Response of Dogs’ Cutaneous Veins to Local and Central Temperature Changes

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ABSTRACT
To study the separate actions of peripheral and central temperature-sensitive systems on the cutaneous veins of the dog, a cross-circulation preparation was made in which hindleg and central temperatures could be varied independently. The lateral saphenous vein of a vascularly isolated hindleg was cross-perfused at constant flow; the difference between perfusion and femoral vein pressures was a measure of veno-motor activity. With central temperature constant, local cooling of one leg from 47°C to 17°C caused the lateral saphenous vein to constrict; sensitivity to cooling was maximal between 42° and 27°C. With leg temperature constant, central cooling caused the lateral saphenous vein to constrict; over the range of 40° to 33°C, the constriction was linearly related to the decrease in temperature. Central heating reduced the response to local cooling, whereas central cooling had the opposite effect. Thus a decrease in central temperature from 38° to 34°C increased the venoconstrictor response to local cooling from 42° to 22°C by a factor of ten or more.

ADDITIONAL KEY WORDS
venous reflexes

Both central and peripheral thermosensitive “receptors” act together to initiate the complex pattern of reactions by which an animal maintains a constant body temperature. The relative importance of central and peripheral controls in the regulation of body temperature, however, has not been exactly defined. The finding that the lateral saphenous vein of the dog shows a constrictor response to both local and central cooling mediated on the efferent side by adrenergic nerve fibers (1) indicated the possibility of studying the separate roles of peripheral and central mechanisms in this response. A cross-perfusion preparation was accordingly devised in which central and right hindleg temperatures could be varied independently.

Methods
In dogs anesthetized with thiopental, 15 mg/kg iv, and chloralose, 80 mg/kg iv, and artificially ventilated with oxygen, a cross-perfusion circuit was set up (Fig. 1).
Right Leg Circuit.—The normal circulation to this leg was cut off by a wire snare drawn tight around the upper part of the thigh. Blood from the left femoral artery of the donor dog was led to a Y junction. One arm of the Y led to a roller pump that delivered blood at a constant flow rate through a heat exchanger (A) into the experimental dog’s right lateral saphenous vein at the ankle. The other arm of the Y was connected to a cannula placed in the experimental dog’s femoral artery. During experiments (which lasted up to 20 minutes), this arm of the Y was clamped, but between experiments the clamp was removed, and the experimental dog’s right femoral artery was perfused with blood from the donor animal. Blood was led back from the right femoral vein of the experimental dog to the left femoral vein of the donor dog through a second heat exchanger (B). Pressures were measured just upstream to the saphenous vein cannula and in the femoral vein of the experimental dog’s right leg. Because, during experiments, flow from the donor dog to the experimental dog’s right femoral artery was arrested, flow to the lateral saphenous vein was provided entirely by
the roller pump; under these conditions of constant flow, the difference between perfusion and femoral vein pressures (driving pressure) was a measure of the venomotor activity. The esophageal temperatures of both dogs and the temperature of the blood flowing into the vein were measured. The latter temperature was altered by changing the temperature of the water flowing through heat exchanger A (placed between the pump and the saphenous vein cannula). The water temperature of heat exchanger B (placed between experimental and donor animals' femoral vein cannulas) was maintained at 38°C. With this arrangement of the heat exchangers, the temperature of the blood flowing through the saphenous vein could be varied from 47° to 17°C, without any changes in esophageal temperature of the donor dog. Because the circulation of the experimental dog's right leg was isolated, this dog's esophageal temperature also did not change.

Left Leg Circuit.—Blood was taken from the experimental animal’s median sacral artery and pumped through a heat exchanger (C) into the left saphenous vein. Changing the water temperature of this heat exchanger made it possible to raise or lower the animal’s central temperature. Esophageal and saphenous perfusate temperatures were measured by thermocouple probes (Yellow Springs Instrument Co.).

Results

Of six successful preparations, four gave satisfactory results, showing the same three features.

Local Cooling of Right Saphenous Vein Perfusate with Central Temperature Constant.—Cooling the blood perfusing the right saphenous vein from 47° to 17°C in the absence of any change in central temperature caused the vein to constrict. Figure 2 is a record from one of the dogs. As the temperature of the blood perfusing the vein was increased from 37° to 47°C, venodilatation occurred. Gradual cooling of the blood from 47° to 17°C caused a progressive venoconstriction. Figure 3 gives the results for the
four dogs. It will be noted that the venoconstriction caused by local cooling was maximal in the range 42° to 27°C and that the constrictor response to local cooling was smallest in the dog whose esophageal temperature was highest.

Central Cooling with Right Saphenous Perfusate Temperature Constant.—The esophageal temperature of the experimental dogs was lowered by reducing the temperature of the blood perfusing their left saphenous veins to 16°C and was raised by increasing this temperature to 43°C. The temperature of the right (vascularly isolated) saphenous vein was maintained at 37°C throughout. The results of such an experiment are plotted graphically in Figure 4. Lowering the esophageal temperature of this dog from 40° to 33°C increased the driving pressure in the right saphenous vein from 12 to 62 mm Hg with right saphenous perfusate maintained at 37.5°C ± 0.5°C. In the other three dogs, esophageal temperature was not varied over such a wide range, but similar results were obtained. In the first of these dogs, the saphenous vein driving pressures at a local

![Graph](https://example.com/graph.jpg)

**FIGURE 3**

Response of cutaneous vein to local temperature changes (results from four dogs). In experiments on each dog, esophageal temperature was held constant at figure shown. Driving pressure is saphenous perfusion pressure minus femoral vein pressure at equilibrium following each change in perfusate temperature. Note that venomotor response to changes in local temperature is least in dog with highest esophageal temperature (38°C).

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Venous Perfusate Temperature.
37.5 ± 0.5 °C

**FIGURE 4**
Driving pressure of right saphenous vein plotted against esophageal temperature. Note that venous responses to esophageal temperature change appear linear over the range 33° to 40°C.

Temperature of 37°C were 10, 19, and 20 mm Hg at esophageal temperatures of 38°, 36°, and 34°C, respectively; in the second dog, they were 20, 25, 41, and 49 mm Hg at esophageal temperatures of 36°, 35°, 34.5°, and 34°C, respectively; and in the third dog they were 25, 36, and 25 mm Hg at esophageal temperatures of 37.2°, 35.2°, and 37°C, respectively.

**Combined Local and Central Cooling.**—The response to identical changes in temperature of the blood perfusing the right saphenous vein was examined at different esophageal temperatures. Figure 5 shows the tracings from an experiment in which the response to changing the temperature of the blood perfusing the right saphenous vein from 37° to 42° to 22°C was examined at esophageal temperatures of 38°, 36°, 34°, 36°, 38°, and 36°C. Comparison of the response to the decrease in temperature of the perfusate from 42° to 22°C after central cooling to an esophageal temperature of 34°C and after central rewarming to an esophageal temperature of 38°C shows that at the lower central temperature the increase in driving pressure caused by the decrease in perfusate temperature was augmented more than tenfold. Figure 6 shows the effect of central cooling on the venoconstrictor response to a decrease of 20°C in venous perfusate temperature, and it will be seen that, in all four dogs, central cooling greatly augmented the venoconstrictor response to the same decrease in local venous temperature.

In both of the unsatisfactory cross-perfusion preparations, changes in temperature of the blood perfusing the right saphenous vein resulted in alterations in tone of that vessel, but a decrease in esophageal temperature failed to cause venoconstriction, and central cooling did not augment the response to local cooling. In the first of these dogs, a decrease in perfusate temperature from 42° to 22°C increased the driving pressure by 8 mm Hg. This response was unaffected by lumbar
TEMPERATURE AND VEINS

Recordings to demonstrate effects of changing esophageal temperature on response of right lateral saphenous vein to standard decrease in temperature of blood perfusing the vein (scale marked °C). Tracing 1 gives temperature of blood perfusing the vein and esophageal temperature (recorded by single galvanometer). Square-wave deflections are caused by switching to read esophageal temperature. Broken line is added to aid the reading of esophageal temperatures; E 36, E 34, E 38 just above this line are the esophageal temperatures at these periods of the experiment. Tracing 2 refers to the temperature of blood perfusing left saphenous vein (scale not shown). This temperature was altered to change the central (esophageal) temperature. Tracing 3 refers to pressure of blood perfusing right lateral saphenous vein, and fourth tracing represents pressure in right femoral vein. Since flow is constant, changes in perfusion pressure are due to active changes in venous wall tension. Note that increase in wall tension in response to lowering the temperature of blood perfusing right saphenous vein is augmented by lowering esophageal temperature.

sympathectomy. Electric stimulation of the right sympathetic chain (10-v, square-wave impulses of 1-msec duration at a frequency of 10 cps) caused an increase in driving pressure of 126 mm Hg. In the second dog, a decrease in perfusate temperature from 42° to 22°C caused an increase in driving pressure of 57 mm Hg; after sympathectomy, the increase was 8 mm Hg.

Discussion

Evidence from lesion and ablation studies (2, 3), combined with that obtained by various methods of localized heating and cooling of the brain (4-12), supports the concept that the hypothalamus is the main integrative center for regulation of temperature. The hypothalamus has been shown to contain thermosensitive cells activated by changes in blood temperature (13, 14).

There is also evidence that stimulation of cutaneous thermal receptors initiates reflexes to control heat transfer from (and heat production by) the body (15-17). Measurements of the total thermal and metabolic responses of the unanesthetized dog to localized heating and cooling of the hypothalamus at various environmental temperatures led Fusco and co-workers (18) to conclude that the thermoregulatory responses were due to a summing of the central and peripheral thermal drives.

A previous study (1) had suggested that both peripheral and central mechanisms were involved in the response of the superficial limb veins to changes in temperature and had indicated that this response depended on the integrity of the sympathetic nervous system. The experimental preparation used (perfusion of the lateral saphenous veins of both hindlegs with unilateral changes in perfusate temperature), however, did not permit the
temperature of the blood perfusing the veins and the central temperature to be varied independently. Thus it was impossible to decide if the two systems showed a summation that was simply additive or mutually facilitative. The results of the present study confirm that either local cooling of the blood perfusing the vein or central cooling produces constriction of the superficial limb veins. With esophageal temperature constant, most of the venoconstriction in response to local cooling occurred over the perfusate temperature range 42° to 27°C. These experiments involved the longest periods of arrest of the arterial circulation to the right leg (up to 20 minutes). The saphenous driving pressures at a perfusate temperature of 37°C at the beginning and end of each experiment were very similar, indicating that arrest of arterial flow to the leg had little or no effect on tone in the vein perfused with arterial blood.

With perfusate temperature constant, central cooling caused a venoconstriction that was linearly related to the decrease in esophageal temperature over the range 40° to 33°C. The sudden changes in the temperature of the left saphenous vein had no immediate effect on the venomotor tone in the vascularly isolated right saphenous vein maintained at 37°C, the change in tone in this vessel occurring only with a change in esophageal temperature. Because local changes in temperature of the blood perfusing the vein do not cause reflex changes in venomotor tone (19), it is likely that central temperature receptors (possibly the temperature-sensitive neurones in the hypothalamus [13, 14]) were responsible for these changes in right saphenous venomotor tone.

Of particular interest is the evidence that central heating reduces the response to a standard local cold stimulus (lowering local temperature from 42° to 22°C), whereas central cooling has the opposite effect. Thus a decrease in central temperature from 38° to 34°C increased the response to the standard local cold stimulus by a factor of more than ten. In this case, the peripheral and central "thermal drives" do not appear to be simply additive, since changes in central temperature can be seen to act by "resetting the gain" of the local thermoregulatory mechanism, central cooling increasing the gain, and central warming having the opposite effect.

In the first of the two unsatisfactory preparations, the powerful venoconstrictor response to electric stimulation of the sympathetic nerves demonstrated that the poor response to local cooling of the venous perfusate and the absence of response to changes in esophageal temperature were not due to lack of responsiveness of the venous smooth muscle to sympathetic nerve impulses. The results in the second animal (see Results)
suggest that the local venous thermoregulatory mechanism could function even though the central receptors had failed.

In summary, the superficial limb veins are controlled by a local thermoregulatory mechanism, the sensitivity of which is governed by central temperature receptors. The nature of the local mechanism is the subject of the study reported in the next paper (19).

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References
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