Responses of the Bronchial Veins in a Heart-Lung-Bronchial Preparation

WITH SPECIAL REFERENCE TO A PULMONARY TO BRONCHIAL SHUNT

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Almost all previous attempts to study the bronchial circulation have been limited to measurements of blood flow in the bronchial arteries and bronchopulmonary anastomoses. There have been two studies devoted to estimations of blood flow in the bronchial veins of the normal dog. In 1931, Berry and Daly perfused in dogs either the posterior bronchial artery of one lung or the entire aortic segment from which the bronchial arteries originate. Perfusion of the pulmonary artery was omitted temporarily to allow collection of outflow of blood into both atria. In each of four dogs, the allocations of the bronchial arterial blood were as follows: 12, 18, 30, and 39 per cent into the right atrium via the bronchial veins, and the remainder into the left atrium via the bronchopulmonary venous anastomoses. A second series of isolated right-lung preparations perfused simultaneously through the pulmonary artery and bronchial artery revealed that, in three dogs, 18, 20, and 87 per cent of bronchial arterial blood, respectively, drained into the right atrium via the bronchial veins. The considerable variation in distribution of bronchial arterial blood reported in both studies is probably because some of the bronchial arterial blood passes through adjacent mediastinal structures and finds its way to the right atrium without actually supplying lung tissues.

The experiments reported herein were intended to obtain direct and continuous measurements of bronchial venous flow in a heart-lung preparation with suitable modifications. The relationships of bronchial venous flow to bronchial arterial flow, bronchomotor tone, and pulmonary arterial pressure have been explored in an experimental preparation in which the central autonomic control has been excluded. Such chemical stimulants to the peripheral autonomic nervous pathways as levarterenol, epinephrine, acetylcholine, and others have been tested. Previously reported measurements of flows in the bronchopulmonary anastomoses and the bronchial artery have revealed that the bronchial veins are more reactive than the bronchopulmonary anastomoses to a variety of chemical agents. The experiments reported herein lend additional support to this generalization.

Methods

Mongrel dogs were anesthetized with morphine sulfate (2 mg./Kg.) and chloralose (70 mg./Kg.). The heart-lung preparation was performed in the way described by Knowlton and Starling, with appropriate modifications to maintain blood flow in the bronchial circulation (fig. 1). The arterial cannula was inserted into the left subclavian artery and the Starling resistance set at 100 to 140 mm. Hg. The venous reservoir was at a level of 15 to 35 cm. above the right atrium, and the venous cannula was inserted into the inferior vena cava. The temperature of the blood entering the right atrium was between 38 and 39 C. A Shipley-Wilson rotameter (P1) was inserted proximal to the Starling resistance for direct measurement of the systemic flow (cardiac output minus coronary flow). The upper part of the descending aorta was isolated and all the branches arising from it were ligated except the posterior bronchial arteries to both lungs.
The bronchial circulation is maintained by blood from the aorta, flowing via a flowmeter (F₁) attached to the aortic pouch and bronchial arteries. Bronchial arterial pressure is measured by a transducer (T) and aortic flow by a rotameter (F₄) attached proximal to the Starling resistance. Bronchial venous flow is collected by a cannula in the azygos vein, recorded by a third rotameter (F₃), and automatically transferred into the venous reservoir.

The blood for perfusion of the aortic pouch was diverted from the systemic circuit by means of a lateral outlet between the systemic rotameter and the Starling resistance, and a second rotameter (F₂) was inserted in the connection to allow recording of the bronchial arterial blood flow. The perfusion pressure was measured by a Statham transducer connected to the entrance of the aortic pouch. A Cournand catheter was inserted through the superior vena cava, either into the right ventricle or the pulmonary artery, and was connected to a second transducer for measurement of blood pressures.

The azygos vein was ligated above the diaphragm and a cannula inserted at its junction with the superior vena cava. The azygos vein blood flow, representing the bronchial venous flow, passing through a third rotameter (F₃) was automatically returned to the venous reservoir by a mechanical device consisting of a reservoir and pump. The bronchomotor tone was estimated by a modification of the Konzett-Rössler method, consisting essentially in recording the ventilation overflow by means of a pneumotachograph. The overflow was, in turn, integrated in an analog computer to volume in milliliters.

These measurements (bronchial arterial blood pressure, systemic, bronchial arterial, and bronchial venous flows, right ventricular or pulmonary arterial pressure, and ventilation overflow) were recorded in a Sanborn polyviso. The drugs were injected either into the aortic pouch (direct bronchial arterial) or at the entrance of the cannula in the inferior vena cava (intravenous), the total volume being less than 1 ml. in every injection.

**Results**

The six successful heart-lung preparations are summarized in Table 1. The mean control value for the group was 45 per cent of bronchial arterial blood draining into the bronchial veins. This figure is based on a wide range of distribution, from 32 to 71 per cent, but four of the dogs had values of 32 to 34 per cent. An attempt will be made to explain such a wide variation of values (see Discussion).

**PROGRESSIVE RISES IN BRONCHIAL ARTERIAL PRESSURE**

Each of the six dogs was initially subjected to an increase in resistance to aortic flow by stepwise increases in pressure exerted on the Starling resistance. Each pressure level was maintained for three to five minutes. As expected, bronchial arterial flow increased at each successive step (Fig. 2, left). The increase in flow is not proportionate to the increase in pressure. This relationship can be expressed quantitatively as bronchial arterial resistance by dividing bronchial arterial pressure by its corresponding flow, with the assumption that the bronchial venous pressure is unchanged. This is a sound assump-
HEART-LUNG-BRONCHIAL PREPARATION

Effects of progressive increases in pressure exerted on the Starling resistance. (Left panel) Each dot represents the bronchial arterial flow at a specified level of bronchial arterial pressure. Connected dots are derived from the same dog. (Right panel) Each dot represents the bronchial arterial resistance calculated by dividing bronchial arterial pressure by the corresponding bronchial arterial flow.

Because the venous outflow was collected in an open reservoir and the height of the collecting tube was kept constant. Such a calculation of bronchial vascular resistance showed that an increase in pressure of about 50 mm. Hg initially caused a reduction in resistance, but a further rise caused no changes. The blood pressure level above which resistance is unchanged varied from 60 to 180 mm. Hg in each of the six dogs (fig. 2, right).

BRONCHIAL VENOUS FLOW

The corresponding venous changes elicited by an increase in bronchial arterial pressure proved to be surprisingly different from bronchial arterial flow described above. There was a progressive increase in venous flow in four dogs, but two other dogs behaved differently. One of them (no. 4) showed an increase when blood pressure was elevated from 50 to 80 mm. Hg, but a decrease beyond this level. The other dog (no. 5) showed no increase in venous flow (fig. 3, left).

BRONCHIAL VENOUS FLOW EXPRESSED AS PER CENT OF BRONCHIAL ARTERIAL FLOW

The response of venous flow to changes in arterial pressure became more consistent if the results were expressed in terms of its fraction of total arterial inflow (fig. 3, right). All dogs showed a reduction in bronchial venous fraction as bronchial arterial pressure increased. If one starts from the 100 mm. Hg pressure level, a reduction in pressure caused an increase in fraction, whereas a rise caused a decrease. Another manner of expressing the relationship is that the increase in bronchial arterial flow brought about by an increase in bronchial arterial pressure is usually greater than the increase in bronchial venous outflow. This means that the bronchopulmonary fraction of bronchial arterial flow was correspondingly increased to a greater extent than the bronchial venous fraction, but the bronchopulmonary fraction was not measured directly in the heart-lung-bronchial preparation.

ROLE OF PULMONARY ARTERIAL PRESSURE

The increase of pressure in the Starling resistance induced a rise in bronchial arterial and pulmonary arterial pressures. In two dogs, the pulmonary arterial pressure was intentionally increased by elevation of the height of the venous reservoir, which in turn augmented pulmonary blood flow without increasing bronchial arterial pressure. When the amounts of bronchial venous flow are compared during both maneuvers, it appears that...
Effects of progressive increases in pressure exerted on the Starling resistance and of elevation of venous reservoir to increase pulmonary blood flow. Each point represents bronchial venous flow at the corresponding level of pulmonary arterial pressure. Left panel is for dog no. 5 and right panel for dog no. 6.

at the same level of pulmonary arterial pressure, venous values are about equal (fig. 4, open symbols). These results suggest that the bronchial venous flow is influenced by pulmonary arterial pressure; the details were examined by interruption of bronchial arterial inflow.

INTERUPTION OF BRONCHIAL ARTERIAL INFLOW
In a heart-lung-bronchial preparation, blood collected in the bronchial veins in the absence of bronchial arterial flow would represent pulmonary vascular blood reaching the bronchial veins (pulmonary to bronchial shunt). The amount of blood collected from the bronchial veins in the presence of the bronchial blood flow was reduced by 30 to 50 per cent when the bronchial arteries were occluded. This means that about 50 to 70 per cent of bronchial venous flow arises from the blood in the pulmonary circulation; this relationship is true when pulmonary arterial pressure is increased by elevation of either the venous reservoir or the pressure on the Starling resistance. When both types of procedures were compared in each of two dogs, the bronchial venous flow values were about equal for the same level of pulmonary arterial pressure (fig. 4). The amount of pulmonary vascular blood which reaches the bronchial veins is dependent on the level of pulmonary arterial pressure, rather than on pulmonary blood flow. When pulmonary arterial pressure...
arterial pressure is elevated, the pulmonary to bronchial shunt is reduced. An attempt will be made to explain the mechanisms involved (see Discussion).

**EPINEPHRINE**

The bronchial arterial injection of 2 μg. of epinephrine elicited a fall in both the bronchial arterial flow and bronchial venous flow (table 2). The percentage reduction in the bronchial venous flow was greater in two dogs and less in the other four dogs than the reduction in arterial flow. One difference seen in all dogs with that the reduction in bronchial venous flow always outlasted the reduction of bronchial arterial flow (fig. 5, left).

**NOREPINEPHRINE**

The corresponding effects of norepinephrine were similar to those described for epinephrine. Like epinephrine, norepinephrine caused a reduction in bronchial arterial and venous flows when injected intra-arterially, and the duration of reduction in venous flow was longer than that of arterial inflow (fig. 5, middle, and table 2). The differences in behavior of both flows were further demonstrated by the intravenous injection of epinephrine (2 μg total). In two dogs, there was no reduction in bronchial arterial flow, but there was a reduction in bronchial venous flow. The latter is another manifestation that bronchial venous flow is more sensitive than bronchial arterial flow to norepinephrine.

**ISOPROTERENOL**

This sympathomimetic amine caused increases in bronchial arterial and venous flows, and the latter outlasted the former (fig. 5, right, and table 2). Similar effects were derived from acetylcholine and histamine (fig. 6 and table 2).

**BRONCHOMOTOR TONE**

The results of the injection of various agents directly into the bronchial artery offered an opportunity to compare vascular changes with those of bronchomotor tone. Isoproterenol, norepinephrine, and epinephrine caused a reduction in ventilation overflow which can be interpreted to mean...
FIGURE 6
Bronchial arterial injections of acetylcholine and histamine.

FIGURE 7
Bronchial arterial injections of DMPP before and after atropine.
bronchodilatation, but the vascular effects on the bronchial arteries were dilatation for the first one and constriction for the other two. Acetylcholine and histamine caused an increase in ventilation overflow, i.e., bronchoconstriction, but the vascular effects were consistently dilatation. It was not possible to dissociate these two types of actions by such agents. The results derived from 1,1-dimethyl-4-phenylpiperazinium (DMPP) helped in the dissociation in the following manner: DMPP caused bronchoconstriction and vasodilatation, but after atropine, DMPP still caused vasodilatation unaccompanied by bronchoconstriction (fig. 7).

Discussion

The heart-lung-bronchial preparation was designed primarily to investigate the factors controlling bronchial venous flow without the use of perfusion pumps. The features of the bronchial venous flow are as follows:

1. The blood flow collected in the bronchial veins of a heart-lung-bronchial preparation does not consist entirely of blood from the bronchial artery. When the latter is interrupted, the remaining 50 to 70 per cent (of venous flow prior to interruption) arises from the pulmonary circulation. The passage of a small proportion of pulmonary arterial blood into the bronchial veins has been previously demonstrated by Daly and von Euler and by Aviado et al. in dogs' lungs in which the pulmonary and bronchial arteries were perfused by separate pumps.

2. The bronchial venous fraction arising from the bronchial artery cannot be calculated simply by measuring both flows, as represented in table 1. Of the wide range of values from 32 to 71 per cent, the lowest figure would probably represent the best estimate in which the pulmonary arterial blood fraction to the bronchial vein is at its minimum. In other experiments in which bronchial arterial flow and bronchopulmonary flow are measured directly, the average figure is 67 per cent of bronchial arterial flow as bronchopulmonary flow, i.e., 33 per cent of bronchial arterial flow to bronchial veins. In both types of experiments, about one-third of bronchial arterial flow drains into the bronchial veins and two-thirds into the bronchopulmonary anastomoses.

3. The bronchial venous flow in a heart-lung-bronchial preparation can be influenced by raising either bronchial arterial pressure or pulmonary arterial pressure (induced by an increase in venous return). The variability in response seen in six dogs appears to depend on two components of bronchial venous flow which change in opposite directions: (a) an increase in the fraction from bronchial arteries; and (b) a decrease in the fraction from the pulmonary vessels (pulmonary to bronchial shunt). The former mechanism is associated with the increase in bronchial arterial flow and the latter with an increase in pulmonary arterial pressure. The mechanisms to explain a reduction in pulmonary to bronchial shunt when pulmonary arterial pressure is increased have not been investigated. It is difficult to conceive of a local mechanism in the lungs in which a rise in pulmonary arterial pressure would lead to a reduction in pulmonary to bronchial shunt. A reflex mechanism is another alternative, but the extrinsic nerves are not likely to be viable in the lungs. The remaining possibility is a reflex involving intrinsic nerve mechanisms, similar to the pulmonary vasoconstriction which can be induced in an embolized lung even after surgical excision of extrinsic nerves.

4. The bronchial venous flow is more sensitive than the bronchial arterial flow to vasoconstrictors such as norepinephrine and epinephrine. The difference is largely on the longer duration of reduction in flow in the bronchial vein. It is not possible to differentiate whether the reduction in bronchial venous flow involves the fraction from the bronchial arteries or from the pulmonary vessels. However, in experiments in anes-
thetized dogs, the injection of such sympathomimetic amines caused a reduction in bronchial arterial flow with an increase in bronchopulmonary flow. This combination of results has been interpreted to mean that the bronchial veins are more sensitive than the bronchopulmonary anastomoses, so that it is probable that the reduction in bronchial venous outflow in the heart-lung-bronchial preparation is due to a reduction in the fraction from the bronchial arteries, with shunting of bronchial arterial flow to the bronchopulmonary anastomoses.

5. The responses of bronchial venous and arterial flows to various agents are independent of changes in bronchomotor tone. Bronchodilators such as epinephrine and isoproterenol induce vasoconstriction and vasodilatation, respectively, on the bronchial vessels. Bronchoconstrictors such as acetylcholine, histamine, and DMPP produce vasodilatation, but it is possible to dissociate the responses to DMPP after administration of atropine. After parasympathetic blockade, DMPP fails to induce bronchoconstriction, but is still able to dilate the bronchial vessels. Considering that DMPP is an autonomic ganglion stimulant, the bronchoconstrictor action should be interpreted as the result of the stimulation by DMPP of parasympathetic ganglia which can be readily blocked by atropine. The vasodilator effect which persists after atropine could be due to stimulation of different nervous pathways or to a direct action on the vessels, as reported by Winbury for the arteries of the hind limb of the dog. All these results point to an independence in the occurrence of bronchomotor and bronchial vascular changes. They further suggest that changes in bronchial venous flow cannot be brought about by a primary bronchoconstriction or bronchodilatation.

Summary

Blood collected from the bronchial veins of a heart-lung-bronchial preparation consists of two components: (a) fraction from the bronchial arteries, and (b) pulmonary to bronchial shunt. It is estimated that the latter is more than half of total bronchial venous flow. The pulmonary to bronchial shunt is reduced by procedures which increase pulmonary arterial pressure. An intrinsic nervous reflex mechanism is suggested to explain such a response, particularly because the bronchial veins are more sensitive than the bronchial arteries to the vasoconstrictor action of epinephrine and norepinephrine, and to the vasodilator action of isoproterenol, acetylcholine, histamine, and DMPP. Alterations in bronchial venous flow induced by such chemical agents are independent of bronchoconstriction or bronchodilatation.

References

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