen at the start of exercise at zero gradient, was present in half of the studies at 7% gradient, but was infrequently seen at the start of exercise at 14% gradient. No overshoot was seen at the start of exercise at 21 and 28% gradient or in the studies with continually increased severity of the work load. This temporary increase in flow was accompanied by a brief tachycardia. In dog 8, the heart rate was 205 beats/min at the peak of the flow response before sympathectomy and 197 beats/min in the study after sympathectomy. This was in contrast to heart rates of 140 to 150 beats/min during the last 20 seconds of each study.

The records of phasic flow showed that in both normal and sympathectomized limbs the
increase in limb blood flow during exercise came not only from an increase in pulse flow but also from a very considerable increase in flow during the diastolic phase. The records reproduced in Figure 9 were selected to illustrate two points. In the resting animal, the heart rate was slow and R-R intervals of 0.8 to 1.0 second were recorded during the respiratory sinus arrhythmia. During the long diastolic phase, limb blood flow remained at a level indistinguishable from complete arrest of limb flow by the occlusion cuff. End-diastolic aortic blood pressure was 50 to 55 mm Hg. Observations of this type were made in normal and in sympathectomized limbs. An effect of muscle tension on limb blood flow is shown on the right. By chance, in this section of the record, the frequency with which each limb supported the dog’s weight was exactly half the heart rate, and the time relations of these two events were almost constant. As a result, a well-defined decrease in flow during systole and diastole occurred alternately in each leg. A reduction in limb blood flow during weight-bearing by the limb was seen in all of the records of exercise examined but could not be defined with such precision as in the example shown.

In the dog with the chronically implanted lumbar electrode, the effect on hind-limb blood flow of stimulating the lumbar sympathetic chain at various frequencies was studied at rest and during light exercise. Figure 10 shows a stimulus-response curve so obtained. In addition, the lumbar chain was electrically stimulated at 6 v, 6 cps, and 5-msec duration for 30 seconds during exercise at different work levels. The data are presented in Figure 11 and show that even at limb blood flows of almost 1,000 ml/min, a reduction to nearly half that value could be obtained through the action of the sympathetic vasoconstrictor nerves. When electric stimulation in the exercising dog was stopped, blood flow...
Blood flow to same hind limb before and after L-2 through L-7 sympathectomy. In dog 7, lumbar sympathetic chain was excised surgically; first and only postoperative study was obtained 13 days later. In dog 8, sympathectomy was first produced by snare technique; first and only postoperative study of this limb was made 24 hours later. Remaining lumbar chain was then excised surgically, and a series of five postoperative studies carried out, first of which was done 3 days after sympathectomy. In this dog, in-situ calibration of flowmeters was not obtained, and thus blood flows in same limbs before and after sympathectomy are presented in millimeters of recorded deflection.

Discussion
Neither in the studies in which the oxygen saturation of blood was measured from the common iliac veins nor in those in which the blood flow was measured directly with electromagnetic flow transducers were there conspicuous differences between the normal and the sympathectomized limbs during graded exercise. This similarity in the pattern and magnitude of the changes in limb blood flow was found over the whole range of exercise, both when each level was studied individually and when the severity of the exercise was increased continuously. The volume of blood delivered per minute to the hind limb was directly related to the work load, and there was no evidence that the rate of inflow was modified by sympathetic adrenergic activity. The studies afford no information on the
distribution of blood flow within the active muscles and the possibility of an alteration in this distribution through the activity of the sympathetic nerves. However, the area drained by the common iliac vein is more extensive than that supplied by the external iliac artery and includes the skin over the tail and the upper part of the hindquarters. The differences in venous \( \text{O}_2 \) saturation of blood from the sympathectomized limb compared to the normal limb during the control period, the milder grades of exercise, and the first minute of recovery thus might reflect a difference in blood flow to the skin of each limb.

Even when exercise was undertaken as early as 4 to 24 hours after sympathectomy, the increases in blood flow in the normal and the sympathectomized limbs were of similar magnitude, as was the decline in blood flow on cessation of running. Duff (9) described differences of blood flow in muscle and skin after sympathectomy and showed that the immediate increase in forearm blood flow was reduced by one-third on the first postoperative day and had returned almost to control values on the second. Similarly, Ederstrom and associates (10) reported a doubling of blood flow to the canine foot immediately after unilateral lumbar sympathectomy (L-2 through L-7). The flow had decreased by 24 hours, and thereafter blood flow on the operated side was less than on the control side.

Strandell and Shepherd (7) observed a reduction in blood flow in the exercising forearm of man during reflex augmentation of...
activity in sympathetic vasomotor fibers by lower body suction. In the present study, blood flow to the exercising hind limb of the dog was reduced by electric excitation of the lumbar sympathetic trunk. The percent of reduction in blood flow became less as the magnitude of the flow was increased, but even blood flows of 1,000 ml/min could be reduced substantially. When lumbar chain stimulation in the exercising limb was stopped, blood flow returned to the prestimulation level without the overshoot in flow observed when a similar reduction in blood flow had been produced mechanically by the occlusion cuff. Studies in man have shown that the metabolic recovery after exercise was not noticeably changed by the reflex reduction in blood flow during and after exercise (7) and that a mechanical reduction in blood flow after exercise did not lead to any prolongation of the postexercise hyperemia (11, 12). The mechanism of interaction between the sympathetic constrictor fibers and the local dilator mechanism is unknown.

The different shape of the stimulus-response curve of limb blood flow at rest and during exercise has been reported previously in a study of anesthetized dogs (13) and has considerable implications for the present study. If in the dog, as in man, there is an
increase in activity of the sympathetic adrenergic nerves that is proportional to the severity of the exercise, then during low or moderate work levels a degree of sympathetic nerve activity which would produce near maximal effects in the resistance vessels of inactive muscles would be almost without effect on active muscles. It is possible that in our studies the conditions associated with even maximal levels of exercise did not engender sufficiently intense sympathetic activity to modify blood flow in the active muscles, and to produce an effect, sympathetic vasomotor activity must be augmented in some manner. However, man and dog may differ in the degree of sympathetic vasomotor activity during exercise. An unchanged or increased blood flow was found in the renal and superior mesenteric arteries (14) and in the splenic artery (15) during treadmill exercise in dogs. Rushmer and associates (16) also have reported that during treadmill exercise in dogs the blood flow in the hepatic, renal, and superior mesenteric arteries remained unchanged from the preexercise values. In a study of blood flow distribution of Alaskan sled dogs during extended exercise, Van Citters and Franklin (17) found no change or a slight increase in renal and mesenteric blood flows. These studies in dogs in which blood flow was measured directly, do not support the view that, during exercise, blood flow in the active muscles is augmented at the expense of blood flow to the viscera.

During graded exercise, the increase in limb blood flow was linearly related to the increase in work load. The average increments in blood flow between 0, 7, 14, 21, and 28% gradients were 143, 149, 144, and 149 ml/min for the
Normal limbs; the corresponding values for the sympathetomized limbs were 122, 134, 122, and 116 ml/min. The oxygen saturation of limb venous blood decreased linearly with increase in work load, but the magnitude of the changes was not large. The average
198 DONALD, ROWLANDS, FERGUSON

% REDUCTION IN FLOW

69 81 68 55 49 46 57 60

STIMULATION

Before

During

HIND LIMB BLOOD FLOW (ml/min)

STANDING 0 7 14 21 0 LIYING

FIGURE 11

Effect of electric stimulation of lumbar sympathetic chain (6 v, 6 cps, 3 msec) for 30 seconds on limb blood flow during different intensities of exercise. Cross-hatched areas show blood flow before stimulation and solid areas, the flow during last 10 seconds of stimulation. Each level of exercise was run separately.

decreases in oxygen saturation between the five work levels were 3, 3, 4, and 2%, for the normal limbs and 4, 3, 4, and 2% for the sympathectomized limbs. The greatest change, both in limb blood flow (average 290 ml/min) and in venous oxygen saturation (average 10%), was between the control value and that measured during the first level of exercise (5.5 km/hour at zero gradient).

Thus, under the conditions of exercise in this study, the metabolic demands of mild exercise were met by an increase both in blood flow and in oxygen extraction. As the severity of the exercise increased, the demand for oxygen was met principally by an increase in blood flow. In this respect, the dog behaves similarly to man exercising in the upright position. Reeves and associates (18) have shown that in man the increased metabolic demands of walking at various gradients are met almost entirely by increased femoral and total blood flow.

The finding that blood flow in the external iliac arteries stopped during late diastole on those occasions when the R-R interval was 1 second or more was unexpected because the arterial blood pressure was between 50 and 60 mm Hg. A slight increase in heart rate and in end-diastolic blood pressure, however, resulted in limb blood flow being continuous throughout the cardiac cycle, although the zero flow line was approached in late diastole. Gregg (19) has remarked on the variable relationship of the flow patterns in different regions to the position of zero flow. In the renal and mesenteric arteries, the flow pattern was widely separated from the zero flow line; in the iliac artery, forward flow declined almost to zero in the latter part of diastole (heart rate 70 beats/min, end-diastolic arterial blood pressure 60 mm Hg). The findings in these two studies would indicate that in the resting, conscious dog the resistance to flow may be sufficiently great in the vascular bed of the normal and the sympathectomized limb that blood flow may cease even at arterial blood pressures of 50 mm Hg or more.

The present study in dogs revealed no significant differences in blood flow to the normal and the sympathectomized hind limb of the dog, either when the dog was standing on the treadmill or when it was performing graded exercise. The severity of the exercise undertaken appeared to be the sole determinant of blood flow to the limb.

References


Similarity of Blood Flow in the Normal and the Sympathectomized Dog Hind Limb during Graded Exercise

DAVID E. DONALD, DEREK J. ROWLANDS and DAVID A. FERGUSON

doi: 10.1161/01.RES.26.2.185

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1970 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/26/2/185

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation Research* 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 Research* is online at:
http://circres.ahajournals.org/subscriptions/