Effect of temperature on reactivity of saphenous, mesenteric, and femoral veins of the dog

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VANHOUTTE, PAUL M., AND ROBERT R. LORENZ. Effect of temperature on reactivity of saphenous, mesenteric, and femoral veins of the dog. Am. J. Physiol. 218(6): 1746-1750. 1970.—The contraction of cutaneous veins of the dog caused by sympathetic nerve stimulation or by vasoactive drugs has been found previously to be potentiated by cooling and depressed by warming. To determine if this effect was specific for cutaneous veins, the thermosensitivity of helical strips of saphenous and femoral veins and of longitudinal strips of mesenteric veins of the dog was investigated. Strips from three types of veins relaxed slightly during cooling (to 29 C) and contracted during warming (to 43 C). In addition, warming augmented the spontaneous activity exhibited by the mesenteric vein strips, whereas cooling had the opposite effect. Electric stimulation caused saphenous and mesenteric vein strips to contract, and these contractions were augmented by cooling and attenuated by warming. The femoral vein strips reacted to electric stimulation, norepinephrine, and 5-hydroxytryptamine; these reactions were attenuated by cooling and enhanced by warming. The data suggest that the potentiating effect of cold on adrenergic reactions is not specific for cutaneous veins but is not a general characteristic of venous smooth muscle.

METHODS

The experiments were performed on helical strips of lateral saphenous and femoral veins and on longitudinal strips of anterior mesenteric veins taken from dogs anesthetized with intravenously administered pentobarbital sodium (20 mg/kg). The preparations were placed in a chamber filled with Krebs-Ringer bicarbonate solution of the following composition in millimoles per liter: NaCl, 118.3; KCl, 4.7; MgSO4, 1.2; KH2PO4, 1.2; CaCl2, 2.5; NaHCO3, 25.0; and glucose, 11.1; aerated with a 95% O2-5% CO2 gas mixture. The strips were connected to a strain gauge (Grass, FT-03) for isometric tension recording. The bath temperature was measured by a thermistor probe (Yellow Springs Instrument Co.). The Krebs-Ringer solution was continuously circulated through a circuit consisting of a roller pump, a heat exchanger, and the bath. Altering, at a controlled rate, the temperature of the water flowing through the heat exchanger produced rapid and reproducible (± 0.5 C) changes in bath temperature.

For electric stimulation of the preparation, two rectangular platinum electrodes were placed parallel to the strips, as described previously (22). Electric impulses consisted of square waves (8 v, 2 msec) provided by a direct-current power supply and switching transistor (RCA 2N-3055) triggered by a Grass stimulator (Model S4). In some experiments, bretylium tosylate (Darenthin) was used. In other experiments the effects of norepinephrine (Levophed) and 5-hydroxytryptamine were investigated. These drugs were infused at a constant rate, by means of an infusion pump (Harvard) upstream of the roller pump, to ensure adequate mixing. The given doses are expressed as final bath concentrations. In these experiments the bath content was not recirculated.

Before the experiments were begun, the preparations were placed at the optimal point of their length-tension relationship (22). In each group of preparations, the number of strips reported in the RESULTS section is also the number of different dogs used.

RESULTS

Saphenous Veins

Basal tension. In experiments on 15 helical strips without external stimulation, a decrease in bath temperature, from 37 to 29 C, decreased the basal tension slightly in most preparations. Increasing the bath temperature, from 37...
to 43°C, resulted in a slight to marked increase in tension. Two preparations exhibited spontaneous activity at the higher bath temperature.

Reaction to electric stimulation. Figure 1 illustrates a typical experiment. During a sustained contraction caused by electric stimulation, an increase in bath temperature depressed the reaction to the stimulation whereas rapid cooling of the bath solution markedly increased the responses in all strips studied. In some preparations, the potentiation by cooling was preceded by a small transient decrease in tension, when the same preparations were returning to the control temperature, a rapid and transient increase in tension preceded relaxation. Figure 2, left, illustrates the effects of temperature changes, noted in strips from eight saphenous veins. It emphasizes the relatively small effects of temperature change in the absence of external stimulation. Since both the basal tension and the active tension developed during electric stimulation differed in the individual preparations, the data are expressed as percentage of the difference between the lowest tension recorded in the absence of electric stimulation and the highest value observed during stimulation. The basal tension of each saphenous strip was the least, and the active tension developed was the greatest at 29°C.

Mesenteric Veins

Basal activity (Fig. 3). Cooling reduced the spontaneous activity exhibited by most mesenteric vein strips and, in most of the preparations, reduced the basal tension in the same way as observed in saphenous strips. An increase in bath temperature augmented the basal tension and the spontaneous activity in the sense of more frequent oscillations of decreasing amplitude. Not all preparations could maintain those initial responses to warming.

Reaction to electric stimulation. Figure 4 compares the effects of identical changes in temperature imposed on a saphenous strip and a mesenteric strip from the same dog. The mesenteric strip reacted to temperature in the same way as the saphenous strip: during a sustained contraction induced by electric stimulation, cooling the bath from 37 to 29°C resulted in a marked increase in tension and warming had an opposite effect. Similar results were obtained in eight mesenteric strips (Fig. 2, center).

In a series of seven experiments, each performed simultaneously on strips of both mesenteric and saphenous veins taken from the same dogs, the effect of a similar decrease in temperature (from 37 to 29°C) was investigated during contractions induced by electric stimulation of increasing frequency, so that frequency-response curves could be constructed. The results (Fig. 5) confirm that there is no important difference in reactivity to cold between mesenteric and saphenous veins, in particular at the higher frequencies.

Femoral Veins

Basal tension. Warming the bath in the absence of external stimulation caused an increase, and cooling it caused a decrease in basal tension of the preparations (Fig. 6, left).

Reaction to electric stimulation. Electric stimulation (2–15 cycles/sec) caused contraction of femoral vein strips (seven preparations). These reactions, even to supramaximal stimulation (15 cycles/sec), were abolished by addition of bretylium tosylate (2 × 10⁻⁶ g/ml) to the bath solution. Figure 6, right, shows, in a typical experiment, the effects of temperature changes: warming increased and cooling depressed the reaction to electric stimulation. Similar results were obtained in strips from seven femoral veins (Fig. 2, right).

Reaction to norepinephrine and 5-hydroxytryptamine. Addition of norepinephrine (1–5 × 10⁻⁶ g/ml) caused contraction of nine femoral vein strips. In all experiments cooling depressed and warming augmented these reactions. However,
quantitative determination of temperature effects was made difficult by the fact that not all preparations could maintain a sustained contraction to pharmacological agents. In five femoral strips relatively stable reactions could be obtained with norepinephrine (10^-6 g/ml). Cooling the bath to 29°C reduced these contractions to 72.8% (SE ± 5.3%) of the contraction (285 mg; SE ± 97) obtained at 37°C. In four femoral strips relatively stable contractions could also be obtained with 5-hydroxytryptamine (2 × 10^-9 g/ml). Cooling the bath to 29°C reduced these contractions to 46.3% (SE ± 8.4%) of the contractions (230 mg; SE ± 57) obtained at 37°C. With both norepinephrine and 5-hydroxytryptamine, the values at 29°C are corrected for the direct effect of cooling on the strips in the absence of stimulation. Thus, the effects of changes in bath temperature during active contraction were similar to those observed in the absence of external stimulation but opposite to those observed during active contractions of strips from saphenous and mesenteric veins.

DISCUSSION

When similar variations in bath temperature were imposed in control conditions, the strips from the three types of veins reacted with a slight decrease in tension with cooling and an increase with warming. The effects of temperature on the spontaneous activity of the dog's mesenteric vein appear to be identical to what has been reported for spontaneously active venous smooth muscle of other mammals (4, 10, 16, 20, 27). In perfusion experiments in the intact dog (24, 26) and in isolated cutaneous vein segments (23), minimal changes in resistance, consistent with the tension changes obtained in these strip preparations, have been observed only occasionally with cooling in the absence of external stimulation. This indicates that, in vivo, the changes in wall tension probably are partially or completely balanced by viscosity changes in the fluids flowing through the veins (6, 7, 15). In mesenteric and saphenous veins the observed changes in wall tension are minimal, especially during cooling, as compared to the very marked effects, in the opposite direction, of temperature variations imposed during active contractions.

Since pharmacologic experiments, using reserpine and
sympatholytic drugs, have shown that electric stimulation, as used in the present experiments (short pulse duration at low frequencies), of isolated venous tissue acts by liberating catecholamines from nerve terminals (11, 12, 21), our experiments confirm the observations by Webb-Peploe and Shepherd (24–26) who described the marked dependency of adrenergic reactions on local temperature in the cutaneous veins in the intact dog. Also, our results indicate that this phenomenon is not specific for cutaneous veins. Increased sensitivity of isolated cutaneous arteries to adrenergic stimulation during moderate cooling has been reported by others (8, 9, 18). A potentiated reaction to adrenergic agents during local cooling has also been reported for the dog’s mesenteric artery by Rogers and coauthors (17).

Femoral vein strips reacted to electric stimulation, and these reactions were inhibited by doses of bretylium tosylate known to inhibit the reactivity of saphenous and mesenteric veins (21), which indicated that electric stimulation also activates sympathetic nerve endings in the femoral vein.

On the other hand, the reactions of femoral vein strips to electric stimulation, norepinephrine, and 5-hydroxytryptamine are depressed by cooling and enhanced by warming, almost in exaggeration of the effects of changes in temperature in control conditions. A difference in reactivity to temperature changes, imposed during adrenergic reactions, between cutaneous and femoral arteries has been described (8), and a depression of the contractile responses with cooling has been reported for different somatic arteries (3, 13, 14). The difference in patterns in thermosensitivity between saphenous and mesenteric veins on the one hand and femoral veins on the other hand is perhaps just another example of the heterogeneity existing among different vascular smooth muscles (1, 2, 19). However, a depressing effect of cooling, similar to the one observed in femoral veins and in different arteries (5, 13, 14), can be evoked even in saphenous veins when the contraction of the venous smooth muscle is induced by either KCl or BaCl₂ (23). This indicates that the intrinsic effect of a decrease in temperature on venous smooth muscle may be a depression of contractility (3). In cutaneous veins, and apparently also in mesenteric veins, this direct depressing effect of cold on the contractile process would be counteracted, during adrenergic contractions, by an opposite effect of temperature on the excitation mechanisms of the smooth muscle cell (25). In preparations which, in the absence of stimulation, reacted to warming with a larger increase in tension, the opposing actions of temperature can be detected when the bath is warmed during a sustained contraction. In the example shown in Fig. 4, right, both saphenous and mesenteric vein strips showed biphasic responses. Why only the more direct effect of temperature changes is apparent in the femoral vein strip is not clear.

The cutaneous veins, in the intact organism, are exposed to variations in temperature in the range of those tested in our study. Therefore, the potentiating effect of cooling, if not specific, probably is of particular importance for the cutaneous venomotor reactivity.

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