bath. Temperatures were monitored with a Honeywell 24-channel recording thermograph verified by a Schultheis mercury thermometer. For validation and discussion of this technique, see B. Bradley, *Limnol. Oceanog.* **21**, 596 (1976).
11. Individually reared F_1 fish in 180-ml plastic containers with holes to allow water circulation were placed in a large (about 100 liters), thoroughly aerated, water bath. Water temperatures were lowered approximately 10°C during the first hour and approximately 5°C per hour thereafter. Temperature at loss of equilibrium was recorded for each fish to 0.1°C. The temperature was raised slowly to 27°C after the experiment; 2 days later, the experimental procedure was repeated, raising the temperature approximately 8°C the first hour and 3°C per hour thereafter. The temperature at cessation of respiratory ventilation was recorded.
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16. We thank A. Bloodgood, C. Farrell, and W. Osbrink for technical assistance. Comments by K. Heck and two anonymous reviewers helped improve the manuscript. This work was supported by grant DEB 77-03897 from the National Science Foundation.
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20 July 1979; revised 27 November 1979

Temperature Sensitivity of Tone in the Rabbit Facial Vein: Myogenic Mechanism for Cranial Thermoregulation?

Abstract. *Intrinsic myogenic tone in the buccal segment of the rabbit facial vein is exquisitely sensitive to small changes in temperature in the range 33° to 44°C. This particular venous segment also exhibits a preponderance of β-adrenergic receptors and receives a dense, medial sympathetic innervation. This area of the vein is proposed to act as a temperature-sensitive sphincter that distributes cooled nasal venous blood between superficial and deep venous drainage systems in the head and neck. Deviation of cool blood to deeper venous sinuses has been shown to be an important thermoregulatory mechanism.*

The buccal segment of the rabbit facial vein exhibits a number of uncommon properties. Isolated rings from this 10- to 14-mm length of vessel dramatically develop myogenic tone in response to stretch (*1*) and display a β-adrenergic receptor-mediated relaxation to sympathomimetic stimulation (*1*, *2*). The smooth muscle cell layers are endowed with a dense, three-dimensional adrenergic innervation (*2*). These characteristics are not observed in more proximal or distal segments of the vein nor in the adjacent part of the facial artery. A physiological role for this segment has not been proposed.

We have observed that the intrinsic myogenic tone of the rabbit facial vein responds to very small changes in ambient temperature. This tone is maintained as long as stretch is applied and is independent of both the sympathetic innervation and known endogenous vasoactive autacoids (*1*). We hypothesize that the temperature-sensitive changes in tone that occur in this restricted vascular segment are responsible for influencing the direction of venous return from the nose, either allowing cooled venous blood to course through the facial vein en route to the external jugular vein or shunting the flow of blood through deep cranial sinuses. These temperature-induced changes in venous flow assist in maintaining brain homothermia.

The right and left facial veins of New Zealand White rabbits (2.0 to 2.6 kg) were excised distal to their confluence with the deep facial vein. Two cleaned 4-mm rings were prepared from each vein and set up in tissue baths so that changes in vessel contractility could be recorded (*2*). They were equilibrated for 1 hour (without tension) in a modified Krebs physiological saline solution of the following millimolar composition: Na^+, 144.2; K^+, 4.9; Ca^{2+}, 1.6; Mg^{2+}, 1.2; Cl^-, 126.7; HCO_3^-, 25; SO_4^{2-}, 1.19; glucose, 11.1; and ethylenediaminetetraacetic acid, 0.024, bubbled with 95 percent O_2 and 5 percent CO_2. Water circulated from a heated reservoir around the tissue bath to maintain temperature normally at 37.5°C. Tissues were washed every 15 minutes during this equilibrium. After 1 hour, rings were stretched so that approximately 0.5 g of tension was applied to the vessel wall. The resulting developed tone was quantified by measuring the extent of relaxation following the addition of sodium nitrite ($5 \times 10^{-2} M$) (Fig. 1A). The temperature of the Krebs saline solution was increased or decreased by 1°C intervals by adjusting the temperature of the reservoir. Bath temperature was monitored by a thermistor probe (Yellow Springs Instrument model 421) suspended in the tissue bath and connected to a telethermometer bridge (Y.S.I. model 425c). The amount of tone recorded with each change in temperature was expressed as a percentage of the maximum tension produced by exogenously added histamine at 37.5°C (*3*).

Figure 1A illustrates changes in intrinsic tone that occur in response to small changes in bath temperature; the relationship between the equilibrium level of tone and bath temperature is shown in Fig. 1B. A fall of only 1°C from the control level of 37.5°C reduced the level of tone by 50 percent; a rise of 1°C

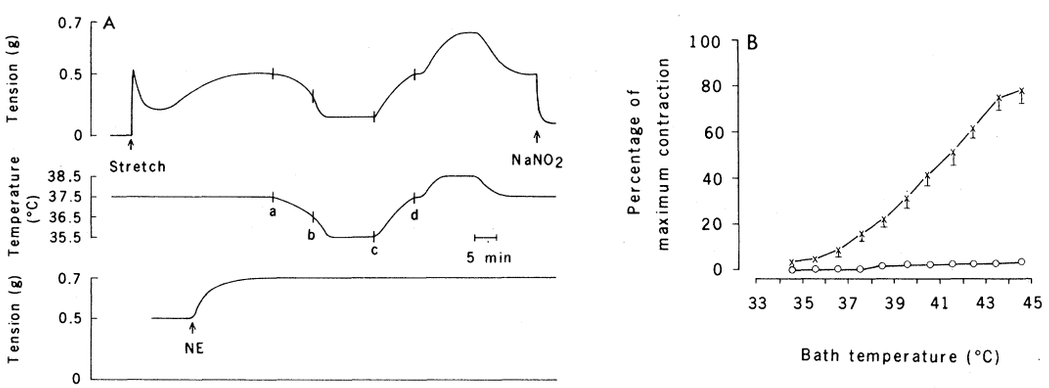

Fig. 1. (A) Typical in vitro tension recording of a rabbit facial vein (top trace). A maintained tone develops after the vein is stretched, but decreases if the tissue bath temperature (middle trace) falls by 1°C (*a*). There is a corresponding increase in the decline of tone if the ambient temperature falls faster (*b*). Tone returns to control levels as the temperature readjusts to 37.5°C (*c*). There is a reversible doubling of the level of tone accompanying a 1°C rise in ambient temperature (*d*). The total amount of developed tone is indicated by the addition of a maximal dose of sodium nitrite. Venous segments distal to the facial vein sphincter failed to show this temperature sensitivity when tone was induced by the addition of *l*-norepinephrine ($10^{-7} M$) (bottom trace). (B) Tone present in control (X) and sodium nitrite-treated ($5 \times 10^{-2} M$) (○) facial vein rings in a 12°C range of ambient temperature, expressed as a percentage of the maximal contraction elicited by histamine at 37.5°C. Data points are means ± standard errors for the control curve.

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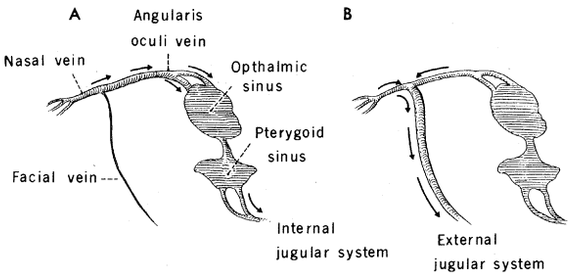

Fig. 2. (A) Proposed route of cooled venous blood from the nasal heat exchange area in hyperthermia. Increased tone in the rabbit's facial vein sphincter directs more cooled blood into the ophthalmic and pterygoid sinuses for cranial thermoregulation. (B) Decreased ambient temperature inhibits tone in the facial vein and allows for drainage of the cooled venous blood into the external jugular system.

caused a 100 percent increase. Tone did not develop at 33.5°C but returned to control levels when the bath temperature was elevated to 37.5°C. The rate of change of tone but not its final level varied with the rate of change of temperature. Changes in the level of tone were observed over a temperature range of 12°C. The same level of tone was achieved at a particular temperature whether it was approached from a higher or lower level. Under these circumstances the maximum temperature-induced tone was approximately 80 percent of the maximum drug-induced tension.

Venous segments taken proximal and distal to this special area did not develop tone. Their resting length and their contractile response to *l*-norepinephrine changed very little over the 12°C range (Fig. 1A). The resting length of facial vein rings maximally relaxed with sodium nitrite ($5 \times 10^{-2} M$) also failed to change significantly with these changes in ambient temperature (Fig. 1B).

Changes in vascular tone of both resistance and capacitance vessels in response to alteration in the ambient temperature occur as part of the mammalian thermoregulatory mechanism (*4*, *5*). Cooling of cutaneous vessels from 37° to 27°C increases their responsiveness to adrenergic stimulation (*5*, *6*), in part because of an alteration in the α-adrenoceptor mechanism (*5*). Increased ambient temperature normally has an opposite effect. Thus, the increase in intrinsic tone with a rise in the temperature of the buccal segment of the rabbit facial vein is opposite to that observed in other cutaneous blood vessels and to the consequences of changes in adrenergic responsiveness with temperature change. Not only the direction but the magnitude of the change in tone of this venous segment with alteration in the ambient temperature differs from other vascular sites. This is another facet of the uniqueness and singularity of this vessel segment.

The exquisite sensitivity of the facial vein sphincter tone to ambient temperature suggests a role in thermoregulation. Blood draining the nasal mucosa is cooled by heat exchange with the air within the nose and by surface evaporation (*7*). In the rabbit, this blood drains either into the facial vein and then into the external jugular system or via the angular and ophthalmic veins into the pterygoid plexus and cavernous sinus (*8*). This latter blood returns to the heart via the deeper or internal jugular system (*8*). The distribution of venous blood flow between these two pathways would depend upon the relative resistance to flow of each system, which in turn would depend on the relative diameter of the smaller veins. There is evidence that cooled blood flowing through the venous sinuses ventral to the brain can cool that structure directly by heat exchange with the cerebrospinal fluid (*9*) and by a countercurrent mechanism that cools carotid arterial blood (*7*). This latter system is functional only in species with a carotid rete, a branching network of thin-walled arterioles coursing through venous blood (*7*). This structure is absent in the rabbit (*8*).

We propose that the buccal segment of the rabbit facial vein acts as a temperature-sensitive sphincter whose tone changes significantly with the temperature of the blood draining the nasal turbinates (Fig. 2). The data suggest that at average external temperature conditions, the tone of the facial vein sphincter is relatively low; therefore a sizable portion of the nasal blood courses through the external jugular system. When the ambient temperature rises, or for some other reason the nasal blood temperature is slightly elevated, the level of sphincter tone increases, shunting a great proportion of the nasal venous blood toward the large central sinuses. Cooled venous blood flowing into the pterygoid and ophthalmic sinuses effectively dissipates heat from the base of the brain in the rabbit (*9*). The direction of human blood flow in the angular vein of the eye changes with external temperature (*10*). When the external temperature is high, blood flows from the face toward the brain. Furthermore, changes in temperature in the region of the angular, ocular, and facial veins of the dog can be interpreted as suggesting the presence of a system that proportions blood flow between superficial and deep venous structures (*11*). Humans and dogs also lack a carotid rete (*7*).

One of the responses of the body to hypothermia is an increased sympathetic drive. In most veins where the α-adrenergic constrictor propensity is greater than the β-adrenergic dilator, this would result in venoconstriction (*5*), especially when, as in the facial vein, the adrenergic innervation is distributed throughout the thickness of the media. In the facial vein sphincter, however, increased sympathetic activity results in vascular smooth muscle relaxation, an effect similar to the direct effect of cooler blood. Thus the local and centrally mediated effects of hypothermia are complementary in this vessel.

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11 October 1979