The removal of indifferent material is easy to bring about, and occurs with much greater regularity than the precipitation of the antibody itself at a more acid point as described in the preceding paper. It would therefore seem to offer a more practical method for partial purification of the antibody.

The material and mice used in these studies were generously furnished by the H. K. Mulford Co., Glenolden, Pa., through the courtesy of Dr. F. M. Huntoon.

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Observations on the extra-cardiac circulation.*

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Experiment (I)

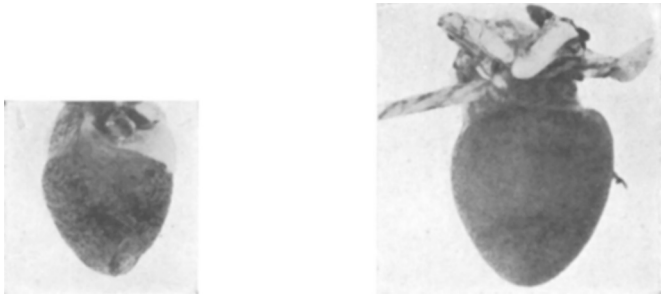
If the bulbus arteriosus of the frog is ligated, the heart gradually dilates. In about ten minutes the heart has more than doubled its size. (Fig. 1.) The heart muscle appears more cyanotic. If at the same time the peripheral circulation in the frog's web is observed microscopically, it is seen that the blood keeps moving in the capillaries for 5-10 minutes after aortic ligature. While corpuscular flow is slower, it simulates the normal as far as direction is concerned, going from the arteries to capillaries, then to the veins.

Thus the enlargement of the heart after aortic ligation is associated with the movement of blood from the large arteries to the capillaries, and from these back to the heart. It appears as though co-ordinated contractions of the vessels themselves were capable of circulating the blood along its usual course. This vascular mechanism comes into play when the cardiac output is prevented by ligation of the aorta.

If now the vessels of a second frog are injured quite another reaction takes place following the ligation of the aorta. In order to produce a profound vascular injury, the spinal cord of the animal was destroyed by pithing. This, as is known, has a tre-

* This work was completed in 1919.

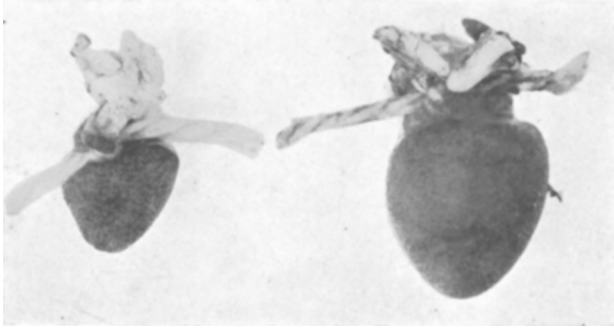
FIG. 1.



Heart before ligation of Bulbus Arteriosus. Heart after ligation.

mendous "shock effect." One of the evidences of this is the cessation of spontaneous arterial contractions in the frog.[1, 2] To further damage the vessels chloroform was applied to the skin of the animal. This caused a marked dilatation of the capillaries, but the corpuscular velocity before aortic ligation did not differ materially from the normal. Now the aorta was ligated. Almost at once the blood-flow in the capillaries stopped, the corpuscles became stagnant. There was now no sign of cardiac enlargement, when the functional integrity of the vessels was impaired (Fig. 2). Hence in the animal with damaged vessels there was neither a peripheral circulation nor an enlargement of the heart after the aorta was clamped. These two effects must therefore be ascribed to the proper functioning of the vessels.

FIG. 2.



[1] Nussbaum, *Pflüger's Archiv.*, 1875, x, 375.
[2] Huzinga, *Pflüger's Archiv.*, 1875, xi, 207.

To further study the reaction of the peripheral vessels when an artery was ligated centrally the following experiments were performed.

Experiment (II)

The aorta of a cat was clamped, and the time elapsing between this procedure and the stagnation of the capillary circulation in the ear was measured. The corpuscular flow lasted 35 seconds in one capillary, 50 seconds in another. The clamp was now released, and the circulation became reestablished. The aorta was again clamped. This time the corpuscular flow in one capillary lasted for six minutes after arterial compression.

Experiment (III)

A frog's leg was ligated above the tibio-tarsal joint, and quickly amputated just above the ligature. The circulation in the web of the foot was studied microscopically. The corpuscular flow lasted 2-3 minutes after the vessels were tied, in some experiments even longer. An interesting phenomenon observed in this experiment was the intermittency of the corpuscular movement. At times the corpuscles oscillated back and forth. There was a striking similarity between these and the corpuscular oscillations in the capillaries of man when pressure measurements were made with the micro-capillary-tonometer.[3]

Experiment (IV)

A ligature was firmly tied around the middle of a frog's thigh, and the web circulation studied microscopically. The periodic to-and-fro movement of the corpuscles was again observed. This lasted as long as the period of the observation, thirty minutes.

The successive phases of corpuscular movement were as follows:

Art. to Vein— 3 min.
Vein to Art.—18 sec.
Art. to Vein—16 sec.
Vein to Art.—15 sec.

Experiment (V)

An incision was made into the skin of the frog's thigh, and a subcutaneous artery was selected. This vessel divided into fine capillary branches which were distributed on the under surface

[3] Danzer and Hooker, *Am. J. Physiol.*, 1920, lii, 136.

of the skin. A skin flap was then made, and the circulation of the vessels was observed under the microscope. For five minutes after the main artery was ligated the corpuscles kept slowly moving in a normal direction in the capillaries. The movement, however, was not steady but oscillatory in character.

Experiment (VI)

A Riva-Rocci blood pressure cuff was placed around the arm, and the capillaries of the finger of the corresponding hand were viewed microscopically. The cuff was inflated to a pressure of 300 mm. Hg. The interval between the compression of the artery and the cessation of the capillary circulation was measured with a stop watch. The direction and duration of the subsequent movements of the corpuscles were also studied. The results are tabulated below.

	Art.→Vein	Stasis	Vein→Art.	Stasis	V→A	Stasis
Miss C.	15 sec.	30 sec.	75 sec.	20 sec.	.....	
D. R. H.	10 sec.	00 sec.	30 sec.	.....	.....	
	20 sec.	....	....	.....	.....	
Miss C.	37 sec.	10	75	43(?)	.....	
C. S. D.	27 sec.	11 sec.	47 sec.	13	70	55

First the arterial then venous limb of the capillary empties.

It is apparent that after the cuff has been inflated up to supra-systolic pressure, the corpuscles still keep moving in their normal direction—from artery to vein—for a period varying from 10 to 37 seconds in normal subjects. In pathological cases, or where the arm has been compressed for some time, this phase becomes much prolonged. It may last 100 or more seconds under such conditions. When this prolongation occurs the flow is not a continuous one, but is separated by short intervals into several parts. In the following few minutes the corpuscles become stagnant, then reverse their course, going from vein to artery, then stagnate and reverse their course once more.

The vascular reactions in man following brachial compression probably consist of a slow peristaltic contraction wave followed by intermittent periods of relaxation of the arterial vessels distal to the cuff. If the veins were not simultaneously obstructed, by the latter, this peripheral vascular motor mechanism might drive the blood in the direction of the heart, just as in the aortic ligation experiment of the frog.

Experiment (VII)

To bring out more clearly the differences in reaction between normal and injured vessels the following experiment was done:

A frog was anesthetized with ether. The sciatic nerve on the left side was cut, and chloroform was applied to the web of the corresponding foot. The right lower extremity was left intact. The webs of both feet were separately fixed on two boards and viewed with two microscopes. By means of a Leitz "Comparison Ocular," the visual fields of both were observed simultaneously.

The bulbus arteriosus was ligated and the circulation in both webs observed.

In the right web: (normal)	In the left web: (sciatic section and capillary relaxation)
The corpuscular after-flow lasted three and half minutes. This represents the vascular reaction in the normal extremity.	The blood corpuscles stopped moving almost immediately after the aorta was ligated. This represents the reaction of severely injured vessels.

This experiment proves that, when the vasomotor function is eliminated and the capillaries are dilated as in the left foot of the frog, aortic ligation is followed by immediate cessation of corpuscular flow in the vascular areas supplied by these vessels.

Injury to the vasomotor system or the local application of vasodilators alone does not produce a very striking effect. The combination of the two procedures, however, paralyses the peripheral vascular mechanism and prevents the filling and enlargement of the heart after aortic ligation.

This and the previous experiments have established for us the following working hypothesis:

(1) The size of the heart after ligation of the aorta is an index of the integrity and function of the peripheral vascular mechanism. The latter is elicited by arterial ligation.

(2) The peripheral vascular mechanism may be inhibited by the combined action of local vasodilator substances (chloroform, etc.) plus the destructive effect on the vasomotors by nerve section or spinal cord pithing.