Peripheral Venoconstriction During Acceleration and Orthostasis

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Active peripheral venous constriction has been demonstrated in dogs by a miniature balloon technic. The magnitude of the venoconstrictor response to acceleration on the centrifuge was strongly correlated with the animal's ability to maintain arterial pressure, suggesting the importance of contraction of the venous reservoir in the support of cardiac output under a hydrostatic load.

The organism exposed to gravitational or accelerative stress would find it advantageous if active venous constriction occurred in the dependent portions of the body. Since the veins contain 60-75 per cent of the total systemic blood volume,1 a relatively small per cent decrease in capacity of the venous reservoir could yield a considerable increase in the volume of the diastolic cardiac inflow and might contribute a great deal to the support of cardiac output and arterial pressure on the centrifuge or tilt table.2

There is indirect evidence that this venoconstriction may in fact occur. Sieker observed an elevation in central venous pressure after centrifugation and ascribed it to peripheral venoconstriction persistent after the hypotensive stimulus.4 Charlier has demonstrated a rise in right atrial pressure despite the increased cardiac output following bilateral common carotid artery occlusion,4 and Fleisch and Heymans have independently shown reflex alterations in the caliber of an isolated but innervated mesenteric vein segment in response to changes in pressure in the carotid sinus.6 More directly, Alexander has described a decrease in the distensibility of mesenteric veins accompanying a reduction in carotid sinus pressure.7 A reflex increase in pressure in an isolated forearm vein segment during tilting was noted by Page and associates.8, 9

To demonstrate reflex changes in peripheral venous tone in response to orthostatic stresses, we have employed a miniature intravascular balloon in dogs on the centrifuge.

**METHOD**

Adult mongrel dogs were anesthetized with chloralose, to avoid brain stem depression. An even plane of anesthesia was maintained by periodic small doses. A modification of the miniature balloon technic of Connolly and Wood10 was utilized. The lesser saphenous vein was exposed through a short incision near the lateral malleolus, and a miniature latex balloon was inserted and threaded proximally about two inches until its tip lay in an untraumatized portion of the vein. The stylet was removed, and after insertion of a blunt needle into the stem of the balloon the system was filled with water and connected by a fluid-filled polyethylene tube to a Statham pressure transducer and an oscillograph using photographic recording. Since the pressure within the inflated balloon was a function of hydrostatic pressure in the vein as well as the tone of the vessel wall, venous pressure at an equivalent point was measured through a catheter in the greater saphenous vein in the same leg. By placement of the strain gages for balloon and venous pressure at the same level relative to the dog, the necessity for hydrostatic corrections was avoided. A catheter was placed in the femoral artery of the opposite leg for arterial pressure measurements. Placement of the arterial pressure transducer at the level of the mastoid process allowed direct recording of blood pressure at head level during centrifugation. The animal was then strapped securely into a frame and placed in the feet-out ("positive G") position on the centrifuge.

The technic described by Connolly and Wood in 1954 employed an overvulcanized flaccid inelastic balloon inflated to only 30 mm. Hg in the dorsal hand veins of man. Their system responded faithfully to changes in venous pressure, but venoconstriction obvious to the eye in response to cold was not registered by their balloons. The failure of the technic to demonstrate a venoconstrictor response was explained by the authors as due either to the passive, unconstricting nature of veins or to their loss of the ability to constrict in the presence of an intraluminal irritant, i.e., the balloon. Neither interpretation seemed tenable in view of the observed decrease in size of the hand veins with cold despite a venous tourniquet around the forearm. An explanation which appeared more likely to us was that their
flaccid balloon simply changed in shape rather than pressure in response to a change in the diameter of the vein containing it. Accordingly, we have used an elastic balloon inflated till turgid, filling the lumen of the vein at its tip.

In vitro studies utilizing U-tubes filled with water or mercury of varying column height or filled with a constant column of water and centrifuged at varying G demonstrated that when our elastic balloons were initially inflated to 80-160 mm. Hg, the initial pressure in the balloons had no effect on the increment of pressure rise with a given change in hydrostatic pressure around the balloon. The change in balloon pressure in response to a constant increment in external pressure was linear over wide limits. On theoretic grounds, therefore, an elastic turgid balloon appeared suitable for an assessment of the pressure around it, the components of which were the tone of the vessel wall and the hydrostatic head.

For validation of the technic in vivo, we have observed the response to local and intravenous sympathetic mimetic drugs and to direct faradic stimulation of the lumbar sympathetic chain. Venoconstriction was recorded as an increase in pressure in the balloon in the absence of, or in excess of an increase in hydrostatic pressure at the same level. In addition, since contraction of the vessel wall was prevented by Dibenzyline, a potent adrenergic blocking agent, the difference in the balloon's response to various experimental procedures before and after the intravenous administration of the drug was a function of the degree of contractility of the vein wall, hydrostatic pressure being relatively unaltered, and it furnished a semiquantitative estimate of the magnitude of the venoconstrictor response. Intravenous epinephrine (1 mg.) or norepinephrine (0.1-0.3 mg.) given in 22 dogs consistently elevated balloon pressure from 2-23 mm. Hg with no equivalent change in venous pressure. This effect was not demonstrated after Dibenzyline was given. A reversal of the normal constriction response to epinephrine was frequently seen after Dibenzyline, as the vasodilating action of the sympathetic mimetic amine was unmasked by the adrenergic block. A rise in balloon pressure was also seen after local application of Aramine to exposed vein segments containing the balloons. In 3 experiments, direct electric stimulation of the lumbar sympathetic chain was performed and was followed by a prompt balloon pressure rise with little or no change in venous pressure in the area.

Results

Twelve animals have been studied on the centrifuge. Each dog was given 2 types of runs, 1 in which a peak of 3 G was reached in 3 to 4 sec. and held for a 15 sec. plateau, the other in which the acceleration was gradually increased at the rate of 1 G/10 sec., the end point being arbitrarily taken as the G level at which mean arterial pressure at head level reached 0. The gradual onset run allows time for maximum reflex protection to come into play from the beginning of the hydrostatic stress and in humans has been shown to add an average of 1.9 G to the individual's relaxed blackout threshold. Each animal was then given 3 mg./Kg. Dibenzyline intravenously and after a 30-45 min. wait for the drug to manifest its full effect, the 2 centrifuge runs were repeated.

A typical set of records for the rapid onset runs is shown in figure 1. The difference in magnitude of the rise in balloon pressure at the same G before and after Dibenzyline is illustrated here. This difference varied from animal to animal, with a maximum of 72 per cent of the rise in balloon pressure in the control. The rise in peripheral venous pressure after Dibenzyline was only a few mm. Hg less than in the control. The arterial pressure at head level fell to a minimum shortly after reaching peak G and began to rise again a few seconds later, generally 6-8 sec. after the onset of acceleration. By the end of the 15 sec. constant G period, considerable reflex recovery of arterial pressure had usually occurred. As the centrifuge slowed, the arterial pressure value...
often showed a transient overshoot before it returned to the baseline. After Dibenzyline was administered, reflex recovery of arterial pressure was not seen during the run, and no overshoot occurred after the run. In general, those dogs which demonstrated the greatest difference in their balloon pressure responses before and after Dibenzyline also showed the greatest degree of arterial pressure recovery in their control runs.

Figure 2 is a set of records from the gradual onset runs of the same dog shown in figure 1. Taking 0 arterial pressure at peak G as an arbitrary end point, the difference in tolerance to acceleration before and after Dibenzyline is illustrated. The rise in balloon pressure at peak G after Dibenzyline was compared with the rise at the same G value in the control, and the difference was taken as a function of the venoconstrictor response in the control. Values ranged from 0 to 34 per cent of the balloon pressure rise in the control in 11 dogs studied. No records of the gradual onset runs of the twelfth dog were available, because of a technical error. The arterial pressure generally fell more rapidly after Dibenzyline than in the control. The relation of the fall in arterial pressure at the same G before and after adrenergic block was expressed as a ratio. In general, those dogs showing the greatest venoconstrictor response in the control runs also showed the greatest difference between their fall of arterial pressure before and after Dibenzyline.

In addition, several dogs showed isolated findings qualitatively suggestive of venoconstriction. Occasionally an abrupt rise in balloon pressure was seen shortly before the onset of reflex arterial pressure recovery. In a few animals, a prolonged elevation of balloon pressure was noted following the control runs but was not observed after Dibenzyline was administered.

A few dogs were studied on the tilt table, but here the results were less clear-cut, perhaps because the circulatory stress and the stimulus to baroreceptors was less severe than on the centrifuge. One animal demonstrated a rise in balloon pressure immediately preceding a recovery of arterial pressure; this response was eliminated by Dibenzyline. In a few instances, an elevation of balloon pressure persisted after return to the horizontal in the control but was blocked by Dibenzyline.

**DISCUSSION**

No conclusions have been based on data derived from the downslope of the balloon pressure curves, since stress relaxation in the balloon as the external pressure is reduced interferes with precise assessment of the course of venous relaxation.

To quantitate the magnitude of the venoconstrictor response to centrifugation, we have taken the difference between the rise in pressure in the intravenous balloon at the same G before and after the administration of Dibenzyline. This is expressed as a fraction of the increment in balloon pressure in the control run. Since the elevation of hydrostatic pressure around the balloon is only slightly less during a centrifuge run after adrenergic block than before, the diminished pressure rise in the balloon after Dibenzyline must be a function of the altered behavior of the local vein wall, i.e., the failure of venoconstriction.

In each dog, the degree of venoconstriction in response to positive acceleration of rapid onset is well correlated with the degree of recovery of arterial pressure measured at head level (fig. 3). A similar relationship is demonstrable in the gradual onset centrifuge runs (fig. 4). Here the behavior of the arterial pressure is described as the ratio of the fall in pressure at peak G after adrenergic block to...
the fall in pressure at the same G value in the control. The greater the numerical value of this ratio in each animal, the greater the effect on the blood pressure of a block at the neuro-effector junction and, by inference, the greater

\[ 10^{-80} \]

**VENOC0MSTR1CTOR RESPONSE**

**RESPONSE**

**OF CONTROL iALLCO**

**FftEtME  70 INCREMENT**

\[ 60 \]

\[ 30 \]

\[ 40 \]

\[ 30 \]

\[ 20 \]

\[ 10 \]

**0**

\[ 20 \]

\[ 200 \]

\[ 162 \]

\[ 171 \]

\[ 92 \]

\[ 141 \]

**Fig. 3. Rapid onset runs. Correlation of the venoconstrictor response with recovery of arterial pressure, expressed as per cent of the initial blood pressure fall. The coefficient of correlation is 0.88, which is highly significant.**

**Fig. 4. Gradual onset runs. Correlation of the venoconstrictor response (ordinate) with the relative fall in arterial pressure at the same G before and after Dibenzyline. The coefficient of correlation is 0.91, which is highly significant.**

**Fig. 5. Time-G tolerance curve for the average relaxed human subject. The delayed recovery after an initial period of low tolerance may be a consequence of peripheral venoconstriction. Ordinate, G units; abscissa, time in sec.**

**BLACKOUT**

The relative influence of the peripheral vasculature in the support of arterial pressure in the control.

The correlation of venoconstriction with the maintenance of arterial pressure on the centrifuge has significant applications. It furnishes a link between arteriolar and venous tone and supports the thesis that in certain situations the two may behave in a parallel fashion, probably in response to the same central governing mechanism.\(^{12}\)

In addition, it emphasizes the importance of the venous system in the maintenance of cardiac output and, thus, of arterial pressure under a hydrostatic load. The classic curve of G-tolerance vs. time (fig. 5) shows a tardy recovery coincident with the delayed climb of arterial pressure at head level, which is difficult to explain purely on the basis of the rise in peripheral resistance from arteriolar constriction. Heymans,\(^{13}\) Dawson,\(^{14}\) and others have shown the lag in arteriolar constriction following carotid occlusion or direct sympathetic stimulation to be only 1–3 sec.; yet the blood pressure rise here is delayed till 6–8 sec. after the onset of acceleration and 4–6 sec. after reaching peak G in a run of rapid onset. The lag period might well be the time required for blood squeezed out of the contracting venous reservoir to reach the left heart and aorta.
VENOCONSTRICTION DURING ACCELERATION AND ORTHOSTASIS

The protection afforded a centrifuge subject by the gradual onset of acceleration is closely correlated with the degree of protection he obtains from an Air Force anti-G suit. Since a principal effect of the anti-G suit is the prevention of blood pooling by venous compression, it appears that the gradual application of G force allows the body to perform this same function reflexly.

A more precise evaluation of the role of active venoconstriction in the support of arterial pressure awaits the development of a technic for the continuous recording of cardiac output during orthostasis and acceleration.

SUMMARY

A miniature balloon technic for demonstrating active constriction of peripheral veins was validated by in vitro studies and by observing the responses to sympathomimetic drugs and to direct stimulation of the lumbar sympathetic chain. By eliminating the constriction with Dibenzyline, an adrenergic blocking agent, the semiquantitative interpretation of results was made possible.

Active venoconstriction was observed in dogs exposed to acceleration on the centrifuge. The magnitude of the venous response in each animal was well correlated with the animal’s ability to maintain its arterial pressure at head level. These findings were interpreted as evidence for the role of contraction of the venous reservoir in the support of the cardiac output under a hydrostatic load.

ACKNOWLEDGMENTS

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ADDENDUM

Subcutaneous tissue tension adjacent to the intravenous balloon was recorded in 3 additional dogs on the centrifuge. Dibenzyline produced no reduction in the effect of acceleration on tissue tension. These findings are consistent with our hypothesis that the decreased balloon pressure rise seen after adrenergic block was a function of venoconstriction eliminated by Dibenzyline.

SUMARIO IN INTERLINGUA

Un technica usante un ballon de dimensione minuscula pro le demonstration de constriction activa de venas peripheric esseva validate per studios in vitro e per le observation de responsas a drogas sympathomimetic e al stimulation directe del catena sympathetic lumbar. Per eliminar le constriction per medio de Dibenzyline, un agent de bloacage adrenergic, le interpretation semi-quantitative del resultatos esseva rendite possibile.

Venoconstriction esseva observe in canes exponite a acceleration per le apparato centrifuge. Le magnitude del responsa venose in cata un del animales esseva ben correlationate con le capacitate del animal de mantener su pressure arterial al nivello del capite. Iste constatazioni esseva interpretate como demonstration del rolo de contractiones del reservoir venose como supporto del rendimento cardiac sub un carga hydrostatic.

REFERENCES

Pressure-Flow Relations in the Portal Hepatic Vessels

It has become apparent in recent years that pressure-flow (P/F) curves determined by progressive increase and decrease in pressures differ owing either to changes in vascular tone or, more probable, to plastic changes in vascular walls that Alexander has called *reduction*. Furthermore, the pattern of P/F curves show marked difference in such organs as the hind legs (Green and associates), kidney (Selkurt), lungs (Wagner, Wezler, Edwards) and the mesenteric venous tributaries of the portal vein (Alexander). Now, Riecker has added characteristics P/F curves for the portal intrahepatic circuit.

The curves show that when portal pressure is steadily increased, P/F relations are not linear up to pressures of 13 cm. H₂O, indicating that intrahepatic resistance decreases markedly. With progressive reduction of pressures the curves have an entirely different pattern depending, among other factors, on the time vessels remain stretched by higher pressures. Vasconstriction induced by anoxia or injection of epinephrine, not only increases resistance but reduces their passive distention by increasing pressures and raises the "closing pressure."

Among important conclusions are: (1) Portal resistance is only about \( \frac{1}{2} \) that of the dog's hind limb; (2) Equivalent increases in portal and femoral pressures augment hepatic flow 38 times as much as in the leg.

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