Experimental Reversal of Capillary Blood Flow

By Ray Heimbecker, M.D., Vivien Thomas and Alfred Blalock, M.D.

Beck, Sciaroni and others have made clinical and experimental attempts to reverse the direction of flow of blood across the capillary bed by the anastomosis of arteries and veins. The present authors have shown by the microscopic observation of capillaries in acute experiments on cats, dogs and rabbits that a reversal of blood flow in mesenteric capillaries will occur following the connection of an artery to a vein provided the collateral arteries and veins are obstructed. Furthermore, it was shown that blood flowing in a reverse direction through capillaries loses oxygen.

A NUMBER of recent investigations in vascular surgery have been based on the hypothesis that reversal of blood flow in capillaries is possible. Experimental and clinical attempts have been made to reverse the direction of the flow across the capillary bed by the anastomosis of an artery to the venous side of the capillary bed. Several groups of investigators have anastomosed a systemic artery to the coronary sinus of the heart in attempts to cause a retrograde flow of blood through the capillaries of the myocardium.1-4 Sciaroni5 and Beck6 have created an anastomosis between the carotid artery and jugular vein in an attempt to increase the blood flow to the brain. Efforts to increase the arterial blood supply to the leg were made by Johnston and associates7 in operations in which they anastomosed the proximal end of the femoral artery to the distal end of the femoral vein.

Both the clinical and experimental studies have given results which are difficult to interpret. The present study was undertaken in an effort to determine whether reversal of the capillary blood flow is physiologically possible.

The capillary bed was observed microscopically both before and after reversal of the circulation in the living tissues of the experimental animal. In addition to the observations on the capillaries, the rate of blood flow and the oxygen consumption of the part were determined.

Methods

Cats were used in most of the experiments and additional studies were performed on dogs and rabbits. Anesthesia was produced by the intraperitoneal injection of Nembutal. Several regions of the body were studied in preliminary experiments but we shall report only those which were made on the mesenteric blood vessels since they yielded the most conclusive results. A short low midline incision was made and the terminal ileum was delivered, thus exposing the mesenteric blood vessels of this area. The blood vessels of the ileocecal region were followed back to the root of the mesentery and large branches of both the mesenteric artery and vein were prepared for cannulation. The femoral artery and vein were similarly prepared. The method is illustrated in figure 1.

The cannulas consisted of polyethylene tubing of suitable caliber. The largest tubing that would fit the blood vessel was used in each case, the outside diameter varying from 2 to 4 mm. The cannulas were prepared by beveling the tips with a sharp scalpel, after which they were treated with DriSilicone. Short couplers of larger tubing, which fitted snugly over the cannulas, were used to connect them together. As can be seen in the illustration in figure 1, ligatures of braided silk were placed around the bowel and its remaining mesentery at the extreme ends of the segment of bowel under study, in order that the collateral blood supply could be eliminated when desired. Shortly before the cannulas were introduced, the animals were heparinized.

The quartz rod technic8 was used for the illumination of the blood vessels of the mesentery and a 500 Watt light source was employed. A constant gentle flow of Ringer's solution at 39 C. kept the tissues moist and warm. Motion of the tissues under study was prevented by the use of a small plastic

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holder. The capillaries were observed using a binocular microscope, and from time to time were photographed on Kodachrome film employing a Kodak special movie camera. The rate of blood flow of the bowel segment was determined by temporarily disconnecting the venous cannula and timing the flow of blood. The oxygen content of the arterial and venous blood was determined by the method of Van Slyke and the rate of blood flow and the arteriovenous oxygen difference were used in computing the oxygen consumption. Pressures in the mesenteric artery and vein were determined by means of small sidearms on the cannulas and a Sanborn Electromanometer.

With the cannulas in place as shown in figure 1, studies were made with the blood flow in the normal direction, that is, from femoral artery to mesenteric artery through the capillaries and returning through the mesenteric and femoral veins. Following this, a retrograde perfusion was produced by attaching the arterial inflow cannula to the mesenteric vein, and the outflow cannula to the mesenteric artery. Under this latter condition, the arterial blood was directed at arterial pressure into the venous end of the capillary and was drained away from the arterial end of the bed. Thus the capillary bed of an area was studied with the flow directed in the normal direction or in the reverse direction, and the direction of flow was altered as desired.

RESULTS

Thirty-one experiments were performed on 19 cats, 3 dogs, and 3 rabbits. Excellent forward capillary blood flow was observed in twenty-seven experiments during the time that the flow was in the normal direction and in seventeen of these good reversal of capillary flow was seen when the inflow was reversed. This reversal of capillary flow was demonstrated both by direct microscopic observation and by motion pictures. Failure of the capillary flow to reverse in ten studies was usually due to incomplete elimination of the collateral arterial inflow to the part, although in some instances there was no adequate explanation.

Fig. 1. Showing the experimental procedure. Part of the small intestine has been delivered through an abdominal incision. A mesenteric artery and vein have been isolated. These vessels are connected by cannulas to the femoral artery and vein. Braided silk ligatures occlude the intestines and collateral blood vessels. The capillaries of the mesentery are studied microscopically.
The longest period that reversal of blood flow was observed was 57 minutes.

The rate of flow and the oxygen consumption of the segment of intestine were determined in ten experiments. The average flow was 4.42 cc. per minute with forward flow, and 3.07 cc. per minute with reverse flow. The oxygen consumption was 0.3 cc. per minute with forward flow and 0.17 cc. per minute with reverse. These figures are given in table 1. Even gross ob-

Table 1.—Capillary Studies

<table>
<thead>
<tr>
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<th>Normal perfusion</th>
<th>Reverse perfusion</th>
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<tbody>
<tr>
<td>Excellent Microscopic Capillary Blood Flow</td>
<td>27 exps.</td>
<td>17 exps.</td>
</tr>
<tr>
<td>Average Rate of Blood Flow cc./min</td>
<td>4.42</td>
<td>3.07</td>
</tr>
<tr>
<td>Average Tissue Oxygen Consumption cc./min</td>
<td>0.3</td>
<td>0.17</td>
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Fig. 2. Showing the effect of collateral pathways on perfusion pressure. A. Pressure in mesenteric artery with flow in normal direction, collaterals open. B. Pressure of inflowing blood in mesenteric vein with retrograde flow, collaterals open, followed by elevation in inflow pressure that occurs when collaterals are tied.

The effects of opening and closing the collateral pathways on the perfusion pressure are shown in figure 2.

Discussion

Two other types of experiments will be commented upon briefly. An attempt was made to produce a chronic reversal of flow in a segment of bowel of heparinized animals but either death occurred or thrombosis at the site of the inflow cannula took place. In other animals, the terminal aorta and the inferior vena cava were severed, the proximal end of the aorta was anastomosed to the distal end of the vein and the distal end of the aorta to the proximal end of the artery but death occurred within 24 hours. We are not certain as to the cause of death.

Transient reversal of the direction of capillary blood flow has been noted previously by several observers. Chambers and Zweifach* reported this phenomenon in the normal capillary bed as a result of a rhythmic variation in the amount of entering blood. Bigelow, Heimbecker and Harrison10 reported reversal of blood flow in capillaries due to alterations in hemodynamics associated with intravascular agglutination of blood. The present experiments show that at least temporary retrograde flow in the capillary bed can be produced by transposing the arterial inflow and the venous outflow. However, the studies indicate that this retrograde flow occurs only if the collateral arterial pathways are closed. This finding may be due in part to the resistance to inflow imposed by the cannulas. The presence of a plexus of collateral veins provides a shunt mechanism through which the blood in a mesenteric vein at an artificial arterial pressure can escape directly into the general venous return, thereby avoiding the capillary bed. The studies reported in figure 2 support this statement. At any rate, this finding in studies on the intestinal tract suggests that the presence of uninterrupted collateral arteries and veins in the heart, brain, or extremity would exert the same inhibitory influence upon the reversal of capillary blood flow. Moreover, if reversal is to occur in these organs, the blood must leave by way of the organs’ arteries.
The tissue oxygen consumption fell from an average of 0.3 cc. per minute during normal perfusion to an average of 0.17 cc. during retrograde perfusion. However, in three experiments there was no decline. The figures should not be compared too critically for it should be remembered that a mesenteric artery and its adjacent vein do not necessarily connect with identical areas of the capillary bed. The figures do show that the tissues will take up oxygen from blood flowing through its capillaries in a reverse direction.

**Summary**

It has been shown in acute experiments on cats, dogs and rabbits that a reversal of blood flow in mesenteric capillaries will occur following the connection of an artery to a vein providing the collateral arteries and veins are obstructed. The blood must be permitted to leave the area by means of the mesenteric arteries. Blood flowing in a reverse direction through capillaries loses oxygen.

**REFERENCES**


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