Centrogenic Pulmonary Hemorrhagic Edema
Induced by Cerebral Compression in Rats

Mechanism of Volume and Pressure Loading in the
Pulmonary Circulation

Hsing I. Chen, Jyh F. Liao, Lih Kuo, and Shung T. Ho

SUMMARY In anesthetized and vagotomized rats, an intense cerebral compression (CC) by intracranial placement of a space-occupying mass evoked systemic arterial hypertension (SAH), pulmonary venous hypertension (PVH), and pulmonary hemorrhagic edema (PHE) in 2–3 minutes. Observation of the regional weight changes revealed an acute increase in pulmonary blood volume with a decrease in the volume of the systemic vascular beds. With chronically instrumented flow probes, we demonstrated that the overall pattern of imbalance in right and left cardiac outputs was characterized by an immediate fall in aortic flow by 52% accompanying a slower decline in pulmonary arterial flow. In 10 rats with a right heart bypass (venous return to reservoir and constant pulmonary inflow), CC produced severe PVH and PHE associated with SAH, reservoir volume reduction, and no significant change in pulmonary vascular resistance. The increases in left atrial pressure and lung index (lung: body weight × 100) were much greater than those obtained with natural circulation. In 20 left heart-bypassed rats (constant aortic flow either with or without a reservoir between the left atrium and a roller pump), CC induced SAH, whereas no significant changes occurred in the lungs. The lung index was not different from the normal value. The results indicate that neurogenic constriction of the systemic capacitance vessels to favor venous return is not an important hemodynamic event in the centrogenic pulmonary pathology. Pulmonary volume loading leading to pulmonary hypertension and PHE is evoked principally by a dramatic pulmonary hypertension decrease in left ventricular output due to ventricular strain in the face of an intense arterial constriction. Circ Res 47: 366–373, 1980

ACUTE FULMINATING pulmonary edema and hemorrhage of neurogenic origin can be associated with various disorders of the central nervous system, such as cerebral compression (CC) (Campbell et al., 1949; Ducker and Simmons, 1968; Ducker et al., 1968; Chen et al., 1973), intracranial injection of chemical irritants (Sarnoff and Sarnoff, 1952; Worthen et al., 1969), preoptic hypothalamic lesions (Maire and Patton, 1956), an ablation of the nucleus tractus solitarius (Doba and Reis, 1973). Sarnoff and associates (Sarnoff and Sarnoff, 1952; Sarnoff and Berglund, 1952) first characterized the neural and hemodynamic mechanisms involved in the pulmonary edema of central nervous origin. They found that activation of the medullary sympathetic mechanism by an intracisternal injection of fibrin evoked striking elevation of systemic arterial pressure (SAP) and pulmonary venous pressure followed by massive pulmonary edema. Since direct sympathetic impulses to the lungs were not essential for the pulmonary damage, they concluded that the pulmonary hypertension and edema were induced by a shift of blood from the systemic vascular beds to the pulmonary circulation as a consequence of systemic vasoconstriction. With regard to the pulmonary pathology associated with intracranial compression, early reports (Campbell et al., 1949; Campbell and Visscher, 1949) suggested that the changes were mediated mainly by vagal pathways and the effects of cardiac slowing. However, many investigators (Ducker and Simmons, 1968; Chen et al., 1973; Chen and Chai, 1974) later argued that this type of neurogenic pulmonary change was induced principally by intense sympathetic activation leading to dramatic hemodynamic alterations, a mechanism similar to that induced by an intracisternal injection of fibrin. The concept of hemodynamic crisis in the production of pulmonary hemorrhagic edema was also supported by one of our studies (Chen and Chai, 1974). In that experiment, massive PHE accompanying systemic and pulmonary hypertension was produced by a large intravenous dose of vasoconstrictor agents, such as epinephrine, norepinephrine, angiotensin, and vasopressin. However, the ultimate mechanism of pulmonary volume and pressure loading resulting from systemic vasoconstriction remained unresolved.

In previous studies (Chen et al., 1973; Chen and
Centrogenic Blood Volume and Pulmonary Changes

Chai, 1974), we used a method of impacting a space-occupying mass into the cranium to induce PHE in anesthetized rats. Although intracranial pressure was not measured, the procedure consistently evoked severe systemic and pulmonary hypertension followed by massive PHE within a period of 2-3 minutes. Gross observation, histological finding, and gravimetric analysis revealed that the pulmonary damage was primarily hemorrhagic, i.e., disruption of blood vessels and extravasation of blood cells. Since intracranial compression causes not only arteriolar constriction but also venomotor reaction (Brown, 1956), it is possible that both the systemic resistance and capacitance vessels are involved in causing the blood volume accumulation in the lungs. We advanced our study by using the same method of CC in rats. The purpose was to determine the relative importance of changes in the right and left cardiac output for the production of volume loading, rise in vascular pressures, and pathological changes in the pulmonary circulation.

Methods

General Preparation for Acute Experiment

Male Sprague-Dawley rats, weighing 350-380 g, were used. Each animal was anesthetized with intraperitoneal sodium pentobarbital, 35 mg/kg. Supplemental doses (10-20 mg/kg) were given intravenously to maintain a state of surgical anesthesia. Through a midcervical incision, the trachea was intubated to provide artificial ventilation with ambient air by a Harvard Apparatus rodent ventilator. The ventilatory rate and stroke volume were 50-60 counts/min and 1.5-2 ml, respectively. The vagus nerves were isolated and looped with threads for easy access for subsequent sectioning before CC. Although vagotomy did not significantly affect the degree of PHE induced by CC (Chen et al., 1973), the experiments were conducted in vagotomized rats to eliminate the interference of acute and profound bradycardia. A femoral vein was cannulated for administration of drugs or fluid. A femoral artery was catheterized to measure the SAP with a Statham P23Db transducer. Heart rate (HR) was monitored with a Grass 7P4F tachograph triggered by arterial pulses or ECG signals. The right atrial pressure (RAP) or central venous pressure was monitored with a Statham P23Db transducer through a jugular vein catheter. We used a Grass model 7 polygraph to display these and the other recordings.

Cerebral Compression

The method of CC to produce acute fulminating PHE in rats by impacting a space-occupying mass into the cranium has been described (Chen et al., 1973; Chen and Chai, 1974). In brief, the device consisted of a metal bar placed vertical to the rat's head which was fixed in a stereotaxic instrument. A piece of sponge was attached to the end of the metal bar. After removal of the parietal bones, a plasticine mass (0.2 cm³) was placed first between the parietal cortex and the sponge. We introduced the plasticine mass completely into the cranium within 8 seconds by pressing the metal bar toward the skull.

Regional Weighing

To use the method of regional weighing first described by Fell and Rushmer (1961), we made several modifications in the present experiment. In support of the stereotaxic instrument, a head holder was used for head fixation to minimize body displacement during CC. The animal was also paralyzed with intravenous succinylcholine (2 mg/kg) to avoid spontaneous movements and irregular respiration. We placed two scale platforms, one (1.5 cm wide) underlying the thoracic region and the other (4 cm wide) under the abdominal and hindquarters regions. The borders of these scales were 6-7 cm apart. The center of each scale platform was attached and fixed on top of a Grass FT-10 force-displacement transducer. The latter was situated inside a wooden block and was connected to the Grass polygraph recorder. We calibrated the transducers by placing a known weight on the part of the animal overlying each scale. The experimental design permitted a gross observation of instantaneous distribution of blood volume between body regions above and below the diaphragm.

Measurement of Aortic Flow and Pulmonary Arterial Flow

Rats were instrumented chronically under sterile conditions, artificial ventilation, and pentobarbital anesthesia. A midline thoracotomy was performed through the sternum. An electromagnetic flow transducer (Biotronex BL-6020 to 6035; 2.0 to 3.5-mm i.d.) was placed around the ascending aorta in one group of rats and around the pulmonary artery in another group. A 21-gauge polyethylene tube was inserted into the left atrial appendage to measure the left atrial pressure (LAP) or pulmonary venous pressure in some rats. After the operation, penicillin was given to prevent infection, and the cannula was flushed with heparinized saline to avoid clotting. Sixteen rats (six with aortic flow probes and 10 with pulmonary arterial flow probes) were selected to enter the acute experiment approximately 7 days after surgery. The selection was based on their food intake, general activity, and response to provocation. Blood flow was measured with a Biotronex BL-613 flowmeter. Calibration was done after the experiment by passing blood through the flow transducer at a constant rate (Kumazawa et al., 1969; Doba and Reis, 1973). The LAP was monitored with a Statham P23Db transducer.

Right and Left Heart Bypass

We used a roller pump (American Optical model 16450), an extracorporeal reservoir, and tubing to control the right or left cardiac output in rats under artificial ventilation and after a right or left thoracotomy (2-3 ribs were removed). The bypass per-
fusion system was primed with heparinized blood from donor rats. For the right heart bypass, short pieces of polyethylene tubing were used to cannulate the right atrium (13 gauge) through the atrial appendage, and the pulmonary artery (16 gauge) through the right ventricle. The pulmonary arterial cannula was connected to the outflow side of the pump with Teflon tubing (1/16-inch i.d., 1/8-inch o.d.). A short piece (3 cm) of large bore Silastic tubing was connected to the right atrial cannula to divert venous return into a reservoir, from which blood was pumped to the pulmonary artery at a constant flow rate. The latter was set to maintain SAP close to the level existing before the bypass procedure. Despite frequent failures, a satisfactory preparation was achieved in 10 rats. Adequacy of left ventricular function was verified by observing a constant LAP and a prompt rise in arterial pressure upon a temporary increase in pump flow rate. Pulmonary arterial perfusion pressure (PAP) was measured from the pump outflow tubing via a side outlet near the pulmonary artery. Two types of left heart bypass were performed in a total of 20 rats to keep a constant aortic flow. In one type, blood was drained from the left atrium to a reservoir and was pumped back to the aorta through a carotid and a femoral artery. In the other type, blood was pumped directly from the left atrium into the aorta without passing through a reservoir. LAP was measured via a side outlet near the atrium. The flow rate was adjusted to maintain a prebypass level of arterial pressure which was measured from the other femoral artery. Blood volume inside the reservoir was monitored with a Statham P23V transducer that was connected to the reservoir bottom. Before CC, the reservoir volume and other parameters remained constant for at least 5 minutes. For comparison, CC was done in control experiments (natural circulation) approximately 30 minutes after open-chest surgery. In the bypass preparations, the pulmonary and systemic vascular resistances (PVR and SVR) were calculated from the PAP, LAP, SAP, RAP, and perfusion flow (Q):

\[ PVR = \frac{PAP - LAP}{Q} \]  
\[ SVR = \frac{SAP - RAP}{Q} \]

**Results**

**Regional Weight Changes**

In 10 vagotomized rats, an intense CC evoked acute increases in SAP and HR. Concomitantly, the regional weight changes (AWT) consisted of an increase in thoracic weight and a decrease in weight of the abdomen-hindquarters regions. The changes reached a maximum of 4-6 g above or below the baseline within 20 seconds after CC. Despite a terminal decline in SAP and HR about 3 minutes after CC, the weight changes stayed around the plateau level (Fig. 1). At approximately the end of the hypertensive plateau, pink-tinged frothy fluid came out from the tracheal tube. At postmortem, the lungs showed dark-red discoloration and were swollen and globular in appearance. The pathological changes in the lungs have been described in detail elsewhere (Chen et al., 1973). The lung weight was about three times the normal value (lung index

\[ \Delta WT \]

**FIGURE 1 Changes in SAP, HR, and WT upon CC in the vagotomized rat. The downward deflection marked on the timer tracing indicates the time of placing a space-occupying mass in the cranium. Note the systemic hypertension and tachycardia accompanying an increase in the thoracic weight and a decrease in the abdomen-hindquarters regions. The \( \Delta WT \) are largely irreversible.**
of 1.62 ± 0.24 comparable with the normal value of 0.55 ± 0.08). The early phase of thoracic weight increase was probably the result of intravascular blood redistribution. With the development of PHE, most of the weight changes became irreversible because of blood extravasation in the lungs.

**Imbalance in Right and Left Cardiac Outputs**

Pulmonary arterial flow was measured in 10 rats, and aortic flow in another six rats with chronically instrumented flow probes. LAP was recorded through chronically implanted catheters in eight of the 16 rats. Since we observed little variation in the time course of changes in SAP, HR, RAP, and LAP, these changes were averaged at different times after CC (Fig. 2). The individual and average changes in systemic flow (ΔQ) were expressed as the percentage increase or decrease from the baseline. The latter were 76 ± 8 ml/min for pulmonary arterial flow and 70 ± 11 ml/min for aortic flow. Accompanying the profound rises in SAP and LAP within 40 seconds after CC, the aortic flow decreased dramatically to 45–58% below the baseline. During the first 10 seconds, the pulmonary arterial flow transiently increased by 4–23.2% in four rats, whereas it decreased by 1.6–7.2% in another six rats. Thereafter, the pulmonary arterial flow declined gradually in all animals, reaching an average of −44.5% at 40 seconds. As shown in Figure 2, the overall pattern of imbalance in systemic flows was characterized by a fast fall in aortic flow associated with a slower decrease in pulmonary arterial flow. In this series of experiments, the value of the lung index was 1.58 ± 0.18.

**Right and Left Heart Bypass**

Severe PHE was observed after CC in 10 rats with a right heart bypass. In this preparation with a constant flow perfusion to the pulmonary circulation, the hemodynamic responses to CC included rises in SAP, PAP, and LAP with a decrease in reservoir volume (Fig. 3). In 20 rats with the left

![Figure 2. Changes in SAP (ΔSAP), HR (ΔHR), Q (ΔQ), LAP (ΔLAP), and RAP (ΔRAP) following CC in 16 rats with chronically implanted flow probes. In this and subsequent figures, the bar on the time axis represents the time when an intracranial mass was positioned. The responses to CC are immediate rises in SAP, HR, and LAP. The change in RAP is relatively small. The upper panel of ΔQ depicts the individual changes in aortic flow (dashed lines) measured in six rats and pulmonary arterial flow (solid lines) in another 10 rats. The lower panel of ΔQ shows the average changes. Note the abrupt and dramatic fall of aortic flow in all animals, the transient rise of pulmonary flow in a few rats, and the imbalance in systemic flows during the early stage. The difference between the changes in pulmonary and aortic flows is significant within a period of 40 seconds. *** P < 0.001; * P < 0.05. For detailed description, see text.](http://circres.ahajournals.org/content/36/4/369/F2.large.jpg)
Hemodynamic responses to CC in 10 vagotomized rats with a right heart bypass. ARRV, the change in right reservoir blood volume. With the venous return bypassed through a reservoir and a constant pulmonary arterial inflow, CC causes acute rises in SAP, PAP, and LAP and a decrease in reservoir blood volume. The increase in LAP is slightly greater than the increase in PAP, reflecting a small decrease in pulmonary pressure gradient or PVR.

heart bypassed to keep a constant aortic flow, lung changes were not discernible following CC. The latter evoked a remarkable rise in SAP and slight changes in RAP and reservoir volume in 10 rats with bypass through a reservoir (Fig. 4). In another 10 rats in which blood did not pass through a reservoir, CC elicited systemic arterial hypertension with a transient and slight rise in LAP (Table 1).

In Table 1, we compare the maximal changes in SAP, LAP, and lung index in the various groups of animals. Although systemic arterial hypertension was greatest in the left heart bypass group, the value of the lung index was not different from that of the normal lungs (groups 4 and 5 vs. group 1). In addition, the rise in LAP (4.6 ± 1.2 mm Hg) observed in the left heart bypass group without a reservoir was much lower than that in the control experiments with natural circulation (41.2 ± 7.1 mm Hg). In contrast, the values of ΔLAP and lung index in the right heart bypass group were much higher than those obtained in the control experiments (group 3 vs. group 2). The changes in PVR and SVR were calculated at 20 seconds after CC (Table 2); at that time, the cardiovascular response usually had reached a maximum. In 10 animals with a right heart bypass the PVR increased in only three rats, whereas it decreased in the other seven rats. The average change was a decrease by -0.06 ± 0.09 mm Hg-min/ml from the control of 0.24 ± 0.06 mm Hg-min/ml (Table 2). The change was, however, not statistically significant. In the left heart bypass preparation, the SVR was consistently elevated to 292% of the control (Table 2).

Discussion

Pulmonary hypertension and PHE can be induced after hemodynamic alterations associated with generalized vasoconstriction either of neurogenic origin (Sarnoff and Sarnoff, 1952; Sarnoff and Berglund, 1952; Chen et al., 1973; Doba and Reis, 1973) or caused by pharmacological intervention (Chen and Chai, 1974). In the present investigation, a method of regional weighing allowed us to observe that an intense CC produces an acute increase of blood volume in the thoracic region and an accompanying decrease in areas below the diaphragm. It has been hypothesized that an accumulation of blood in the lungs is the result of a shift of blood from high constrictor area (systemic circulation) to an area of low constrictor potential (pulmonary circulation) (Sarnoff and Sarnoff, 1952; Sarnoff and Berglund, 1952; Chen and Chai, 1974). The results of the present study appear to modify this concept and explain the mechanism of transfer in blood volume between the pulmonary and systemic circulation. The pulmonary volume and pressure loading after CC or perhaps other neurogenic disorders is initiated principally by a profound decrease in left cardiac output. An increased venous return subsequent to a reduction in the systemic vascular

![Figure 3](http://circres.ahajournals.org/)

**FIGURE 3** Hemodynamic responses to CC in 10 vagotomized rats with a right heart bypass. ARRV, the change in right reservoir blood volume. With the venous return bypassed through a reservoir and a constant pulmonary arterial inflow, CC causes acute rises in SAP, PAP, and LAP and a decrease in reservoir blood volume. The increase in LAP is slightly greater than the increase in PAP, reflecting a small decrease in pulmonary pressure gradient or PVR.

![Figure 4](http://circres.ahajournals.org/)

**FIGURE 4** Hemodynamic responses to CC in 10 vagotomized rats with a left heart bypass via a reservoir. ΔLRV, the change in left reservoir blood volume. Note the marked elevation in SAP and the slight change in RAP. The ΔLRV is an initial increase followed by a decrease. However, the changes are slight compared with the ΔRRV in Figure 3.
TABLE 1 Comparison of the Maximal Changes in SAP, LAP, and Lung Index in Various Groups of Vagotomized Rats after CC

<table>
<thead>
<tr>
<th>Group Description</th>
<th>n</th>
<th>Increase of SAP (mm Hg)</th>
<th>Increase of LAP (mm Hg)</th>
<th>Lung index</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Normal lungs (without CC)</td>
<td>20</td>
<td>0.56 ± 0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2) Control (open chest, natural circulation)</td>
<td>10</td>
<td>83.6 ± 14.1</td>
<td>128.8 ± 13.8</td>
<td>1.42 ± 0.19</td>
</tr>
<tr>
<td>(3) Right heart bypass (via a reservoir)</td>
<td>10</td>
<td>128.8 ± 13.8</td>
<td>194.2 ± 20.4</td>
<td></td>
</tr>
<tr>
<td>(4) Left heart bypass (via a reservoir)</td>
<td>10</td>
<td>194.2 ± 20.4</td>
<td>192.6 ± 19.8</td>
<td></td>
</tr>
<tr>
<td>(5) Left heart bypass (without a reservoir)</td>
<td>10</td>
<td>192.6 ± 19.8</td>
<td>4.6 ± 1.2</td>
<td>0.54 ± 0.07</td>
</tr>
</tbody>
</table>

P values

(2) vs. (1) <0.001
(3) vs. (1) <0.001
(4) vs. (1) >0.2
(5) vs. (1) >0.2
(3) vs. (2) <0.001
(4) vs. (2) <0.001
(5) vs. (2) <0.001

Values are means ± SD.

capacity is not important for the genesis of the centrogenic pulmonary pathology.

It has been well documented that arteriolar constriction and increased peripheral resistance are the major hemodynamic events involved in the Cushing pressor response to CC (Cushing, 1901; Brown, 1956; Ducker and Simmons, 1968; Ducker et al., 1968; Chen et al., 1973). Cardiac output may rise or fall, depending on the degree of intracranial hypertension (Ducker et al., 1968; Brashear and Ross, 1970). There is little information with respect to the effect of CC on the venous capacitance vessels or the systemic vascular capacity. In response to a moderate intracranial compression, vasomotor tone in the intestine (Brown, 1956) and venous return through both venae cavae (Rodbard and Stone, 1954) have been shown to increase. To produce an accumulation of blood in the lungs, the pulmonary inflow must exceed the outflow for a period of time. In the present study, we illustrate that the overall pattern of imbalance in right and left cardiac outputs is characterized by an immediate and profound fall in aortic flow accompanying a slower decline in pulmonary arterial flow. A transient rise of pulmonary inflow by about 20% was observed in only three of the 10 rats (Fig. 2). The dramatic decrease in cardiac output in the face of intense systemic vasoconstriction is probably the result of left ventricular overload secondary to tremendous increase in total peripheral resistance (Guyton et al., 1973; Doba and Reis, 1973; Dampney et al., 1979). The imbalance in both sides of the heart and the transfer of blood into the pulmonary circulation can be initiated by acute left ventricular failure without a simultaneous and equal weakening of the right heart (Lindsey et al., 1957) and can be independent of a neurogenic reduction in the systemic vascular capacity (Guyton et al., 1973). In contrast to a marked increase in SVR, the PVR is affected slightly after CC (Table 2). This factor may enable the right heart to pump more blood into the pulmonary circuit as the left heart fails to pump adequate flow out of the lungs. However, at this point, we cannot preclude the possible involvement of an active constriction of systemic capacitance vessels until we examine the results obtained in the heart bypass studies.

The relative importance of changes in pulmonary

TABLE 2 Effect of CC on Cardiovascular Dynamics in Vagotomized Rats with Right and Left Heart Bypass with a Reservoir

<table>
<thead>
<tr>
<th>Group Description</th>
<th>Control (before CC)</th>
<th>Response (20 sec after CC)</th>
<th>Change</th>
<th>% of control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right heart bypass (n = 10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>96.8 ± 7.7</td>
<td>216.9 ± 9.9</td>
<td>+120.1 ± 10.2</td>
<td>223</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>21.2 ± 3.5</td>
<td>73.6 ± 6.6</td>
<td>+52.4 ± 6.4</td>
<td>347</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAP (mm Hg)</td>
<td>3.9 ± 1.7</td>
<td>60.8 ± 7.3</td>
<td>+56.9 ± 7.1</td>
<td>1559</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q (ml/min)</td>
<td>72.5 ± 3.1</td>
<td>(constant flow)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVR (mm Hg·min/ml)</td>
<td>0.24 ± 0.05</td>
<td>0.18 ± 0.08</td>
<td>-0.06 ± 0.09</td>
<td>75</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Left heart bypass (n = 10)

| SAP (mm Hg)                                            | 95.0 ± 6.6          | 279.1 ± 15.7                | +184.1 ± 15.5 | 294 | <0.001     |
| RAP (mm Hg)                                            | 1.3 ± 1.1           | 5.9 ± 2.0                   | +4.6 ± 1.8    | 439 | <0.001     |
| Q (ml/min)                                             | 75.1 ± 3.0          | (constant flow)             |        |              |       |
| SVR (mm Hg·min/ml)                                     | 1.25 ± 0.10         | 3.65 ± 0.28                 | +2.40 ± 0.25  | 292 | <0.001     |

Values are means ± sd.
inflow and outflow for the production of pulmonary volume and pressure loading is evaluated by data obtained in rats with a left or right heart bypass. In the rats with the left heart bypass by which the aortic flow is kept constant and the change in pulmonary outflow is minimized (with a reservoir) or prevented (without a reservoir), CC evokes a marked rise in SAP, whereas little change occurs in pulmonary vascular pressure and lung weight (Table 1). In Figure 4, the slight rise in reservoir volume may reflect a slight increase in venous return. However, this is soon followed by a decrease which probably is consequent to pooling of blood in the systemic arterial tree because of severe arterial hypertension (Shoukas and Sagawa, 1973). Nevertheless, the experiment indicates that, under the condition of a constant aortic flow, a possible increase in venous return is not essential for the production of pulmonary volume and pressure loading. On the contrary the extent of rise in left atrial pressure and the degree of pulmonary pathology after CC are more profound during right heart bypass than with natural circulation (Table 1). Therefore, central to the mechanism of blood mobilization between the greater and lesser circulation is the performance of the left heart, not an active change in the systemic blood reservoir. In essence, the pulmonary volume loading is produced by a backward instead of a forward process. In addition, we observe a significant decrease in reservoir volume in the right heart bypass preparation (Fig. 3). In a similar preparation, the change in reservoir volume is used to represent a change in systemic vascular capacity of the opposite direction; for instance, epinephrine causes reservoir volume to increase, whereas nitroprusside causes a decrease (Mitzner and Goldberg, 1975; Rubin et al., 1979). The correlation of the reservoir volume with the systemic vascular capacity probably is valid only when the pulmonary blood volume and the left cardiac output remain unchanged. Our observation of a decrease in the right heart bypass reservoir volume certainly does not indicate an expansion of the systemic vascular capacity; rather, it may reflect volume pooling and blood loss in the pulmonary circulation and probably in the large arteries due to systemic hypertension (Shoukas and Sagawa, 1973).

Based on a finding that intracranial compression did not cause significant change of PVR in the dog’s lung perfused with constant flow, Lloyd (1973) concluded that the pulmonary circulation did not play an active role in the centrogeneric pulmonary pathology. However, a later study (Hessler and Cassin, 1977) demonstrated active constriction of pulmonary resistance vessels in the neonatal goat as a result of increase in intracranial pressure. In the present study, the hemodynamic data (Table 2) for the right heart bypass indicate that CC causes a slight decrease in PVR, although the decrease is not statistically significant. The change is probably a result of passive dilation due to an elevation of transmural pressure (Carlill and Duke, 1956; Lloyd and Schneider, 1969) that outweighs active pulmonary vasoconstriction, if any. However, we do not mean to suggest that direct sympathetic impulses to the lungs have entirely no effect on the rise of pulmonary vascular pressures in the face of passive volume loading. Under some circumstances, sympathetic effects on the pulmonary circulation may cause a significant decrease in distensibility or capacity, despite no change in resistance (Ingram et al., 1968; Aarseth et al., 1971). It is possible that an active pulmonary vasomotor reaction may not affect the resistive property, but it may alter the pressure-volume characteristics and thereby exaggerate the degree of pulmonary hypertension and pathology. Such a contention cannot be concluded from the data of the present experiments.

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