Effective Compliance of the Total Vascular Bed and the Intrathoracic Compartment Derived from Changes in Central Venous Pressure Induced by Volume Changes in Man

By Martin Echt, Johannes Düwel, Otto H. Gauer, and Lothar Lange

ABSTRACT

In eight male subjects the blood volume was changed (± 10%) by hemorrhage and transfusion. One cycle of blood infusion and withdrawal or hemorrhage and reinfusion was completed within 9 minutes. The effective compliance of the total circulation was calculated from the changes in central venous pressure recorded simultaneously with the changes in blood volume. The effective compliance was 2.3 ml/mm Hg kg⁻¹ body weight. This procedure was repeated while the capacity of the circulatory system was restricted by infusion of norepinephrine (15 μg/min), lower body positive pressure, or both. The compliance values thus obtained were: norepinephrine 1.7 ml/mm Hg kg⁻¹ body weight, lower body positive pressure 1.2 ml/mm Hg kg⁻¹ body weight, and both norepinephrine and lower body positive pressure 0.9 ml/mm Hg kg⁻¹ body weight. The effective compliance of the intrathoracic vascular bed was assumed to be between 1.2 ml/mm Hg kg⁻¹ body weight (lower body positive pressure) and 0.9 ml/mm Hg kg⁻¹ body weight (norepinephrine and lower body positive pressure). These values constitute 55% and 42% of the effective compliance of the total circulation, respectively.

KEY WORDS lower body positive pressure hemorrhage transfusion intrathoracic vascular bed blood volume peripheral venous pressure norepinephrine

In the overall regulation of the circulation, the filling pressure of the heart plays a crucial role because it regulates cardiac performance (1) and originates reflexes influencing peripheral vascular tone (2) and kidney function (3). For volume regulation, a well-defined correlation must exist between blood volume and filling pressure of the heart (1, 3). When the heart is not beating, the central venous pressure is the same as pressures in other parts of the circulation: it rises and falls with changes in blood volume, allowing the compliance, ∆V/∆P, of the total system to be determined (4, 5). As the present experiment demonstrates and as previous studies (6, 7) have shown, a similar relationship between blood volume and central venous pressure can also be established when the heart is beating. In this case, the pressure change in the central veins is not entirely due to the elastic properties of the vascular bed. Secondary effects of blood volume changes on arterial hemodynamics and venous tone may contribute to changes in central venous pressure; therefore, the term “effective compliance” is preferable for describing the correlation.

In the anesthetized dog, a linear relationship between right and left atrial pressures and blood volume has been established (6). Plotting changes in right atrial pressure against changes in blood volume has shown that the volume elasticity coefficient of the total human circulation is 7 dynes/1000 ml, which corresponds to a compliance of 2.7 ml/mm Hg kg⁻¹ body weight (7). These results were obtained from subjects in the lateral decubitus position, and pressure was recorded from a vein in the dependent arm (8). In view of the importance of the compliance of the intact circulation, the experiments were repeated recording right atrial pressures with the catheterized subject in the standard prone position. Effective vascular compliance was also measured during norepinephrine infusion. Furthermore by the use of a pressure box to neutralize the distensibility of the vascular bed of the lower body, it was possible to estimate the compliance of the intrathoracic compartment, which is functionally the most important section of the low-pressure system.
**Methods**

The subjects were eight healthy male students (24.5 ± 2.6 years old) who had consented to the experimental procedure. Their mean body weight was 66.3 ± 8.9 kg, and their mean height was 175 ± 5.6 cm. The subjects reclined in a wooden box (135 × 55 × 45 cm), which enclosed the lower body up to the processus xiphoideus sterni. Constant pressure was maintained in the box at various levels between 0 and 60 mm Hg for various durations by an air compressor and an overflow pipe in a water tank. A polyethylene catheter (1.5 mm, o.d., 1 mm, i.d.) was introduced into the antecubital vein of the left arm and advanced to the right atrium. The central venous pressure was recorded with a Statham P23BB strain gauge and with electronic damping. A comparison between the planimetric means of the undamped central venous pressure and those of the damped central venous pressure showed differences of less than 0.1 mm Hg. The peripheral venous pressure was measured with a Statham P23BB strain gauge via a polyethylene catheter in a vein in the distal third of the left forearm. An imaginary line above and parallel to the experimental table and at one-third of the distance between the anterior chest wall and the table was used as a base line for the Statham strain gauge. The largest vein of the right cubital fossa was punctured by a Braunula (2 mm, i.d., Braun Melsungen Inc., Germany) for infusion and bleeding. The arterial blood pressure was monitored by the Riva-Rocci method. The heart rate was counted from the R waves of the electrocardiogram. An eight-channel dynograph was used for recording.

Plasma volume was determined by the dye-dilution method with Evans blue dye. Total blood volume was calculated from the plasma volume and the hematocrit; the mean blood volume of the subjects was 5136 ± 537 ml.

Forearm venous tone was measured to estimate capacitance changes in the venous system within the first 5 minutes after moderate expansion and diminution of the blood volume. Venous occlusion plethysmography was applied at the left forearm. Forearm volume was measured with a mercury strain gauge, and venous pressure was recorded simultaneously in a skin vein in the distal third of the forearm. The volume elasticity coefficient ($E'_v$) determined at an intravenous pressure of 15 mm Hg was used as a measure of venous tone. Details of the technique employed in this study have been described previously (9).

**EXPERIMENTAL PROCEDURE**

The experiments were started after the subjects had adapted to a room temperature of 25 ± 1°C; adaptation was indicated by a constant temperature of the finger tip of 34 ± 1°C. To have blood available for expansion of blood volume, 500 ml of 6% dextran solution (Macrodex) was infused within 3 minutes, and an equal volume of blood was withdrawn 10 minutes later. Thus the blood volume of the subjects returned approximately to the control value. It was assumed that the slight capillary inward filtration due to the high colloid osmotic pressure of the dextran did not continue after 10 minutes and that a substantial part of the infused dextran solution remained in the vascular system for the following 2 hours of the experiment (10, 11).

In the first experiment (control group), the 500 ml of blood that had been withdrawn was reinfused in 3.3 minutes. After a pause of 1.8 minutes, the same amount of blood was withdrawn again within 4.3 minutes. Following this procedure, the subjects were bled another 500 ml in 3.9 minutes. This volume was reinfused 1.3 minutes later within 2.9 minutes. Thus the time taken to complete the two cycles was 9.3 minutes for infusion and 8.1 minutes for bloodloss, i.e., a total of 17.4 minutes. The cycle was run in the shortest time possible to keep secondary effects due to capillary filtration and delayed compliance at a minimum. The blood volume changes amounted to ± 500 ml or ± 9.74% of the total blood volume.

In the second experiment, lower body positive pressure was slowly increased up to 50 mm Hg within 2 minutes. The central venous pressure was recorded simultaneously. During the increase in lower body positive pressure, blood from the dependent parts of the body was shifted into the upper body. This blood displacement led to a rise in central venous pressure. However, increasing lower body positive pressure above 30 mm Hg did not lead to further increases in the central venous pressure. Therefore, a lower body positive pressure of 30 mm Hg was sufficient to shift the maximum available volume of blood from the lower body into the upper body. A lower body positive pressure of 30 mm Hg was then applied in the second experiment when the same procedure of changing the total blood volume by ± 500 ml described for the first experiment was undertaken.

In the third experiment, conditions were the same as they were in the first experiment except that norepinephrine (15 μg/min) was infused.

In the fourth experiment, a lower body positive pressure of 30 mm Hg was combined with the simultaneous administration of norepinephrine (15 μg/min). Again the blood volume changes were ± 500 ml. Heart rate was counted throughout the experiments.

**Results**

Figure 1 (left) shows the changes in central venous pressure and peripheral venous pressure during a change in blood volume (± 500 ml) in the control group. For clarity the standard deviations have been omitted from Figures 1 and 2, but they can be seen in Figure 3. The arrows indicate the pressure course during transfusion and hemorrhage. The central venous pressure rose from 6.6 mm Hg to 9.8 mm Hg after infusion of 500 ml of blood. In the following pause (1.8 minutes), the central venous pressure descended to 9.6 mm Hg and decreased further to 6.3 mm Hg when the infused blood was withdrawn. During hemorrhage of 500 ml, the central venous pressure decreased to 3.3 mm Hg and reached nearly the initial value of 6.6 mm Hg when the blood was reinfused at the end of the experiment. The peripheral venous
pressure increased from 10.2 mm Hg to 12.9 mm Hg after infusion of 500 ml. It decreased to 7.4 mm Hg after hemorrhage.

When lower body positive pressure was applied (Fig. 1, right) (second experiment), the central venous pressure increased from 6.6 to 11.3 mm Hg, and the peripheral venous pressure increased from 10.2 to 13.9 mm Hg. After infusion and subsequent withdrawal of 500 ml of blood, the central venous pressure was decreased from 11.3 mm Hg to 9.2 mm Hg. Conversely, the central venous pressure was increased after hemorrhage and successive reinfusion. At the end of the lower body positive pressure experiment, the central venous pressure was decreased to 10.7 mm Hg compared with the initial value of 11.3 mm Hg (P < 0.01). The peripheral venous pressure behaved similarly. Pressure-volume diagrams of central venous pressure and peripheral venous pressure are markedly steeper and wider during lower body positive pressure compared with those during the control experiment.

Figure 2 shows the changes in central venous pressure during all four experiments for all eight subjects. The distensibility of the total vascular bed was greatest in the control group followed by that in the group receiving norepinephrine; it was minimum in the group subjected to lower body positive pressure combined with a norepinephrine infusion.

All pressure-volume curves showed hysteresis. Although the hysteresis loop was narrow in the control subjects, a very wide loop was observed with lower body positive pressure and norepinephrine infusion. This condition made calculation of the systemic vascular compliance difficult. Mean distensibility curves (Fig. 3) were obtained by calculating the mean of the pressure values of the ascending and the descending limbs corresponding to a given volume. The mean compliance curves thus calculated had the same slope for blood infusion and hemorrhage. The compliance curves for hemorrhage were displaced in parallel to lower pressures probably because of the
Changes in central venous pressure (CVP) during a change in blood volume of ± 500 ml in the control group, the group given norepinephrine (NE), the group with lower body positive pressure (LBPP), and the group given norepinephrine and subjected to lower body positive pressure (NE + LBPP). Number of subjects and procedure are the same as they are in Figure 1. In the group given norepinephrine and subjected to lower body positive pressure, the volume change was started at a and the experiment was terminated at c.

Fluid loss by filtration which occurred since the infusion of blood always preceded blood volume reduction. This effect was very pronounced in the experiments using both lower body positive pressure and infusion of norepinephrine: central venous pressure rose to 22 mm Hg and approached pulmonary edema levels (12). The attempt to quantify filtration in four subjects by measuring changes in hematocrit was not satisfactory. However, the
tendency toward outward filtration with transfusion and inward filtration with hemorrhage was apparent.

Figure 3 clearly demonstrates, the different steepness of the pressure-volume curves in the four experiments. The pressure-volume relationships are practically linear. The coefficients of volume elasticity (E') (Frank) and the vascular compliance values calculated from these data and the mean body weight are listed in Table 1. The normal effective compliance amounted to 2.3 ml/mm Hg kg⁻¹ body weight. With lower body positive pressure the volume changes were mainly restricted to the upper half of the body and the
COMPLIANCE OF THE VASCULAR BED OF MAN.

**TABLE 1**

**Effective Vascular Compliance (C) and Volume Elasticity Coefficient (E')**

<table>
<thead>
<tr>
<th></th>
<th>C (ml/mm Hg kg⁻¹ body wt)</th>
<th>(% of control value)</th>
<th>E' = ΔP/ΔV (mm Hg/20% body wt)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.3</td>
<td>100</td>
<td>6.5</td>
</tr>
<tr>
<td>Lower body positive pressure</td>
<td>1.2*</td>
<td>55</td>
<td>12.5</td>
</tr>
<tr>
<td>Norepinephrine (15 μg/min)</td>
<td>1.7</td>
<td>75</td>
<td>9.2</td>
</tr>
<tr>
<td>Norepinephrine and lower body positive pressure (15 μg/min)</td>
<td>0.9†</td>
<td>42</td>
<td>16.4</td>
</tr>
</tbody>
</table>

*55% of the control value.
†56% of the norepinephrine value.

compliance was reduced to 55% of that of the total normal circulation. Infusion of norepinephrine reduced the compliance to 1.7 ml/mm Hg kg⁻¹ body weight. Induction of lower body positive pressure with infusion of norepinephrine led to a further reduction in compliance to 0.9 ml/mm Hg kg⁻¹ body weight. Compared with the compliance during norepinephrine infusion the compliance with both lower body positive pressure and infusion of norepinephrine decreased to nearly 55% of normal, and compared with the compliance of the control group it was reduced to 42% of normal. Therefore, the effective compliance of the intrathoracic vascular bed is between 42% and 55% of that of the intact normal vascular bed.

Peripheral venous tone (9) showed no significant changes during a blood volume change of ± 500 ml. The mean volume elasticity coefficient (E'₁₃) was 18.9 mm Hg/ml 100 g⁻¹ tissue before infusion. It increased slightly to 19.6 mm Hg/ml 100 g⁻¹ tissue after infusion of 500 ml of blood and decreased to 17.6 mm Hg/ml 100 g⁻¹ tissue after a bleeding of 500 ml. These fluctuations in venous tone, however, were not significant.

There were only slight changes in heart rate during infusion and hemorrhage. The heart rate tended to increase during hemorrhage and to decrease during blood volume expansion (Table 2). Infusion of norepinephrine per se caused a decrease in heart rate which was highly significant (P < 0.0001).

Arterial blood pressure was measured before each experiment. The mean systolic and diastolic pressures (mm Hg) were: control 105/60, lower body positive pressure 115/70, norepinephrine 140/80, and norepinephrine and lower body positive pressure 155/90. Since both arms were catheterized, the blood pressure was not monitored during infusion and hemorrhage.

**Discussion**

Generally, for a normal man (75 kg), the volume elasticity coefficient of the arterial system at a mean blood pressure of 100 mm Hg is 1 mm Hg/ml (13). From this figure a compliance of 0.013 ml/mm Hg kg⁻¹ body weight can be calculated. This compliance is an insignificant fraction of the effective compliance of the total circulation of approxi-

**TABLE 2**

**Heart Rate (Beats/Min) with Changes in Blood Volume**

<table>
<thead>
<tr>
<th></th>
<th>Transfusion (500 ml)</th>
<th>Normal blood volume</th>
<th>Hemorrhage (500 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>76.7 ± 7.4*</td>
<td>78.9 ± 7.5</td>
<td>78.6 ± 6.5</td>
</tr>
<tr>
<td>Lower body positive pressure</td>
<td>74.8 ± 9.3*</td>
<td>76.5 ± 8.6</td>
<td>83.0 ± 6.4*</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>62.8 ± 5.4*</td>
<td>66.0 ± 5.7</td>
<td>70.0 ± 6.2*</td>
</tr>
<tr>
<td>Norepinephrine and lower body positive pressure</td>
<td>61.6 ± 7.3*</td>
<td>65.8 ± 7.3</td>
<td>70.9 ± 6.8*</td>
</tr>
</tbody>
</table>

*P < 0.025 compared with heart rate at normal blood volume (paired t-test).
mately 2.3 ml/mm Hg kg\(^{-1}\) body weight. Therefore, the compliance of the total circulation is mainly determined by the properties of the low-pressure system which holds 80–85% of the total blood volume. The pressures in this system depend largely on the blood volume and the distensibility of the capacitance vessels. The pressure gradients are small due to the very low flow resistances. When the pressure is continuously recorded along the main venous trunk from the iliac vein to the innominate vein in man (14), a sudden pressure drop of 3–4 cm H\(_2\)O occurs at the level of the diaphragm; above and below this level the pressure gradients are too small to be measured. This characteristic pressure drop is due to a partial collapse of the caval vein below the entrance into the thorax (15). A similar pressure difference of 3–4 cm H\(_2\)O has been found between the anticubital vein and the right atrium (8) (Fig. 1). With changes in blood volume the slope of venous pressure in the central compartment is steeper than that in the peripheral compartment.

In model experiments in the rat, which has a more pronounced caval constriction at the diaphragm and a relatively smaller blood volume than does man, the two pressures have been observed continuously during a blood volume change of 30% (16, 17). During infusion the peripheral pressure measured in the iliac vein changes little, but the central pressure rises at a nearly constant rate, according to the effective compliance of the circulation of the rat (3–4 ml/mm Hg kg\(^{-1}\) body weight). When the blood volume is increased by 10–15%, the slope of the peripheral pressure increases and a condition similar to that in Figure 1 results. When the transfusion exceeds 20%, the slope of the central venous pressure reaches that of the peripheral pressure. Subsequently the two pressures increase together, but the original slope of the central pressure-volume curve is maintained.

In view of the low flow resistances in the low-pressure system, possible changes in cardiac output due to volume changes have only a minor effect on the pressure changes. In dogs the change in central venous pressure induced by changes in blood volume is the same whether the heart is arrested (18) or the circulation is perfused at a constant rate (19) (Table 3).

Because of a redistribution of blood volume, even minor changes in posture may change the compliance of sizable sections of the vascular bed and, hence, the effective compliance. Our previous measurements were performed with the subjects in the lateral decubitus position (7, 8). Although the deviation of posture from the standard supine position was obviously not great, we felt that a comparison of the data obtained in the two positions was highly desirable. As Table 3 shows the difference is small. In the upright posture the diaphragmatic constriction of the venous trunk disappears (14) and up to 10% of the estimated blood volume is pooled in the dependent vascular bed, which is distended under high hydrostatic pressures (14). At the same time, the capacitance

### TABLE 3

Comparison of Effective Vascular Compliance and Intrathoracic Compliance Measured in Several Different Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Reference</th>
<th>Compliance (ml/mm Hg Kg(^{-1}) body wt)</th>
<th>Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gauer et al.</td>
<td>7</td>
<td>2.7</td>
<td>Man</td>
</tr>
<tr>
<td>Harlan et al.</td>
<td>18</td>
<td>2.3</td>
<td>Dog arrested circulation (calculated data)</td>
</tr>
<tr>
<td>Ungewiss</td>
<td>22</td>
<td>3.0</td>
<td>Man</td>
</tr>
<tr>
<td>Shoukas and Sagawa</td>
<td>19</td>
<td>2.0–2.4</td>
<td>Man, essential hypertension</td>
</tr>
<tr>
<td>Present study</td>
<td>2.3</td>
<td>1.7</td>
<td>Dog constant perfusion of circulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Man, norepinephrine infusion</td>
</tr>
</tbody>
</table>

### Effective Vascular Compliance

- Man
- Dog arrested circulation (calculated data)
- Man
- Man, essential hypertension
- Dog constant perfusion of circulation
- Man, norepinephrine infusion

### Intrathoracic Compliance

- Dog (calculated data)
- Man, lower body positive pressure
- Man, norepinephrine infusion and lower body positive pressure
vessels in the upper half of the body show a strong tendency to collapse. It is unlikely that the loss in compliance of the vascular beds below the hydrostatic indifference point (14) is canceled out by the gain in compliance of the vascular beds of the upper half of the body. Therefore, an effective compliance different from that obtained in standard dorsal recumbency should occur. Data obtained in man are not available.

When the rat is tilted in the vertical position, the pressures in the central and the peripheral veins rise and fall in parallel with infusion and hemorrhage throughout the whole range of blood volume changes. The effective compliance rises to 7 ml/mm Hg kg⁻¹ body weight compared with a compliance of 4 ml/mm Hg kg⁻¹ body weight in the horizontal posture (16).

Previous studies (14, 20, 21) and the observations in this paper of venous tone in the arm have failed to reveal changes in venous tone with moderate (±10%) changes in central blood volume. There may have been changes in other parts of the capacitance system; however, the data show that such changes, if they exist, are insufficient to stabilize the central venous pressure, which rises and falls predictably with these modest changes in blood volume. Heart rate (Table 2) also indicates that moderate changes in blood volume of ±500 ml have only a minimal influence on sympathetic activity.

In spite of numerous possible complications, a linear, well-defined relationship results when the changes in total blood volume are plotted against the changes in central venous pressure. This compliance which is easily measured and which determines the filling pressure of the right heart may be designated the effective compliance of the circulation. This compliance, when it is related to body weight, agrees with previous measurements in man and in dogs (Table 3). The finding of Ungewiss (22) that the compliance in essential hypertension is significantly higher than that in normal man is interesting and needs further confirmation.

Lower body positive pressure limits the distensible part of the circulatory system mainly to the upper half of the body. The effective compliance of the intrathoracic vascular bed lies between 55% and 42% of the effective compliance of the normal circulation; it must be smaller than 55% because with lower body positive pressure alone the vessels of the surface of the thorax, the upper extremities, and the head contribute to the distensibility. With the addition of norepinephrine the compliance of these vessels is grossly reduced. If the compliance of the intrathoracic vascular bed is not affected by infusion of norepinephrine this compliance would be approximately the correct effective compliance of the intrathoracic vascular compartment. Since this condition is unlikely, the effective compliance of the intrathoracic circulation must be higher than 42% but lower than 55% of that of the normal circulation. For all practical purposes this value is identical with that in the dog obtained by Harlan et al. (18) using a different experimental technique. It also agrees with the observation of Glaser (23) that during a blood transfusion half the transfused volume is accommodated in the intrathoracic compartments.

Acknowledgment
We are grateful to Professor J. L. Thron for lending us the positive-pressure box and to Miss L. Schepeler for help in the preparation of the manuscript.

References
12. Guyton, A.C., and Lindsey, A.W.: Effect of elevated left atrial pressure and decreased plasma protein con-


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Circ Res. 1974;34:61-68
doi: 10.1161/01.RES.34.1.61

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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