ATPase in vitro. Further purification of the fraction will be necessary to establish whether these properties arise from a single molecular species.

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Effect of Thoracic Blood Volume Changes on Steady State Cardiac Output

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SUMMARY We have investigated the extent to which shifts of blood volume out of or into the thoracic region influence the steady state cardiac output. The systemic circulation of anesthetized dogs was replaced with an artificial circuit which simulated the pertinent mechanical characteristics of an intact circulation. As in the normal animal, the steady state venous return was proportional to the pressure gradient for venous return (i.e., mean systemic minus right atrial pressure). Cardiac function was altered either by administration of epinephrine or by changes in left ventricular afterload. At a constant mean aortic pressure of 100 mm Hg, epinephrine administration increased the steady state cardiac output by 55%. Half of this increase resulted from the lowered mean right atrial pressure (caused by improved cardiac function); the remainder resulted from an increased mean systemic pressure (caused by the volume shift to the systemic circulation). Increases in afterload transferred sufficient volume to the heart-lung compartment to reduce significantly the mean systemic pressure and, hence, the steady state venous return. Our results indicate that the heart-lung compartment contains a significant volume which is under cardiac control. In addition to being able to alter the right atrial pressure, the heart can modulate the steady state cardiac output by adjusting the mean systemic pressure. To this degree the heart can adjust its own venous return.

SHIFTS OF volume into or out of the thoracic region have been thought to be too small to cause any significant changes in the systemic blood volume and mean systemic pressure ($P_{sys}$). In the steady state, the cardiac output must equal the venous return; and since the steady state venous return is a function of the pressure gradient for venous return (i.e., $P_{sys}$ minus right atrial pressure ($P_{ra}$)), it follows that such shifts of thoracic blood volume by

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themselves should have only minimal effects on the cardiac output.

We propose that there may be a significant volume of blood in the heart-lung compartment which can be translocated either by changes in cardiac function or by the action of pharmacological agents. This volume may be either from the cardiac chambers or from the pulmonary vasculature. Since volume in either location does not normally influence the $P_{ma}$, transfer of this volume to the systemic circulation would act as an autotransfusion to increase the $P_{ma}$. For example, the systemic compliance of a normal 20-kg dog is about 40 mg/mm Hg, so that for a normal $P_{ma}$ of 7 mm Hg there is only a total of 280 ml (14 mg/kg) of stressed volume (volume under tension, i.e., volume which is equal to systemic pressure times systemic compliance) in the systemic circulation. This is only about 15% of the dog's normal total blood volume of 1,850 ml (92.5 ml/kg). If 50 ml were transferred from the heart-lung segment to the periphery, the $P_{ma}$ should rise by nearly 20%. However, if we consider the pulmonary compliance to be 1/7 of the systemic compliance and mean pulmonary pressure to be less than 10 mm Hg, then there would be barely 50 ml of stressed volume in the pulmonary circuit. Since the total blood volume of the thoracic compartment is 20-25% of the total blood volume of the dog, approximately 20 mg/kg or 400 ml for a 20-kg dog, there clearly exists a large volume relative to the stressed volume of the periphery. In this regard, we have used the data of Harlan et al. and assumed a systemic compliance of 2 ml/kg per mm Hg to calculate that if the total blood volume of a dog is changed, nearly 25% of this change is accommodated by the thoracic compartments. Considering the relatively small pulmonary compliance, it is clear that in the absence of changes in unstressed volume most of this accommodation by the thoracic compartment occurs in the heart.

Guyton has presented a graphic analysis of control and regulation of steady state cardiac output which includes consideration of the pulmonary circuit. In this analysis he considers only that part of the pulmonary blood volume which affects the return of blood to the left heart, i.e., the stressed volume. Because he tacitly assumes the cardiac volume and unstressed vascular volume of the lungs to be unchanged, his analysis has led to the conclusion that, except in extreme situations, shifts in pulmonary blood volume can be absorbed easily by the relatively large systemic compliance, with little change in mean systemic pressure and cardiac output.

According to our hypothesis, changes in cardiac function would translocate significant amounts of blood out of or into the stressed reservoir of the systemic circuit. To test this hypothesis, we established an experimental preparation in which the systemic vascular bed was replaced with a mock circulation which allowed quantification of volume shifts from the heart-lung segment. We changed cardiac function either by changing the afterload on the left heart or by administering epinephrine. We then measured the hemodynamic changes that occurred independently of any reflex changes or direct effects of epinephrine on the systemic vasculature.

Methods
Our experimental model consists of an in situ heart-lung preparation which pumps blood into a mock systemic circulation. A schematic diagram of the preparation is shown in Figure 1. Eight dogs ranging in weight from 20 to 25 kg (average, 23.2 kg) were anesthetized with pentobarbital (25 mg/kg, iv). The chest was opened through a midline incision and loose ligatures were placed around the subclavian and brachiocephalic arteries, the aorta immediately distal to the subclavian artery, the azygos vein, and the inferior and superior vena cavae. Heparin (500 U/kg) was administered, and an arterial cannula then was placed in the brachiocephalic artery. The subclavian artery was ligated, and after a period of about 2 minutes (a time sufficient to drain the cephalic regions) the venous cannula was inserted into the superior vena cava and directed toward the right heart. We carefully removed all air from the venous cannula by drawing blood out of the vena cava, and clamped the filled cannula. The aorta was ligated, and the heart then perfused the external perfusion circuit against an arterial pressure of 80 mm Hg (set by the pressure around the Starling resistor) until the reservoir and tubing of this circuit were primed sufficiently with the dog's own blood, which continued to drain from the systemic circulation. The azygos vein and inferior vena cava then were ligated and the clamp on the venous cannula was removed to complete the external circulation. The surgery was completed in less than 1 hour.

Left atrial pressure ($P_{la}$) was measured through a catheter placed either in a pulmonary vein or in the left atrial appendage. With the exception of the small incision in the pericardium required for placement of the left atrial cannula (when this approach was used) the pericardium remained intact. We determined the effect of the pericardium on our results by repeating the series of experiments (see below) with the pericardium cut open. Right atrial pressure ($P_{ra}$) was measured through a catheter placed in the venous

![Figure 1](http://circres.ahajournals.org/)

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cannula, and aortic pressure ($P_a$) was measured through a catheter placed in the arterial cannula. The zero baseline reference for all pressures was set to the hydrostatic level of the tricuspid valve. Cardiac output (less coronary flow) was measured with an electromagnetic flow probe (Carolina Medical Electronics, model 202) in the external circulation. All pressures were measured with Statham strain gauges (P23 series) and all variables were recorded continuously on a Grass model 7 polygraph. The lungs were ventilated with a Harvard respirator (with a positive end-expiratory pressure of 3–7 cm water) and ventilation was reduced appropriately to maintain a nearly normal PCO$_2$. Bicarbonate was added if needed to keep pH near normal. One hour after the heart-lung preparation had been isolated the mean PCO$_2$ was $44 \pm 8$ (SEM) mm Hg and mean pH was $7.33 \pm 0.05$. Oxygen was administered to maintain full saturation of the arterial blood. A solution of 5% dextrose in water was allowed to drip into the reservoir at a rate of 1–2 ml/min. When epinephrine was administered (at 10 $\mu$g/min) it was first diluted in the dextrose solution, administration of which was continued at the same rate.

The external systemic circulation was designed to simulate the pertinent characteristics of the normal systemic circulation. The left heart pumped through a Starling resistor which was used to control the aortic pressure. Outflow from the Starling resistor entered a reservoir with a fixed but adjustable resistance (which we refer to as $R_v$, the resistance to venous return).

As in the normal circulation, the venous return to the right heart of the dog then was determined by mean systemic pressure (which in our model equals the height of the column of blood in the reservoir, with respect to the level of the right atrium), $P_{ra}$, and the resistance to venous return. The hydrostatic pressure of the venous reservoir relative to the level of the right atrium was measured. This reservoir pressure is analogous to the mean systemic pressure and we refer to it as $P_m$. Volume shifts then were equal to the changes in $P_m$ times the constant reservoir compliance. The reservoir was placed on an adjustable stand so that the level of the right atrium was measured. This reservoir was warmed to maintain a blood temperature of 38°C in the reservoir. Temperature gradients through the circulation were not monitored. Outflow from the reservoir was returned to the superior vena cava through a fixed but adjustable resistance (which we refer to as $R_v$, the resistance to venous return).

As in the normal circulation, the venous return to the right heart of the dog was determined by mean systemic pressure (which in our model equals the height of the column of blood in the reservoir, with respect to the level of the right atrium), $P_{ra}$, and the resistance to venous return. The hydrostatic pressure of the venous reservoir relative to the level of the right atrium was measured. This reservoir pressure is analogous to the mean systemic pressure and we refer to it as $P_m$. Volume shifts then were equal to the changes in $P_m$ times the constant reservoir compliance. The reservoir was placed on an adjustable stand so that $P_m$ could be adjusted by raising or lowering the reservoir. For any given fixed array of linear resistances and compliances in the systemic circulation, the parameters of our simple model could be selected to duplicate the mean pressure, flow, and volume relationships of that fixed array as determined from the inflow and outflow ends (i.e., as seen by the heart).

In the control state $P_m$ and $R_v$ were adjusted to give a value for $P_m$ in the range of 6–9 mm Hg, and a cardiac output of about 1 liter/min with an aortic pressure of 100 mm Hg. This required an average value of $R_v$ of 4 mm Hg/liter per min. The experimental procedure consisted of the following. After a 10-minute control period with mean aortic pressure at 100 mm Hg and a cardiac output of 1 liter/min, the aortic pressure was raised or lowered in multiples of 25 mm Hg by changing the pressure around the Starling resistor appropriately. Each new aortic pressure was held until a steady state was reached (always less than 2 minutes) and then pressure was returned to the control, 100 mm Hg.

Figure 2 shows part of a record from the control state. With each elevation of aortic pressure, $P_m$ transiently rose and then returned to a new level. Although not shown in Figure 2, this steady state level of $P_m$ frequently was below control levels after an elevation of aortic pressure during epinephrine administration. The $P_m$ always fell as the afterload increased, and this resulted from a volume transfer into the heart-lung segment. The $P_{ra}$ response to increased aortic pressure was variable, sometimes increasing and sometimes decreasing. The cardiac output always fell with an increased afterload.

Following the series of changes in afterload in the control state, aortic pressure was returned to 100 mm Hg and epinephrine administration (10 $\mu$g/min) was begun. Aortic pressure was kept fixed at 100 mm Hg, and $R_v$ and venous compliance were not changed. Fifteen minutes after the onset of epinephrine administration, a new steady state level was reached and another series of aortic pressure changes was made. The pericardium was then cut away and a third and fourth series of afterload changes were made, first with epinephrine (immediately after opening the pericardium) and then 20 minutes after the administration of epinephrine was discontinued.

**Results**

Figure 3 shows the control results. The mean heart rate in the control state was 100 ± 5 (SEM) beats/min and was not

![Figure 2](http://circres.ahajournals.org/) Sample record from one dog. Shown are aortic pressure ($P_a$), left atrial pressure ($P_{ra}$), mean systemic pressure ($P_m$), right atrial pressure ($P_{ra}$), and cardiac output (CO). Units of pressure are mm Hg and units of flow are liters/min. At the arrow markers the aortic pressure was changed.
affected significantly by changes in aortic pressure. We have plotted $P_{ms}$, $P_{la}$, $P_{ra}$, and steady state cardiac output as a function of mean aortic pressure. It is obvious from the figure that any increase in afterload was associated with an increase in heart-lung volume, because the reservoir volume ($P_{ms} \times C_{ms}$) decreased. Increases in afterload also were associated with increases in both $P_{ra}$ and $P_{ms}$. Therefore, the cardiac output (which is proportional to $P_{ms} - P_{ra}$) fell with increases in aortic pressure. Over the range of aortic pressures (50–150 mm Hg), the average $P_{ms}$ fell 1.9 mm Hg, and thus the blood volume in the heart-lung compartment increased by 100 ml. Over this range of aortic pressures, $P_{ra}$ increased by 1.5 mm Hg and $P_{ma}$ by 5.7 mm Hg.

Figure 4 shows the results obtained during epinephrine administration. The mean heart rate was 134 ± 6 (SEM) beats/min. At the control pressure of 100 mm Hg, epinephrine caused an increase in steady state cardiac output from 1.03 liters/min to 1.59 liters/min ($P < 0.01$, paired t-test), an increase of 5.5%. The solid block squares in Figure 4 represent the control values of all the variables at an aortic pressure of 100 mm Hg. $P_{ma}$ fell from 5.5 to 2.9 mm Hg and $P_{ra}$ fell from 3.7 to 2.7 mm Hg ($P < 0.01$). $P_{ms}$ rose from 7.7 to 9.0 mm Hg ($P < 0.01$), an increase of 1.3 mm Hg, corresponding to a shift of 68 ml into the systemic circuit. At an aortic pressure of 100 mm Hg about half of the 55% increase in steady state cardiac output resulted from the improved cardiac function (which reduced $P_{ra}$) and the remainder resulted from an increased $P_{ms}$ (which, of course, resulted in part from the augmented cardiac function as well).

In contrast to the control state, increases in aortic pressure over the range 50–150 mm Hg resulted in a decrease in $P_{ms}$. Over this range of aortic pressures $P_{ra}$ remained nearly constant. It should be emphasized that these changes in mean right and left atrial pressures occurred over a range in which the volume of the heart-lung compartment was increased. As the aortic pressure was increased, $P_{ms}$ fell, but the cardiac output fell less then in the control state because $P_{ra}$ did not rise (except at high $P_{a}$). The fall in $P_{ms}$ over the 50–175 mm Hg range of aortic pressures was 1.2 mm Hg and corresponded to a volume shift of 63 ml.

Figure 5 shows the results obtained after the pericardium had been cut open and with the epinephrine administration continuing, and with $P_{a}$ at 100 mm Hg. The squares in Figure 5 are the values for 100 mm Hg from Figure 4. The results are very similar to those shown in Figure 4 for intact pericardium. Both $P_{ms}$ and $P_{ra}$ were slightly lower ($P < 0.02$, at 100 mm Hg): $P_{ma}$ still fell as aortic load was increased in the range 50–150 mm Hg. In contrast to the state obtained when the pericardium was intact, $P_{ra}$ fell over the entire range of increased values of aortic pressure. The $P_{ms}$ was unchanged after removal of the pericardium and responded similarly to changes in aortic pressure. Steady state cardiac output was increased slightly after removal of the pericardium, and the output still fell with increasing aortic pressure. The flow, however, was maintained more nearly constant in this case, since $P_{ra}$ fell with increasing aortic load.

Figure 6 shows the results obtained 20 minutes after the epinephrine infusion was discontinued. As in the original control state, $P_{ra}$ rose monotonically with increases in aortic pressure. As afterload increased the $P_{ms}$ fell markedly (3.2 mm Hg over the range 50–175 mm Hg), corresponding to an increased heart-lung volume of 167 ml. As in the case with epinephrine and no pericardium, $P_{ra}$ fell over the entire range of increased values of aortic pressure. The steady state cardiac output also decreased as aortic pressure was in-
Discussion

Our experimental results demonstrate that volume sufficient to significantly alter $P_{ma}$ can be transferred into or out of the heart-lung segment from the systemic circulation. This volume appears to be under cardiac control. Increasing the cardiac afterload has been shown to depress cardiac function curves, and we have found this increased afterload to be associated with variable degrees of volume uptake by the heart-lung system. Starling, in his original work with the heart-lung preparation, also found a significant increase in heart volume as the afterload was increased. However, his preparation maintained cardiac inflow nearly constant as afterload was changed. In our preparation with the simulated systemic circulation, we allowed the inflow to adjust itself according to the shifts of blood volume and $P_{ra}$, which occurred with changes in afterload. In this regard, our preparation simulates an intact dog without any reflex or humoral changes.

In the control state we have shown that, as mean aortic pressure increased from 50 to 175 mm Hg, there was an increase of 100 ml in thoracic volume. $P_{ra}$ and $P_{ra}$ increased by 1.9 and 5.7 mm Hg, respectively, over this range. We did not measure the pulmonary artery pressure, but since the cardiac output fell over this range of aortic pressures, the pulmonary arterial pressure could not have risen any more than did $P_{ra}$. If we assume that all thoracic pressures rose as much as $P_{ma}$, we can estimate a minimal value for the compliance of the entire heart-lung system. This minimal estimate is 17.5 ml/mm Hg, about $1/5$ of a normal systemic compliance and considerably in excess of the pulmonary compliance, which is usually considered to be $1/10$ of the systemic compliance. The actual magnitude and distribution of this compliance and the relative distribution of volume within the four cardiac chambers and pulmonary vasculature is difficult to characterize, but consideration of the magnitude of the observed volume shifts, changes in $P_{ma}$, and the nominal values of pulmonary compliance leads us to the conclusion that most of the increased heart-lung volume was accommodated in the cardiac chambers. The data obtained during administration of epinephrine show that in response to step increases in aortic pressure from 50 to 150 mm Hg, $P_{ma}$, $P_{ra}$, cardiac output, and presumably pulmonary arterial pressure all decreased—yet the heart-lung compartment volume increased! In this case it is clear that since the vascular pressures within the lung fell, all the increased heart-lung volume was accommodated in the cardiac chambers. This increase in volume was quite substantial (44 ml) and we are forced to conclude that increases in left heart afterload cause changes in the distensibility of the heart, such that the cardiac chambers may contain greater volume at the same or lower distending pressures. We suspect that increases in coronary blood flow (which would increase the delivery of oxygen and epinephrine to the myocardium) or the mechanisms underlying homeometric autoregulation may play important roles in these phenomena.

The steady state cardiac output was increased by epinephrine at all levels of aortic pressure. At the control aortic pressure of 100 mm Hg, epinephrine increased the steady state cardiac output by 55%, decreased $P_{la}$ and $P_{ra}$ by 2.7

![Graph](image-url)
and 1.0 mm Hg, respectively, and shifted 68 ml into the systemic circuit thereby increasing the $P_{ms}$ by 1.3 mm Hg. Since the $R_a$ was not changed, we could calculate that about half of the increased steady state cardiac output resulted from the increase in $P_{ms}$ from 7.7 to 9 mm Hg which was caused by the volume shift, and the other half from the reduction in $P_a$ from 3.7 to 2.7 mm Hg (caused by the augmented cardiac function). To transfer the volume back to the heart-lung segment required an elevation of mean aortic pressure to 200 mm Hg. At this pressure the cardiac output, $P_a$, and $P_{ms}$ all were near their control values (i.e., without epinephrine and with aortic pressure of 100 mm Hg), but $P_a$ still was reduced. This suggests an increased cardiac or pulmonary compliance.

The volume shift of 68 ml that occurred with epinephrine could have come from either the cardiac chambers or the pulmonary vasculature. Since flow rose and $P_{ia}$ fell, we cannot speculate on what happened to the pulmonary artery pressure. It is possible that some of this transferred volume resulted from a decrease in unstressed volume of the pulmonary vasculature. Epinephrine has been shown to reduce the unstressed volume of the systemic vasculature. We cannot estimate the magnitude of such a change, because there are no reports of studies which deal with this aspect of the pulmonary vasculature. In our preparation epinephrine increased heart rate and cardiac stroke volume, and both of these changes would be expected to reduce the mean cardiac volume (i.e., the average total cardiac volume over one heart beat), and thereby shift volume to the systemic circulation. Increases in contractility or decreases in cardiac compliance likewise would reduce the mean cardiac volume.

With aortic pressure at 100 mm Hg and epinephrine infusion continuing, opening the pericardium had only minimal effects. Both atrial pressures were reduced slightly and the $P_{ms}$ did not change. Thus there was a slight increase in steady state cardiac output. Over the low range of aortic pressure, $P_a$ decreased as aortic pressure increased. The main difference between the heart with and without the pericardium was the response of $P_{ia}$ to changes in aortic pressure. Without the pericardium $P_{ia}$ fell as aortic pressure increased over the entire range, whereas with the pericardium intact the $P_{ia}$ fell slightly at the low aortic pressure but then increased in the high pressure range. This response without the pericardium occurred with or without epinephrine (compare Figs. 5 and 6). This experimental observation probably is the result of mechanical coupling or interdependence between the cardiac chambers. With the pericardium intact, the coupling must be tighter so that the $P_{ia}$ is more closely linked to the $P_{ia}$. Removal of the pericardium increases the independence of the chambers. In this condition (i.e., without pericardium) the responses of $P_{ia}$ are similar to those observed with an intact pericardium. However, $P_{ia}$ is more influenced by the falling $P_{ms}$ than by changes in $P_{ia}$, and cardiac output falls less as aortic pressure is increased. This was true with or without epinephrine (compare Figs. 4 and 5 and Figs. 3 and 6). These results are consistent with the findings of Berglund and associates, who previously have shown that increased left heart afterload significantly depresses right heart function only when the pericardium is intact.

With our preparation we examined only direct mechanical effects on the heart-lung segment; there were no central nervous influences and no systemic humoral effects. We feel that the condition of these hearts was as near normal as can be obtained with a heart-lung preparation. (We should point out that in all heart-lung preparations the circulating catecholamine level must be abnormally low, and the tonic central nervous system input is absent. Thus the normal heart in the intact dog might respond in a manner intermediate between our control and epinephrine conditions.) The surgery was performed rapidly, the dogs' own blood was used without dilution, and at a mean aortic pressure of 100 mm Hg, both transmural atrial pressures were within a normal range. Control cardiac output was kept to about half the normal value for a 20-kg dog, but this was done deliberately to ensure a stable and reproducible preparation over the 1- to 1 1/2-hour experimental procedure. By reducing the resistance to venous return of the external peripheral circulation, we could double the steady state cardiac output; this indicates that the hearts were not in failure. Indeed, during the epinephrine infusion, the hearts easily pumped 2 liters/min with low atrial pressures against a mean aortic pressure of 200 mm Hg. Although the transmural right atrial pressures were normal in our preparations, the atrial pressures were higher (with respect to atmospheric pressure) than they would have been in intact dogs because the hearts were surrounded by atmospheric rather than negative pleural pressure. This resulted in a smaller gradient for venous return ($P_{ms} - P_{ra}$). Changes in either $P_{ra}$ or $P_{ms}$ in this preparation will, therefore, cause proportionally larger changes in the venous return than would occur in the intact animal. However, the actual magnitude of the volume shifted and the resultant absolute change in $P_{ms}$ in our

$$\begin{align*}
P_a & \quad 100 \quad \text{[mm Hg]} \quad \text{[mm Hg]} \quad \text{[liters/min]} \\
0 & \quad 1 \text{ min} \\
P_{ia} & \quad -5 \quad \text{[mm Hg]} \\
0 & \quad -0 \\
P_{ms} & \quad -5 \quad \text{[mm Hg]} \quad \text{[liters/min]} \\
0 & \quad -0 \quad \text{[liters/min]} \\
P_{tg} & \quad -5 \quad \text{[mm Hg]} \quad \text{[liters/min]} \\
5.02 | 9 | 47 | 10 | 0.90 & \quad -0 \\
0 & \quad -0 \\
CO & \quad -1.0 \quad \text{[liters/min]} \\
0 & \quad -0 \\
\end{align*}$$

FIGURE 7. Chart record from one dog showing changes in the measured variables caused by stepwise reductions in the resistance to venous return ($R_v$). Shown are aortic pressure ($P_a$), left atrial pressure ($P_{ia}$), mean systemic pressure ($P_{ms}$), right atrial pressure ($P_{tg}$), and cardiac output (CO). Units of pressure are mm Hg; units of flow are liters/min; units of $R_v$ are mm Hg/liters per min.
preparation would be similar to those occurring in the intact dog.

In addition to studying the effects of epinephrine and afterload on the volume shifts between the heart-lung and peripheral segments, we examined the effects of altering the resistance to venous return. Figure 7 shows a record from one dog (in the control state) where Rv was reduced in step-wise fashion from 5.0 to 0.90 mm Hg/liter per min. As Rv was reduced, there was a significant shift of volume (65 ml over the whole range) into the heart-lung compartment. This resulted in a decrease in Pml. Thus, there was a smaller increase in steady state cardiac output than would be expected on the basis of a change in Rv alone. This situation would have been further augmented from that shown in Figure 7 had we permitted aortic pressure to rise by an amount corresponding to the rise in cardiac output. We already have shown that an increased aortic pressure results in an increased heart-lung volume and a decreased Pma, so that an even smaller increase in cardiac output after reduction in Rv would have occurred. In terms of the venous return curves described by Guyton,16 these observations strongly imply that any change in the slope of the venous return curve would tend to cause a significant shift in Pma. If such a change in slope does not alter the Pma in an intact animal, then there must be simultaneous compensatory changes in other vascular parameters.

The results obtained with changes in afterload also would indicate a shift in the venous return curve as cardiac function is changed. Whether the increased aortic pressure caused an increase or decrease in atrial pressure, the mean cardiac volume always increased, and this resulted in a shift of the venous return curve to the left and a further reduction in the steady state cardiac output. In the same context, administration of epinephrine, which increases cardiac function (i.e., shifts the cardiac function curve up and to the left), caused a significant shift of volume into the systemic circulation, thereby raising Pma and shifting the venous return curve to the right.

In our preparation the administration of epinephrine clearly can have no effect on the resistance and compliance of the artificial peripheral circulation. If the results of this study can be applied to the intact dog they have important implications concerning the regulation and control of cardiac output. We previously have shown in the intact anesthetized dog that epinephrine (60 ìg/min) increases cardiac output about 110%.18 In the intact dog epinephrine affects both resistance and compliance of the systemic circulation and arterial pressure as well, so that the conditions of the present experiments are greatly simplified. However, we have demonstrated that volume shifts out of the thoracic compartment are significant, and any explanation of the effects of epinephrine (or of any other state change) on cardiac output must take into consideration these volume shifts. Indeed such volume shifts may play an important role in the regulation of cardiac output in exercise. Rushmer18 has demonstrated clearly a reduction of mean cardiac volume in exercising dogs, and similar observations have been made in exercising man.19 Trained athletes are known to have much larger resting heart volumes, and the increased heart rate and stroke volume associated with exercise must translocate a significant amount of this volume.18,19 In this regard, the results of a recent study by Ehrlich et al.,20 who showed a significant increase in the steady state cardiac output of unanesthetized dogs in response to paced tachycardia, are consistent with the results of our present study.

In conclusion, we have demonstrated that a significant fraction of the blood volume in the heart-lung circuit can be translocated to the systemic circulation and is under local cardiac control. Thus, in addition to being able to alter Pma, the heart is capable of modulating the steady state level of cardiac output by adjusting Pma. To this degree the heart is able to adjust its own venous return.

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