Changes in Central Venous Pressure after Moderate Hemorrhage and Transfusion in Man

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Changes in central venous pressure were recorded continuously before, during and for 40 to 50 minutes after hemorrhage and transfusion in the amounts of 6.5 cc. per Kg. and 8.1 cc. per Kg. The pressures obtained 15 to 20 minutes after onset of blood volume changes were independent of the rate of hemorrhage or transfusion. In the average subject of 70 Kg., \( \Delta P/\Delta V \) for zero time was 0.7 cm. of water pressure change per 100 cc. volume change. Recovery from hemorrhage was imperceptible during the one hour observation period, but recovery from transfusion was slightly faster.

With moderate hemorrhage or transfusion, it has been shown in animals that the pressures at all locations from the great veins to the left atrium change in unison and by approximately the same amount. Human studies also suggest that these volume-conditioned pressure changes are of approximately the same magnitude throughout the low-pressure system and that the changes may persist for a period of time. The general opinion, however, as recently reviewed by Landis and Hortenstine, maintains that the venous pressure is regulated in much the same way as arterial pressure; with hemorrhage, for example, peripheral vasoconstriction, particularly venoconstriction, quickly restores the central venous pressure. It is the purpose of this paper to investigate the degree of central venous pressure change associated with relatively small alterations in total blood volume and to determine the length of time the pressure changes persist.

METHOD

In 12 male subjects, 25 to 44 years of age, changes of central venous pressure were recorded continuously during and for 40 to 50 minutes following hemorrhage or infusion of 400 to 600 cc. of blood. The change in central venous pressure was recorded from a vein in the right arm by the method previously described. With a paper speed of 0.2 mm./sec. the recording camera photographed a band, the width of which was determined by the pulsatile and respiratory oscillations of the venous pulse. The mean pressure was derived by planimetry from interspersed fast records taken at a camera speed of 25 mm./sec. The arterial pressure was recorded simultaneously from a radial or brachial artery by an indwelling needle attached to a Statham pressure transducer. Following a 20 to 40 minute rest period a control record of the venous pressure was obtained for seven to eight minutes. A no. 15 needle was then introduced into the vein of the antecubital space of the left arm. At the end of a 10-minute control recording period, bleeding of 400 to 475 cc. was started into a commercial blood donor bottle. The time taken for the venesection varied between 4 and 15 minutes and venous pressure was recorded during the bleeding and for the following 40 to 50 minutes. The blood was stored and after a period of 4 days, using the same technics, was rein infused in 8 to 12 minutes together with the anticoagulant dextrose solution in the bottle which made a transfused volume of about 600 cc. The venous pressure was continuously recorded as in the bleeding experiments.

RESULTS

Figure 1 is an example of a transfusion experiment. A total of 550 cc. blood was injected within nine minutes, and during the first five minutes with a constant rate of infusion, the venous pressure increased in a linear fashion. When the infusion was stopped the pressure made a sharp decline, but did not return to the control value, and within the next ten minutes

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maintained a new higher level. The record sample of the last 10 minutes of the experiment indicates that the pressure was still approximately 3 cm. of water above the control value. There was no substantial change of arterial pressure with the transfusion. Bleeding experiments showed almost a mirror image of this pattern.

Figure 2 is a summary of the pressure changes observed in 12 bleeding and 10 infusion experiments. Three sets of repeat experiments were done about 6 months apart. The control venous pressures which varied between 2.5 and 12.9 cm. water have been superimposed in one point. The various points therefore indicate pressure changes (ΔP) as a function of time (t) for a given volume change (ΔV). The pressures in figure 2 have not been corrected for different weights of the subjects and variations in blood volume changes which were, due to circumstances, not always exactly 475 cc. for the bleeding and 600 cc. for the transfusion. The subjects represented a rather homogeneous group, and the basic character of the adjustment of central venous pressure to the volume changes can clearly be seen in spite of the somewhat exaggerated scatter. If the volume was changed at a rate not exceeding 50 cc. per minute, the new pressure levels were reached without overshoot. The pressure level observed 15 to 20 minutes after the beginning of hemorrhage or transfusion appeared to be independent of the rate of the blood volume change. During the ensuing observation period the pressures showed only a slight return toward the control value. The equation of the regression line for the hemorrhage of 6.5 cc./Kg. is

$$\Delta P_h = -3.23 + 0.0005 \cdot t$$

and for the infusion of 8.1 cc./Kg. is

$$\Delta P_i = +3.85 - 0.0265 \cdot t$$

As indicated by the arrows in figure 2, these regression lines intercept the ordinate (t = 0) at

$$\Delta P_h = -3.23 \text{ cm. H}_2\text{O}$$

$$\Delta P_i = +3.85 \text{ cm. H}_2\text{O}$$

It is noteworthy that the ratios of the pressure changes and the induced volume changes are almost identical:

$$\frac{\Delta P_h}{\Delta P_i} = 0.84 \quad \frac{\Delta V_h}{\Delta V_i} = 0.80$$
This fact, together with the observation of a linear change of pressure during constant rates of infusion (fig. 1), suggests a linear relationship between blood volume and venous pressure under the condition of our experiments (fig. 3).

By solving the equations for $P = 0$ we find the times ($t_H$ and $t_I$) necessary for the pressures to return to normal after hemorrhage or infusion:

$t_H = 107$ hours  $t_I = 2$ hours 26 minutes

These figures are only valid under the assumption of a constant control level of venous pressure. However, in control recordings lasting 10 to 40 minutes a continuous fall of venous pressure of 5 to 10 mm. water per hour was usually observed. This slightly sloping base line, as indicated in figure 2 by the dotted line, intercepts the regression line for hemorrhage sooner, and the regression line for infusion later, than the
above figures of 107 hours and 2 hours 26 minutes indicate. These figures, therefore, represent the minimum recovery time from infusion and the maximum recovery time from hemorrhage as determined by the regression lines.

In order to establish the pressure-volume relationship in greater detail, regression lines were calculated for each subject from the points in figure 2 and the pressure at zero time plotted against the individual volume changes per Kilogram of body weight. As shown in figure 3, the mean venous pressure change with infusion or hemorrhage was 0.49 ± 0.12 cm. of water for 1 cc. of blood volume change per Kilogram of body weight. In a man of 70 Kg., a blood volume change of 1000 cc. will induce a pressure change of 7.0 cm. of water. The volume elasticity coefficient for the total circulation of a 70 Kg. man is therefore

$$E' = \frac{7.0 - 981 \text{ dynes}}{1000 \text{ cm.}^5} = 7 \text{ dynes/cm.}^5$$

**DISCUSSION**

In contrast to the wide variations in absolute venous pressure (2.5–12.9 cm. H$_2$O) observed in normal human subjects, the relative constancy of the volume elasticity coefficient is remarkable. This constancy together with the prolonged recovery time for pressure changes induced by moderate volume alterations question the existence of a very alert venomotor mechanism for the maintenance of a constant central venous pressure when small blood volume changes are induced.

It has been shown in chloralosed dogs that moderate blood volume changes are accompanied by persistent pressure changes in the central veins, and almost identical changes of mean pressure in the pulmonary arteries and the left atrium. Whether this relationship is purely passive or is controlled by the heart is irrelevant to this discussion. From the point of view of pressure-volume relationships the extraarterial circulation reacts to volume changes like a system of interconnected elastic bags. Although the physical properties of all compartments contribute to the overall volume elasticity coefficient, the final pressure will be greatly influenced by the most distensible compartments which absorb the greatest portion of the volume change with the least change of pressure. Glaser and McMichael's estimate that in a simple blood transfusion approximately 50 per cent of the infused volume can be accounted for in the pulmonary bed and the heart. Sjostrand's figures, collected under more extreme conditions, showed that up to 80 per cent of induced volume changes may be handled by the intra-thoracic blood spaces. The changes in central venous pressure therefore observed in our experiments reflect to a large degree the elastic properties of the intra-thoracic circulatory organs.

Although the elasticity of the arterial system theoretically contributes to the pressure-volume relationship of the total circulation, it has to be ruled out as a potential reservoir. The arterial volume elasticity coefficient can be estimated from the pulse pressure (40 mm. Hg) and the systolic uptake (40 cc.) to be 1 mm. Hg/1 cc. blood or

$$1.36 - 981 \text{ dynes/cm.}^2$$

and is approximately 1400 dynes. This figure as compared to 7 dynes/cm.$^4$ for the total vascular bed, indicates the arterial resistance to stretch is 200 times greater than that of the total circulation. Therefore with infusion of 500 cc. the arterial system can only accept 2 to 3 cc. while the bulk of the volume is accommodated in the low pressure system.

It should be emphasized that the linear relationship between blood volume and central venous pressure can only be expected under resting conditions and with moderate volume changes. The example of subject D.S. who experienced presyncope during a bleeding experiment showed that with stress the venous pressure is no longer a linear function of volume. This observation may also help to explain the discrepancy between our results and earlier experiments in which as a rule considerably greater volume changes were induced and no persistent change in venous pressure was noted.$^8,9$

The moderator effect on venous pressure, so clearly visible after fast changes of blood volume (fig. 2) may be the expression of a redistribution of blood between the systemic veins.
and the pulmonary and splanchnic beds. It may also be due to a redistribution of extra-cellular fluid caused by the initial, fleeting change of venous pressure and hence of the effective filtration pressure in the capillaries. How much the equilibrium, attained through these possible mechanisms, is modified by a readjustment of vascular tone, as observed in isolated vascular beds cannot be derived from these experiments. Following the preliminary fast adjustments the pressure returned only very slowly toward the control level, suggesting that the homeostatic mechanisms involved did not aim for constancy of central venous pressure, but that the return to normal pressure was achieved by a rectification of the volume. From this point of view, the much faster recovery from transfusion than from hemorrhage should be expected under the conditions of our experiments. Thirty minutes to two hours after removal of 760 to 1040 cc. of blood, the plasma volume is reported to be increased only by 145 to 230 cc, but the loss is probably completely replaced in 72 hours. Although the question of the exact recovery times from moderate changes of blood volume cannot be answered accurately, they are in the order of several hours. The concurrent imbalance of volume and pressure in the intrathoracic region may therefore constitute the long lasting adequate stimulus not only for a volume regulatory mechanism effecting renal function, but also for other circulatory adjustments pertaining to changes in blood volume and its distribution which cannot be explained through the arterial homeostatic reflex mechanism alone.

SUMMARY

Changes of central venous pressure were recorded in 9 normal male subjects bled 6.5 cc. per Kg. and infused 8.1 ml per Kg of blood. The pressure changed by 0.49 ± 0.12 cm H₂O/ml/kg or approximately 0.7 cm H₂O per 100 ml of blood in a 70 Kg subject. After an initial fast recovery phase, the pressures returned slowly to the control value, but remained altered during the 50-minute observation period. The results indicate that with moderate changes of blood volume, the low pressure system reacts like a distensible container. The persistent changes of volume and pressure may serve as the adequate stimulus for regulatory mechanisms pertaining to changes of blood volume.

SUMMARIO IN INTERLINGUA

Alterationes del pression venose central esseva registrate in 9 masculos normal, post sanguination de 6,5 ml per kg de peso corporee e infusion de 8,1 ml per kg de peso corporee. Le pression cambiava per 0,49 ± 0,12 cm H₂O/ml/kg o circa 0,7 cm H₂O per 100 ml de sanguine in un individuo de 70 kg de peso corporee. Al initio il habeva un phase de recuperation rapide; postea le pressiones retornava lentemente verso le valores de controlo; sed perdurante le 50 minutas del periodo de observation illos remaneva alterate. Le resultatos indica que con moderate alteraciones del volumine de sanguine, le basse persistente alterationes de volumine e pression pote servir como stimulos adequate in le mecanismo regulatori relative al alterationes del volumine de sanguine.

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Thus Spoke Lavoisier

"When we begin the study of any science, we are in a situation, respecting that
science, similar to children; and the course by which we have to advance, is precisely
the same which Nature follows in the formation of their ideas . . . . He who enters upon
the career of science, is in a less advantageous situation than a child who is acquiring
his first ideas. To the child, Nature gives various means of rectifying any mistakes he
may commit respecting the salutary or hurtful qualities of the objects which surround
him."

"In the study and practice of the sciences it is entirely different; the false judg-
ments we may form neither affect our existence nor our welfare; and we are not com-
pelled by any physical necessity to correct them. Imagination, on the contrary, which
is ever wandering beyond the bounds of truth, joined to self-love and that
self-confidence we are so apt to indulge, prompt us to draw conclusions which are not
immediately derived from facts; so that we become in some measure interested in de-
ceiving ourselves. Hence it is by no means surprising, that, in the science of physics
in general, men have so often formed suppositions, instead of drawing conclusions.
These suppositions, handed down from one age to another, acquire additional weight
from the authorities by which they are supported, till at last they are received, even
by men of genius, as fundamental truths."

"The only method of preventing such errore from taking place, and of correcting
them when formed, is to restrain and simplify our reasoning as much as possible . . . .
We ought, in every instance, to submit our reasoning to the test of experiment, and
never to search for truth, but by the natural road of experiment and observation."

"Thoroughly convinced of these truths, I have imposed upon myself, as a law, never
to advance but from what is known to what is unknown; never to form any conclu-
sion which is not an immediate consequence necessarily flowing from observation and
experiment; and always to arrange the facts, and the conclusions which are drawn
from them, in such an order as shall render it most easy for beginners in the study of
chemistry thoroughly to understand them."

Extract from Preface, — A. L. Lavoisier: Elements of Chemistry.
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