A Study of Reflex Venomotor Reactions in Man

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By the use of simple clamps, a segment of a forearm vein was temporarily isolated from the circulation so that change in pressure within the segment measured change in venous tone. Reflex venoconstriction was elicited by appropriate stimuli. These reactions could be blocked by interruption of the sympathetic pathway to the vein under study. The magnitude of the responses obtained supports the concept that neurogenic venomotor reactions may be quantitatively significant in circulatory adjustments.

Considerations of cardiovascular adjustments are commonly concerned with the responses of the heart and arterioles with less regard for the remainder of the circulatory system. However, the larger part of the total blood volume lies within veins and the larger part of the venous system, including the splanchnic and superficial vessels, is provided with smooth muscle and with autonomic innervation. Thus, there is an anatomic basis for neurogenic venomotor tone and for reflex venomotor reactions which will affect the capacity of, or pressure in, an important segment of the circulatory system. Methods for measuring the contribution of the reactive veins to circulatory homeostasis are not at hand, but the potential importance of these vessels is apparent.

In animals, venomotor nerve fibers have been shown to be part of the sympathetic outflow, and veins have been found to participate in a number of circulatory reactions. In man, the demonstration of specifically venous reactions is difficult. Venous pressure cannot be accepted as a direct index of venous tone for it is also influenced by other factors, notably the competence of the heart, the state of the small vessel circulation and the total blood volume. Lewis and Landis observed that the veins in a sympathectomized extremity were larger than those on the unoperated side, the pressures being equal, and inferred that the removal of sympathetic innervation led to diminution in venous tone. The plethysmographic technic of Capps did not distinguish venous from capillary and small vessel responses. In a single subject, Doupe and co-workers were able to isolate a segment of forearm vein from the circulation. However, these investigators were able to demonstrate change in pressure in the segment only in response to a blast of cold air to the exposed body, and this response amounted to only 3 to 4 mm. of water.

This study was undertaken in order to demonstrate reflex reactions in an accessible venous bed, and to identify the efferent nervous pathway involved.

Materials and Methods

Eight subjects were found to have suitably long segments of forearm vein, without communicating vessels, which could temporarily be isolated from the circulation. These included five normal young men, ranging in age from 21 to 29 years; two men of 32 and 28 years, with normal cardiovascular systems, convalescent from peptic ulcer and pneumococcal pneumonia respectively; and a man of 54 years, an alcoholic, with nutritional deficiency.

Fisher Castaloy Versatile Clamps were applied to the forearm in such a fashion that a rubber stopper fitted to the single prong would occlude the vein on the volar aspect of the forearm when pressure was applied (fig. 1). It should be noted that the opposing prongs closed against the ulna so that the general venous return from the forearm was not compromised. Commonly, the vein selected was such that a valve maintained the compartment distally, so that only a single clamp was necessary. A 1 inch, 20 gage needle was inserted into the vein to be studied through a small procaine wheal at the

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distal limit of the compartment, and connected through a three-way stopcock with an infusion bottle of heparinized saline and a Sanborn electromanometer. Pressure within the vein and a pneumogram were simultaneously recorded on a Sanborn Polyvisocardiette.

The integrity of the venous compartment was tested before and after each procedure. It was assumed to be intact when there was no inflow from infusion bottle at a height of 1 meter above the vein. The initial pressure was found to be determined largely by the pressure applied externally to the vein by the occluding clamp, and was commonly of the order of 45 to 50 mm. Hg. It ranged from 36 to 60 mm. Hg with a mean value of 47 mm. Hg. Further, the responses were quantitatively variable in a given normal subject from day to day and from hour to hour, even though the external environment was kept essentially constant. These observations preclude use of the technic as a measure of an absolute level of venomotor tone. However, acute changes in tone are reflected by changes in pressure within such a segment, since the volume of contained blood remains constant.

The stimuli used were of a simple sort: inspiration against the resistance of pursed lips; immersion of the opposite hand in ice water for one minute; rebreathing of a 5 per cent carbon dioxide-95 per cent oxygen mixture from a standard Benedict-Roth machine, with the soda lime removed; and voluntary hyperventilation. No sedatives were used, except for 100 mg. of Seconal before stellate ganglion block. The effect of apprehension was observed on occasion. Procaine, 1 per cent, was used for perivenous and stellate infiltration. Tetraethylammonium chloride was given intravenously in a dosage of 7 mg. per kilogram of body weight.

**RESULTS**

1. **Inspiration Against Resistance.** Increases in pressure in the segment under study ranged from 4 to 24 mm. Hg.* This maneuver was used repeatedly and a venoconstrictor response was consistently obtained. The response was transient and served as a quick check on the integrity of the compartment, for general venous pressure falls during inspiration.

2. **Apprehension.** The effects of apprehension were observed fortuitously, usually when the subject was approached with ice water or a needle. The most impressive reaction was seen in a medical student who had had previous painful experiences with cold water (fig. 2).

3. **Immersion of the Opposite Hand in Ice Water** (fig. 2). Increases in pressure ranged from 7 to 44 mm. Hg. (See table 1.) It was our impression that the effective stimulus was pain rather than cold, although both stimuli may have been operative. Response was greatest

*The individual readings are shown in table 1.

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**Fig. 1.** Venogram demonstrating a suitable venous segment. A 12 cm. segment of forearm vein is shown to be free of communicating vessels by injection of contrast medium under pressure. For clarity, digital pressure was used for proximal occlusion.

**Fig. 2.** Change in pressure in isolated venous segment in response to apprehension and to immersion of the opposite hand in ice water.

**Table 1.** Increase in pressure, in millimeters of mercury, within isolated segment of vein in response to various stimuli. Each of the ice water and carbon dioxide studies was done during an individual period of occlusion and each had its own baseline level.
in those who experienced significant pain, least in those who were not much disturbed.

4. Rebreathing of 5 Per Cent Carbon Dioxide—95 Per Cent Oxygen Mixtures (fig. 3). Increases in pressure ranged from 7 to 52 mm. Hg. (See table 1.) In general, the venomotor response appeared slowly, becoming sharp only during the second or third minute. Comparable results were obtained by voluntary hyperventilation or by repeated inspirations against resistance. The stimulus was a useful one, but its physiologic significance was not established by these experiments.

5. Perivenous Infiltration with Procaine. Careful infiltration with procaine about the circumference of the vein just proximal to the segment being studied led to the disappearance of the above reactions in three of four subjects, and to nearly complete disappearance in the other.

6. Tetraethylammonium Chloride. Intravenous injections of tetraethylammonium chloride in a dose of 7 mg. per kilogram of body weight likewise blocked the reactions in three of four patients, and largely eliminated them in the other.

7. Stellate Ganglion Block. In one of three subjects, procaine block of the stellate ganglion eliminated the responses studied. However, significant responses persisted in the others, despite the appearance of Horner's syndrome, dilatation of the conjunctival vessels, and abolition of temperature gradient in the extremity.

**DISCUSSION**

Anatomically, the superficial forearm veins are less muscular than the veins of the lower extremity, and considerably less muscular than those of the splanchnic bed. The observation that even forearm veins are capable of producing pressure rises of the magnitude of 40 to 50 mm. Hg during isometric contraction suggests that the contractile power of the muscled veins is considerable.

The efferent neural pathway for the regulation of venomotor tone and venomotor reflexes has been found in animals to be a part of the sympathetic nervous system. Our observations point to a similar distribution in man. The reactions studied were blocked by the infiltration of procaine about the wall of the vein in the forearm, by the administration of an autonomic ganglionic blocking agent, and, though irregularly, by stellate ganglion block. The failure of stellate block regularly and completely to eliminate venomotor reflexes may be due to incomplete infiltration, or to the distribution of the sympathetic system in the upper extremity.

The importance of venomotor tone was indicated by the classic experiment of Goltz in 1864. Dilatation of the mesenteric veins of the frog in response to tapping brought about sequestration of so much blood in these vessels that the heart became bloodless and circulation ceased. So long as their nerve supply was intact, tone quickly returned to the veins, the heart filled, and circulation was restored.

A variable venomotor tone might then be useful in two fashions: in the accommodation of the capacity of the circulatory system to changes in blood volume, and as a factor in the regulation of cardiac output. Active venoconstriction will help to maintain blood pressure and blood flow in the presence of a lowered blood volume. Blood volume remaining constant, venoconstriction will tend to augment venous return and thereby cardiac output. As Landis and Hortenstine have pointed out, the heart represents the important "peripheral resistance" to venous flow. Insofar as the heart is incompetent, venoconstriction will be reflected by increased venous pressure.

Consideration of the function of neurogenic venomotor reactions requires certain qualifications. First, in the intact organism, venomotor reactions do not occur as isolated phenomena, but rather as part of integrated...
cardiovascular adjustments. Second, the innervated, muscled veins are in the circulatory system in parallel circuit with the veins of skeletal muscle in which capacity and pressure are determined largely by extraneous factors. Changes in one system may be opposed or aided by changes in the other. For instance, quiet standing may lead to hypotension and syncope due to inadequate venous return in subjects whose neural mechanisms are intact. If neural pathways are blocked, the effect of quiet standing is enhanced. Conversely, muscular exercise may alleviate the orthostatic hypotension produced by autonomic blocking agents. Further, veins are subject to humoral stimulation, and even muscled veins are relatively thin-walled and subject to external forces so that variations in intra-abdominal pressure, for instance, may influence the vessels of the important splanchnic system.

It is difficult to estimate the contribution of any single factor in circulatory adjustments. However, our observations of venomotor reactions of some magnitude in relatively poorly muscled veins suggest their potential importance elsewhere in the body.

In view of the effectiveness of tetraethylammonium chloride in blocking venomotor reflexes in these experiments, it is of interest that others have had to postulate an effect upon venomotor tone in order to explain certain actions of ganglionic blocking agents in man. Paton has pointed out that the effectiveness of methonium salts in maintaining a bloodless operative field can hardly be explained on the basis of arteriolar dilatation, but can readily be explained by sequestration of blood within relaxed venous reservoirs. Further, orthostatic hypotension due to the methoniums outlasts changes in the supine blood pressure and may be alleviated by exercise of the leg muscles, suggesting that the postural defect lies within the venous side of the circulation. Werko and co-workers have found that hexamethonium may produce a fall in cardiac output in association with diminished pulmonary vascular pressures and diminished cardiopulmonary blood volume. This again suggests relaxation of the systemic venous bed.

Summary

Reflex venomotor reactions of significant magnitude are demonstrated in the human subject. Evidence is presented that the efferent nerves mediating such reactions traverse the sympathetic nervous system, passing through autonomic synapses. Certain implications of neurogenic venomotor tone are discussed.

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Sumario Español

Por medio de pinzas sencillas, un segmento de vena del antebrazo se aisló de la circulación de manera que cambios en presión dentro del segmento comprendido determinan cambios del tono venoso. Vasoconstricción refleja se produjo con estímulos apropiados. Estas reacciones se pudieron bloquear mediante la interrupción de la enervación simpática a la vena bajo estudio. La magnitud de las respuestas obtenidas sostiene el concepto de que las reacciones neurogénicas venomotoras pueden ser cuantitativamente significativas en ajustes circulatorios.

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