Factors Influencing Collateral Blood Flow to the Dog’s Lung

By Peter F. Salisbury, M.D., Ph.D., Peter Weil, M.D. and David State, M.D., Ph.D.

The collateral circulation of the lung, i.e., that part of the bronchial flow which drains into the pulmonary veins, was studied by a heart-lung arrangement in which the lesser and systemic circuits of dogs could be perfused separately. In this preparation the collateral supply amounted to 0.5 to 1 per cent of the total arterial flow under approximately normal conditions. The changes in this collateral flow under a variety of experimental conditions were studied. These included variable systemic, venous and pulmonary pressures, lung collapse, air embolism, and actions of CO₂ and serotonin.

The importance of collateral blood flow to the lung has long been recognized. Obliteration of the bronchial arteries is often followed by necrosis of the bronchi and dilatation of the bronchial vessels or increased collateral blood flow to the lung have been reported in certain types of cardiac and pulmonary disease. While there have been reports of the measurement of flow in isolated bronchial arteries, isolated lobes, estimates of bronchial flow in dogs and humans by means of gas analysis data and measurements of bronchial arterial flow in lung-thorax and lung-esophagus preparations the literature does not contain reports of experiments in which the total collateral blood flow to the normal lung was measured. The opportunity for making such direct measurements presented itself with the development of equipment for total body perfusion. While the “heart-lung machine” diverts the entire venous return from the right ventricle and supplies the arterial tree with blood, the lesser circulation can be perfused separately when the pulmonary artery is tied. The experiments reported here report data concerning collateral circulation to the lungs which were obtained with the aid of this technic—separate perfusion of the greater and the lesser circulation.

Methods

Acute experiments were performed on 25 mongrel dogs, 8–30 Kg. in weight. They were anesthetized with pentobarbital sodium, 5 mg./Kg. and given heparin, 2 mg./Kg. intravenously.

The heart-lung arrangement used is shown in figure 1. Pressures in the femoral artery and in a branch of the pulmonary artery were registered with plastic cannulae connected to strain gages, amplifiers and a multi-channel direct writing oscillograph. Pressure in the inferior vena cava was read directly in a plastic tube inserted via a femoral vein. The heart and great vessels were exposed under positive pressure endotracheal respiration by a bilateral trans-sternal thoracotomy through both fourth intercostal spaces. Plastic cannulae for the withdrawal of venous blood were inserted into the right ventricle (R.V.) through the right atrial appendage and into the superior vena cava through a jugular vein. The pulmonary artery (P.A.) was then ligated at its base and, therefore, all venous blood from the right heart was diverted through the heart-lung machine (P₁, O₂, P₂) described elsewhere whence it was returned to the systemic circulation through a femoral or carotid artery. The left ventricle (L.V.) was cannulated at the apex and all blood from it was drained into a graduated reservoir placed 10 cm. below the dog’s spine. Blood from this reservoir was reinjected into the right atrial appendage and into the superior vena cava through a jugular vein. The pulmonary artery (P.A.) was then ligated at its base and, therefore, all venous blood from the right heart was diverted through the heart-lung machine (P₁, O₂, P₂) described elsewhere whence it was returned to the systemic circulation through a femoral or carotid artery. The left ventricle (L.V.) was cannulated at the apex and all blood from it was drained into a graduated reservoir placed 10 cm. below the dog’s spine. Blood from this reservoir was reinjected into the pulmonary artery through a cannula distal to the ligature. With this arrangement the volume of blood which issues from the pulmonary veins through the left heart into the reservoir must be the sum of the volume pumped from the reservoir into the pulmonary artery plus the volume of the collateral circulation to the lungs. When a steady state obtains in this system the volume of blood injected into the pulmonary artery per minute is known and constant; when the blood from the pulmonary veins exceeds the flow to the pulmonary artery the difference must be due to collateral circulation. The quantity of this collateral flow per standard observation period can
thus be read directly from the blood level in the reservoir. In some experiments a recording pH meter measured and registered the pH of the blood going from the machine to the animal or from the reservoir to the lung.

The systemic circulation of the animals was perfused with volume flows ranging from 25 to 70 ml./Kg./min. This resulted in systemic arterial pressures ranging from 40 to 110 mm. Hg systolic. Pressures in excess of this were observed after administration of pressor agents such as phenylcphrine hydrochloride (Neosynephrine) or arterenol. During cardiopulmonary bypass with the machine, leakage of the blood through the aortic valve into the left ventricle was prevented by a clamp on the ascending aorta. When this clamp was applied blood flow through coronary arteries and veins ceased with resulting cyanosis, dilatation and arrest of the heart. After each variation a short period of perfusion of both circulations was necessary to obtain a steady state during which further observations were made.

Using this method, the collateral blood flow to the lungs can be measured consistently over prolonged periods of time, provided certain precautions are observed. The data reported here are taken from animals with intact reflexes and with excellent jaw tone (there is some evidence, not reported here, that damage to the central nervous system may cause changes in the volume of the collateral circulation to the lungs). When factors such as pH are changed the resulting changes in collateral flow do not occur immediately but a period of transition is noted until a new steady state is established. On the other hand, changes in systemic arterial or venous pressures cause immediate changes in the collateral flow to the lungs. During positive pressure respiration the residual blood volume in the left atrium and the left ventricle may vary inversely with the distension of the lungs so that the level of the reservoir will not rise at a steady rate but will resemble a staircase because the flow of blood into the reservoir is temporarily increased when the distending lungs press on the heart. In order to control this factor one must take reservoir readings only during identical phases of the respiratory cycle. All data reported here were taken from significant observations, when all the above precautions were observed and when at least four measurements of the collateral blood flow to the lungs during successive 1-min. periods indicated a steady state.

**Results**

**Variation of Systemic Arterial Pressure and Collateral Blood Flow.** The arterial pressure was varied in 25 dogs by means of changes of the blood flow in the arterial tree or by the injection of pressor agents into the arterialized blood. In each instance there was a direct relationship between the mean arterial pressure and the collateral flow (fig. 2). In several experiments the arterial blood delivery by the machine was changed while the systemic pressure was kept constant by means of hexamethonium. When the arterial blood flow was varied without simultaneous changes of the arterial pressure collateral flow tended to follow the arterial pressure rather than the arterial flow.

The parallelism between the changes in systemic arterial pressure and the simultaneous variations of collateral flow has been consistently observed in every one of the experiments. At control systolic arterial pressures of 90 to 120 mm. Hg the volume of collateral blood flow to the lungs was in the range of 0.5 to 1.0 per cent of the total systemic blood flow when the flow in the pulmonary circuit was of a magnitude comparable to the systemic perfusion volume.

**Variation of Pulmonary Artery Perfusion and Collateral Blood Flow.** In 35 observations other factors were kept constant but the blood flow in the pulmonary circuit was varied by
changing the speed of the pump. No consistent changes in collateral blood flow were noted when the pulmonary perfusion rate varied between 0 and 30 per cent of the total systemic flow; at this rate the collateral flow was about 2-3 per cent of the total systemic flow. At pulmonary flows in excess of 30 per cent of the systemic flow there was an inverse correlation between the collateral and the pulmonary arterial flow to the lungs. When the pulmonary and the systemic flows were of approximately equal magnitude the collateral flow to the lungs amounted to 0.5 to 1 per cent of the total systemic flow (fig. 3).

In several experiments the pulmonary vessels were not perfused and the collateral blood flowing to the lungs was collected through open cannulae tied into the pulmonary artery and into the left atrium or ventricle. When the pulmonary circuits were not perfused, but the systemic circulation was maintained with the machine, part of the collateral blood flowing to the lung issued from the pulmonary artery (retrograde flow) and another part followed the normal course through the pulmonary veins and the left side of the heart into the reservoir. The partition of the outflowing collateral blood between the pulmonary artery and the pulmonary veins was variable and a consistent pattern was not observed.

Venous Pressure. In 11 observations on 5 dogs the venous pressure of the animals was increased by infusion of heparinized blood into the systemic veins while other factors were kept as constant as possible. It was found that in the 11 observations the collateral flow to the lungs increased up to 400 per cent of the control value with simultaneous increases of systemic venous pressure. In the same dogs 9 reductions of systemic venous pressure (decrease of blood volume) were followed by decreases of collateral flow to the control values (fig. 4).

Pulmonary Ventilation and Collateral Flow. In 6 of 10 significant observations (table 1) collapse of the lungs and arrest of positive
Table 1.—Effect of Pulmonary Ventilation on Collateral Flow

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Collateral flow ml./min. Respiration</th>
<th>Arterial systolic pressure mm. Hg Respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>On</td>
<td>Off</td>
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<tr>
<td>227</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>231</td>
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<td>258</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>265</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>266</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>271</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>275</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>276</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Pressure respiration caused a decrease of collateral blood flow to the lungs down to 40 per cent of the control value. When positive pressure respiration was resumed after its arrest the collateral blood flow increased in 5 of 9 observations. There was no significant variation of the arterial pressure during these observations.

Ventilation with 10 Per Cent Carbon Dioxide in Oxygen. In 12 experiments total body perfusion was carried out when the independently perfused lungs were temporarily ventilated with 10 per cent carbon dioxide in 90 per cent oxygen instead of the 100 per cent oxygen used during the control periods. In these experiments the pulmonary blood was passed through a rubber tube which incorporated glass electrodes and permitted registration of the pH of the pulmonary perfusion blood. Upon ventilation of the lungs with the carbon dioxide mixture, a rapid fall of the pH of the pulmonary, but not of the systemic blood, became evident. In 9 of 11 experiments, when the systemic arterial pressure remained constant, the change of respiratory gas mixture from oxygen to 10 per cent carbon dioxide in oxygen resulted in an increase of the collateral blood flow up to 160 per cent above the control values (table 2).

Table 2.—Effect of Inhalation of Ten Per Cent Carbon Dioxide-Ninety Per Cent Oxygen Mixture on pH of Pulmonary Blood and Collateral Flow

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>pH of pulmonary blood</th>
<th>Collateral flow ml./min.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>From</td>
<td>To</td>
</tr>
<tr>
<td>258</td>
<td>6</td>
<td>14*</td>
</tr>
<tr>
<td>262</td>
<td>7.69</td>
<td>7.03</td>
</tr>
<tr>
<td>266</td>
<td>7.74</td>
<td>7.18</td>
</tr>
<tr>
<td>270</td>
<td>7.5</td>
<td>6.7</td>
</tr>
<tr>
<td>273</td>
<td>6.7</td>
<td>7.42</td>
</tr>
<tr>
<td>274</td>
<td>7.85</td>
<td>7.07</td>
</tr>
<tr>
<td>275</td>
<td>7.75</td>
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</tr>
<tr>
<td>274</td>
<td>7.28</td>
<td>7.23</td>
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</tbody>
</table>

* Experiments denoted by * indicate observations in which pulmonary ventilation was changed from 100 per cent oxygen to 10 per cent carbon dioxide-90 per cent oxygen; in others, ventilation was changed from 10 per cent carbon dioxide-90 per cent oxygen to 100 per cent oxygen. In experiments below line pulmonary ventilation was constant and machine ventilation was varied.

When the ventilation of the lungs with carbon...
dioxide mixture was discontinued and when
ventilation with pure oxygen was resumed the
collateral flow decreased in 8 of 11 significant
observations.

Hypercapnia and Respiratory Acidosis. When
the separately perfused lungs were ventilated
with 100 per cent oxygen, but the heart-lung
machine supplied with 10 per cent carbon di-
oxide in 90 per cent oxygen, instead of the
usual pure oxygen, significant and consistent
changes of the collateral blood flow to the
lungs were not observed (exp. 269, 270, 273,
274, table 2).

Serotonin Injection into the Pulmonary Ar-
tery.* In 4 experiments 1-10 mg. serotonin
were injected into the separately perfused pul-
monary circuit when other factors were held
constant. This caused the well-known pro-
nounced increase of pulmonary arterial pres-
sure, but was not followed by marked changes
in collateral blood flow to the lungs in 2 cases,
and resulted in complete suppression of col-
lateral blood flow in 2 other observations. In 3
of the 4 experiments a minor decrease of the
fenoral artery pressure was observed after in-
jection of serotonin into the separate pulmo-
nary circuit.

Serotonin Injection into the Systemic Circula-
tion.* In 7 of 9 significant observations injec-
tions of 10 mg. serotonin into the arterial cir-

cuits of the heart-lung machine caused a pro-
nounced, sustained rise of the collateral blood
flow to the lungs. The resulting elevations of
collateral flow remained for periods up to 60
min. and diminished only gradually. Repeated
administration of serotonin caused further in-
creases in collateral flow. Systemic administra-
tion of serotonin caused increased collateral
flow even when "local" injection of serotonin
into the pulmonary arteries had produced no
change of collateral flow in the same animal
and was usually followed by a slight transitory
rise in systemic arterial pressure and by pro-
nounced, sustained elevation of pulmonary ar-
tery pressure.

Air Embolism.* In 5 of 6 significant observa-
tions on 3 dogs embolization of the pulmonary
arteries with air resulted in significant in-
creases of collateral blood flow to the lungs,
when other factors were kept constant. Air
embolism was characterized by marked, pro-
longed increases of the pulmonary artery pres-
sure.

Discussion

When the lesser circulation is perfused sepa-
rately from the systemic circuits, as in the
present investigations, an increase in the blood
volume of the lesser circulation can come only
from blood vessels which connect the two sys-
tems. In our experiments these connections
are limited to those with the bronchial vessels.
When blood is injected from the heart-lung
machine into the arterial tree and when the as-
cending aorta is clamped there is no coronary
flow and therefore no Thebesian venous return
to the left side of the heart. It is therefore felt
that communications between the systemic
and pulmonary circulations via the coronary
circulation and via incompetent aortic valves
did not exist and therefore did not introduce
ers into our system.

The complete myocardial ischemia and ar-
rest of the heart beat which obtained in our
experiments would seem to preclude observa-
tion of cardiogenic reflexes which might in-
fluence collateral circulation to the lungs.

The term "collateral blood flow to the lungs" was
used deliberately inasmuch as our method
is capable of measuring only that part of the
bronchial artery flow which drains into the
pulmonary veins, but not the portion which
flows into the systemic venous system.

Our data indicate that under control condi-
tions in which normal or near normal systemic
blood pressure existed 0.5-1 per cent of the
total arterial flow is carried into the lungs by
way of the bronchial collateral circulation.

This is comparable to previous estimates.4,7,8

Our data also confirm earlier investigations
which described the direct relation between
the systemic arterial pressure and collateral
blood flow to the lungs.4,8

Indeed, we showed that the hemodynamic
effects of increasing the pressure head at the
ostia of the bronchial arteries outweigh any
contraction of the bronchial arteries which
may occur as a result of pressor agents. Pre-

* Tabular data of these observations may be ob-
tained from the author on request.
Previous studies which suggested an inverse relationship between pulmonary artery flow and collateral blood flow to the lungs were also confirmed.

Our data offer no proven explanation for the increased collateral blood flow to the lungs which was observed following increases in systemic venous pressure. However, a logical explanation suggests itself: Elevation of venous pressure may cause a reversal of flow in the bronchial veins and in the drainage of systemic venous blood into the pulmonary channels. In the open chest, collapse of the lung through abrogation of artificial respiration may compress the bronchial channels, resulting in the reduction of collateral flow. The effect of carbon dioxide is obviously due to its local action; addition of carbon dioxide to the systemic circulation sufficient to produce systemic, but not pulmonary acidosis, was without effect on the collateral flow. Other investigators have also shown that ventilation of the lungs with carbon dioxide mixtures causes pulmonary vasoconstriction.

The reason for the opposite effects of serotonin when injected systemically or locally is not clear. Its systemic injection may increase collateral flow through a neurogenic mechanism which overrides constriction of the pulmonary bed. Local administration, on the contrary, contracts the pulmonary vasculature first and may constrict the bronchi to such an extent that the collateral vessels are secondarily constricted. The increase of collateral flow after air embolism and its decrease after serotonin offers evidence that elevation of pulmonary arterial pressure per se does not affect collateral blood flow but that the mechanical obstruction of pulmonary blood flow can increase collateral flow. The effect of pulmonary embolization in collateral blood flow may be comparable with the effect of reduced pulmonary artery perfusion. Whether the increased collateral flow to the lungs in chronic disease is mediated by any of the factors shown to cause acute changes would seem to deserve further investigation.

**Summary**

Collateral circulation to the lungs was measured by a technic utilizing independent perfusions of the systemic and pulmonary circulations. This method permitted independent variation of factors.

The following conclusions were reached: with blood pressures in normal ranges the anastomotic channels between bronchial arteries and pulmonary veins carry 0.5 to 1.0 per cent of the total arterial blood flow per minute. The magnitude of collateral blood flow to the lungs is directly related to systemic arterial pressure. Changes in pulmonary artery flow rate did not consistently influence collateral blood flow to the lungs at pulmonary flow rates below 30 ml./Kg./min. At higher pulmonary flow rates there was an inverse relationship between flow in the pulmonary artery and collateral flow. Increases in systemic venous pressure resulted in parallel increases of the collateral blood flow to the lungs. Deflation of the lungs in the open chest caused a decrease in bronchial arterial flow that can be as high as 50 per cent of control values.

The use of 10 per cent carbon dioxide in oxygen to ventilate the lung (but not the pump oxygenator) increased bronchial flow markedly over control values when 100 per cent oxygen was used. Serotonin markedly increased collateral flow when the drug was injected into the systemic circuits but decreased it when injected into the pulmonary circuit. Air embolism resulted in augmentation of collateral blood flow to the lungs.
collateral de sanguine al pulmones quando le velocitate del fluxo pulmonar esseva infra 30 ml per kg per min. Con plus alte velocitates, un relation inverse esseva constatate inter le fluxo in le arteria pulmonar e le fluxo collateral. Augmentos del systemic pression venose resultava in augmentos parallel del affluxo collateral de sanguine al pulmones. Le deflation del pulmones in le thorace aperte causava un reduction del fluxo broncho-arterial per usque a 50 pro cento del valores de controlo. Le uso de 10 pro cento de bixoxyde de carbon in oxygeno pro ventilar le pulmon (sed non le pumpa oxygenator) augmentava le fluxo bronchial marcatemente in comparation con valores de controlo obtenite con le uso de 100 pro cento de oxygeno. Serotonina augmentava le fluxo collateral marcatemente quando le droga esseva injectite in le circuitos systemic sed reduciva lo quando illo esseva injectite in le circuito pulmonar. Acor-embolia resultava in un augmento del affluxo collateral de sanguine al pulmones.

REFERENCES

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