Reflex Alterations in Venomotor Tone Produced by Venous Congestion

By Robert S. Alexander, Ph.D.

Changes in venous tone produced by partial occlusion of the thoracic inferior vena cava, or of the mitral orifice, have been studied in acute experiments on anesthetized dogs, employing distensibility diagrams obtained from injections into the veins of a loop of intestine to measure venous tone. The results demonstrate a reflex mechanism producing venous dilation in response to venous congestion which is mediated by vagal afferents and inhibition of sympathetic efferents.

A important requisite for circulatory homeostasis is the adjustment of vascular capacity to the blood volume so as to maintain normal blood pressures. The venous system should be expected to play a major role in this adjustment, since it comprises about seventy five per cent of the capacity of the vascular bed and since the dynamics of capillary-venous flow indicate that the venous musculature acts primarily to adjust capacity of the system rather than flow resistance through the system. Direct evidence that such capacity changes are actually involved in circulatory regulation is afforded by the observation of venous constriction in association with pressor reflexes and the demonstration of marked compensatory venoconstriction in response to hemorrhage.

This suggests that there might be some specific mechanism for adjusting venous capacity to venous load, comparable to the vaguely defined "volume receptors" which have been proposed as capable of initiating such adjustments. This possibility has been investigated in anesthetized dogs, using the distensibility technic for assessing venomotor tone and a reflex mechanism has been found which regulates venous capacity in response to changes in venous pressure.

METHODS

Dogs were anesthetized with sodium barbital (180 mg./Kg.) after morphine sedation. The circulation to an exteriorized loop of intestine was isolated with careful preservation of its nerve supply. Venomotor tone was measured by the venomotor index calculated from distensibility diagrams obtained by injections into the veins of this loop, as described in previous publications. In brief, this index was defined as the ratio:

\[
\frac{\text{volume required to raise pressure from } 20 - 30 \text{ cm.}}{\text{volume required to raise pressure from } 10 - 20 \text{ cm.}}
\]

Venoconstriction is indicated by an increase in this index and venodilation by a decrease. Between distensibility determinations, circulation of the loop was maintained through an external circuit supplied from a carotid artery and returning venous drainage to a jugular vein. A "T" connection in the carotid circuit was used for continuous recording of arterial pressure.

Acute congestion of the abdominal vena caval system was produced by a double lumen polyethylene catheter introduced by way of a femoral vein. The tip of one lumen of this catheter was enclosed by a balloon which was positioned just below the entrance of the inferior vena cava into the right atrium. The other lumen, which opened 5 cms. below the balloon, was connected with an optical membrane manometer for recording pressure within the abdominal vena cava. Distending the balloon with appropriate volumes of saline produced any desired elevation of pressure in the abdominal vena cava. It should be emphasized that the venous drainage from the test loop was led out externally to an open tube emptying into a funnel connected with a jugular vein. Venous drainage from the test loop therefore by-passed the region of venous congestion, so that there could have been no direct mechanical effect of the elevated venous pressure on the venous bed whose distensibility was measured.

To establish that partial occlusion of the inferior vena cava was exerting its action by producing congestion of the abdominal caval system rather than by the coincidental oligemia of the right heart and pulmonary circulation, a second series of experiments was conducted in which venous congestion was produced by stenosing the mitral valve.
was accomplished by the simple maneuver of invaginating the wall of the left atrium into the mitral orifice with the tip of the finger, the chest having been opened in the mid-line with the animal maintained on artificial respiration. In these experiments, venous pressures were recorded from a catheter placed either in the thoracic vena cava or in the right atrium.

Preliminary experiments revealed that either of these maneuvers tended to produce an intense venoconstriction associated with the precipitous fall in arterial pressure which resulted from acute reduction of venous return to the left ventricle. To minimize this fall in arterial pressure, a compensating reservoir was introduced into the femoral artery and elevated to a height equivalent to approximately 80 mm. Hg. The dog was initially allowed to bleed into this reservoir until the arterial pressure became stabilized at this level. The tendency for the arterial pressure to fall when a stenosis was produced was then largely offset by the automatic reinfusion of blood. To achieve pressure stabilization, an interval of at least two minutes was allowed after producing the stenosis before determining the venomotor index.

RESULTS

In all experiments employing inferior vena caval obstruction, the rise in inferior vena caval pressure was associated with a reduction of the venomotor index, indicating relative venodilation, provided the compensating reservoir prevented any serious fall in arterial pressure. Reproducibility of the effect is illustrated in figure 1, which shows the results of three complete cycles of elevating the caval pressure and returning it back to normal over a total time lapse of 60 minutes. This experiment was selected for illustration because it showed unusual stability of the control values throughout the period of observation. Other experiments exhibited some drift in the control values as the experiment progressed, but the relative lowering of venomotor tone with the rise in caval pressure was always evident.

Since venous drainage from the test loop bypassed the area of venous congestion, this change in venomotor tone must have been the result of a reflex mechanism. To explore the nature of this reflex further, a series of experiments were conducted as illustrated in figure 2. After an initial test recording in which caval pressure elevation evoked the typical fall in the venomotor index, the animal was given 2 mg. of atropine. It has been observed repeatedly in previous experiments that atropinization in itself has minimal effects on the control venomotor tone, indicating a dominance of sympathetic influences which are not susceptible to parasympathetic blocking agents. Furthermore, when caval pressure was elevated following the atropinization, the usual fall in venomotor tone persisted. This excludes parasympathetic efferents from making any significant contribution to the reflex fall in venomotor tone observed with caval
congestion. Finally, both vagi were transected in the neck. In the majority of these animals in which blood pressure had been lowered by bleeding into the compensating reservoir, vagal section evoked evidence of the Pavlov-McDowell depressor effect, illustrated by increased blood flow through the loop, significant drainage of blood from the compensating reservoir, and some fall in the control venomotor index. When, however, caval pressure was elevated following the vagotomy, an elevation of the venomotor index was observed (fig. 2). This elevation can be explained by the moderate fall in arterial blood pressure, acting through the carotid sinus to produce venous constriction. In no case could the venodilator effect of inferior caval obstruction be obtained after vagal section, even though in several experiments the compensating reservoir was elevated slightly so as to prevent any change in arterial blood pressure. The reflex response to inferior vena caval congestion therefore must arise dominantly from afferent fibers ascending in the vagus trunks.

It was of interest to measure blood flow in the test loop of intestine in order to ascertain whether the reflex response also involved changes in peripheral resistance. These measurements were made in five of the dogs studied and yielded results similar to those shown in the upper two plots of figure 2. Blood flow through the loops showed some reduction correlating with the small fall in arterial pressure associated with the caval obstruction. In no case was there any evidence of increased blood flow, signifying arteriolar dilatation, to correlate with the venous dilatation. These results should be stated with some reservation, since the flow measurements were made before blood flow through the loop was occluded for carrying out the distensibility determination, and the pressure changes produced by venous obstruction had not always completely stabilized. Prolonging the period of caval obstruction so as to achieve complete stability for both determinations was not practical because of the shock-inducing properties of venous obstruction. Nevertheless, we were not impressed with any reflex arteriolar effects produced by the venous congestion under the conditions of our experiments.

Acute obstruction of the inferior vena cava, in addition to producing congestion in the abdominal caval system, also results in oligemia of the right heart and pulmonary system. To exclude the possibility that the latter might be responsible for the observed change in venomotor tone, comparable experiments were carried out by producing obstruction at the mitral valve. Results of this procedure again showed a reproducible reduction in venomotor tone elicited by acute mitral stenosis, provided that the arterial pressure was reasonably well maintained.

Comparison of the results obtained by the two methods indicated that when inferior caval obstruction was produced in 23 experiments on nine dogs, the average fall in the venomotor index was .17 (S.D. ±.08); with mitral obstruction, 11 experiments in 4 dogs produced an average fall in the venomotor index of .15 (S.D. ±.05). In this limited series of experiments, there was obviously no significant difference between the two sets of results. However, the inferior vena caval obstruction produced an average pressure rise in the abdominal cava of 8.9 cm. saline, while the mitral obstruction produced an average pressure rise in the thoracic cava of only 1.8 cm. saline. Attempts to ascertain whether there might be some unique reflex effect arising from the pulmonary bed proved futile in this particular experimental analysis because of quantitative variability in the results. Data from any one series or even the same animal did not show any clear correlation between the magnitude of the measured reflex response and the degree of elevation of venous pressure. The major source of variability seemed to reside in the sensitive reflex responses to changes in arterial pressure, which could not be entirely prevented by our technique. This variability overshadowed any quantitative differences between the degrees of caval or pulmonary congestion and the associated venous dilatation.

DISCUSSION

Increase in venous return to the right heart with a concomitant rise in venous pressure acts to increase diastolic filling of the heart and hence increase cardiac output. Other
things being equal, an increased cardiac output would in turn increase systemic pressures and tend to augment venous return, thereby further augmenting cardiac output. There appear to be two mechanisms available to break this cycle. First and apparently most important are the buffer reflexes on the arterial side of the circulation, which respond to an elevation of arterial pressure by applying a brake to the heart and dilating the peripheral vascular bed, including the veins. A subsidiary mechanism is involved in the reactions here, whereby the rise in venous pressure associated with an increased venous return will in itself evoke some dilatation of the venous system and thereby minimize the venous pressure rise.

Quantitatively, the degree of venodilatation observed in these experiments was not great. This may in part relate to the experimental conditions in which the arterial pressure was purposely lowered at the outset in order to be able to compensate for the arterial effects of venous obstruction. Initial lowering of the arterial pressure evoked considerable venous constriction, as evidenced by the relatively high values obtained for the venomotor index in the control determinations. The reflex response to venous congestion, as superimposed on this, was a moderate lessening of the degree of venous constriction rather than a frank venous dilatation. It should be recalled, however, that in addition to this reflex venous dilatation, venous congestion in itself has a mechanical effect in dilating the venous system. Owing to what has been termed the "delayed compliance" of the venous system, maintained pressure elevation leads to a progressive increase in the volume of the venous bed. Reflex lessening of venomotor tone should act synergistically with this direct mechanical effect to increase the capacity of the venous system.

To our knowledge, there has previously been no specific description of a venous distension reflex of the type described here, but scattered reports in the literature are suggestive. Fleisch, for example, observed a biphasic response of the veins to vagal bradycardia. An initial constrictor phase was attributed to the arterial hypotension, while a subsequent dilator phase could have represented the reflex response to the concomitant venous congestion. The studies of Schwiegk give clear evidence of a depressor reflex elicited by pulmonary congestion, presumably making use of the afferent vagal fibers which are excited under such conditions. This depressor reflex response could include a venous dilatation as observed here with mitral obstruction, but it is of no assistance in explaining the response observed to caval obstruction.

The experiments with mitral obstruction were performed chiefly to exclude the possibility that the results with vena caval obstruction were not due to pulmonary oligemia. The fact that this technic appeared equally effective in lowering venous tone in spite of much less of an elevation in venous pressure could suggest that additional reflexes originating in the lungs were involved, a possibility that would be in accord with evidence of others cited above. Further investigations of this problem under better controlled conditions are needed to clarify this aspect.

Considerable caution must be exercised in transferring results in acute experiments over to the situation encountered in chronic venous congestion. It is obvious that a reduction in venous tone and hence increased venous capacity would be compatible with the plethora associated with chronic congestive heart failure. The observation that significant increases in blood volume may occur in cardiac patients with only slight increases in the resting venous pressure also suggests increased venous capacity. On the other hand, Burch has interpreted plethysmographic tracings from patients in severe heart failure as indicative of venous constriction. The concept of a dilated venous bed in the moderately well compensated cardiac patient giving way to venous constriction during bouts of acute decompensation could explain many clinical features of the disease, but further studies will be essential to clarify the balance of factors contributing to venomotor tone in the cardiac patient.

**Summary**

Measurements of venomotor tone in anesthetized dogs reveal a reflex mechanism capable
of dilating the intestinal veins in response to an elevation of pressure in the abdominal caval system. This reflex appears to be initiated by afferents ascending in the vagus nerve and to be effected by a reduction in the sympathetic tone to the venous musculature. Central congestion produced by mitral stenosis produces a similar response. Acting subordinate to the buffer reflexes on the arterial side of the circulation, these veno-venous reflexes would serve to adjust venous capacity to venous load so as to contribute to homeostasis in the vascular system.

**SUMMARIO IN INTERLINGUA**

Mesurationes del tono venomotor in canes anesthesiaste revela un mechanismo reflexe que es capace a dilatar le venas intestinal in responsa a un elevation del pression in le sistema caval abdominal. Iste reflexo es apparentemente inititate per afferentes que ascende in le nervo vage; illo es effectuate per un reduction del tono sympathetic al musculatura venose. Congestion central producite per stenosis mitral resulta in un simile responsa. Iste reflexos veno-venose age subordinatemente al reflexos tampon al latere arterial del circulation e servirea a adjustar le capacitate venose al carga venose lo que contribuere al homeostase in le sistema vascular.

**REFERENCES**


Reflex Alterations in Venomotor Tone Produced by Venous Congestion

ROBERT S. ALEXANDER

Circ Res. 1956;4:49-53
doi: 10.1161/01.RES.4.1.49

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/4/1/49

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/