EXPERIMENTAL STUDY ON PERIPHERAL CIRCULATION DURING EXTRACORPOREAL CIRCULATION, WITH A SPECIAL REFERENCE TO A COMPARISON OF PULSATILE FLOW WITH NON-PULSATILE FLOW

by

JUN TAKEDA

The 2nd Surgical Division, Kyoto University School of Medicine
(Director : Prof. Dr. YASUMASA AOYAGI)

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INTRODUCTION

The cardiac surgery recently developed, especially prolonged open-heart-operation, can be performed safely only when artificial heart lung machine is employed successfully.

However, it is the fact generally accepted that peripheral hemodynamics due to extracorporeal circulation using artificial heart-lung machine is a not physiological state for a living body, this state is beyond a comparison with a normal physiological state.

There are many extensive studies about hemodynamics and pathologic physiology during extracorporeal circulation, but there are still many unsolved problems as to peripheral circulation during total by-pass. Investigations of this problem seem to contribute a great deal for the development of the open cardiac surgery.

Currently the question whether the pulsatile flow or non-pulsatile flow should be employed for extracorporeal circulation is still being discussed.

WESOLOWSKI et al[53] demonstrated in 1955 that arterial pressure, balance of in- and out-flow and physiologic function of the whole organism were successfully maintained as long as three hours under extracorporeal circulation by means of non-pulsatile flow. Therefore, it seems as if the question was solved completely, and almost all the conventional artery pumps have never been deviced so as to generate an efficient pulsatile flow.

However, it is easy to suppose that a certain changes in peripheral circulation of organism should occur if the normal pulsatile flow is switched to non-pulsatile flow.

The purpose of this paper is to investigate the peripheral circulatory changes during extracorporeal circulation with a view to compare pulsatile and non-pulsatile flows.

CHAPTER I EXPERIMENTAL METHOD

§ 1 Materials and method

The materials used in the experiments were adult mongrel dogs weighing 8～

12 kg. These were anesthetized by intravenous injection of 25～30 mg of pentobarbital sodium per kg of body weight, and the trachea was immediately intubated with an endotracheal tube in order to establish adequate ventilation by pure oxygen until onset of the extracorporeal circulation. Both donor and recipient dogs were injected with 3 mg of Heparin sodium per kg of body weight to prevent coagulation.

Artificial heart employed is a new type of pulsatile pump reported by us previously[38], and was constructed in our laboratory under the direction of Dr. GORO KAMIMOTO, Professor of the Faculty of Technology, Kyoto University.

For aeration of blood a foam oxygenator of Waud type was employed. For arterial delivery of blood a metal cannula of 3 mm in caliber was inserted through the left carotid artery into the aorta, and for venous cannulation two vinyl tubes of 5～6 mm in caliber were passed through the right atrium.

Care was taken to keep the rectal temperature above 36°C during extracorporeal circulation.

When a non-pulsatile flow was required pulsation was removed by an air chamber interposed in delivery tube as shown in Fig. 1.

The animals were divided into two groups, namely pulsatile and non-pulsatile, and observations were made on each group under the same flow rate of extracorporeal circulation for a period of sixty to ninety minutes.

1. Arterial blood pressure

It was recorded from the femoral artery by Statham straingage electromanometer or kimograph.

2. Venous blood pressure

It was recorded from the inferior vena cava by a catheter inserted through the femoral vein using the water manometer.

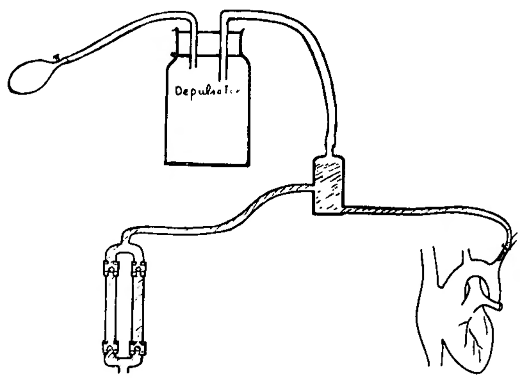

Fig. 1 Schematic illustration of depulsator system.

3. Omentum volume

The omentum was carefully withdrawn through a median abdominal incision and was separated into two parts[25], one of which was nourished from the right gastroepiploic artery, the other from the left.

By this procedure, omentum became a single separated stieled organ, and only a part nourished by the right gastroepiploic artery was used in this study.

This was inserted in a specially constructed double chamber. Then this chamber was filled by warm Ringer's solution and was set gummiplug. The exterior part of this double chamber was filled warm water which circulated through constant water bath in order to maintain the temperature in the interior part of this double chamber at body temperature. The pressure in this chamber was recorded on an ossilographic paper using optic system consisted of a small mirror attached on the

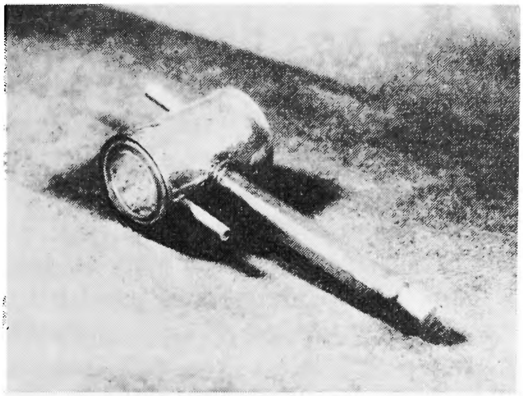

Fig. 2 Specially constructed double chamber for oncograph of omentum.

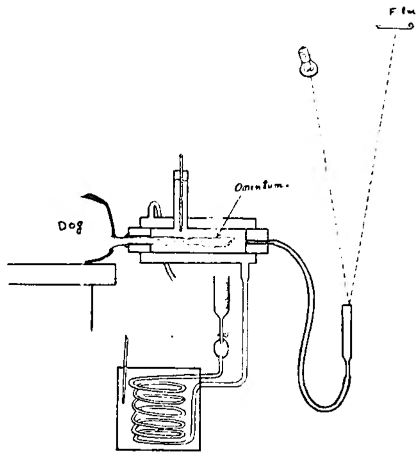

Fig. 3 Schematic illustration of oncograph of omentum.

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4. Microscopic study of omentum capillary

A part of the omentum was carefully withdrawn through a median and transverse abdominal incision and was spread in a specially constructed moist warm

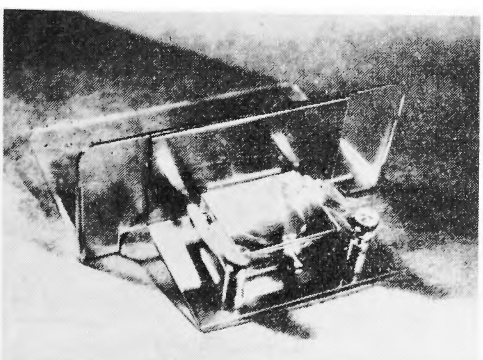


Fig. 4 Specially constructed warm moist chamber for observation of omentum capillary

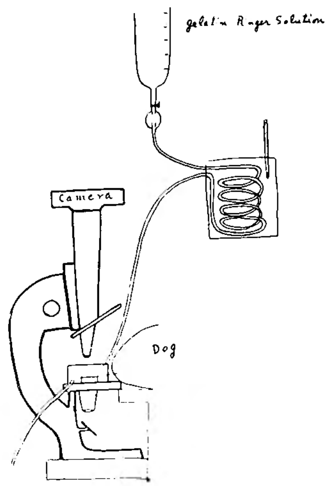


Fig. 5 Schematic illustration of observation's method of omentum capillary.

chamber mounted on the stage of a microscope. The exposed portion of the omentum outside the chamber was covered with a Rubber shirt, and the inside of the chamber was maintained at body temperature and moisture with constant drip of warm 1% gelatin-Ringer's solution prepared by Zweifach's recipe[55][56].

The observations were made on selected vessels throughout the course of an experiment under magnification of 100 times. Light source was a tangsten lump of 6～12 volt, 5 amp. Infrared filter was used to prevent the heating by the incident light. Recording were made by using 8～16 mm movie camera and 35 mm static camera.

5. Plethysmograph of leg

Right leg was inserted into specially constructed metal chamber as shown in Fig. 6, and pressure in this chamber was recorded on an ossilographic paper using optic system consisted of a small mirror attached on the tanbul.

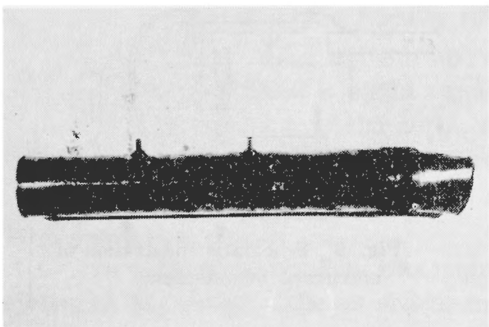


Fig. 6 Specially constructed metal chamber for plethysmograph of leg.

6. Small artery pressure

Polyethylene tube with an outer diameter of 0.7 mm was inserted into the right saphenous artery following Haddy's[21] method, and was connected to electromanometer, thus the pressure of the saphenous artery was measured.

7. Blood flow rate

The blood flow rate was determined using a electromagnetic flow meter made by Hokushin Denki Co. L. T. D.

8. Portal pressure

The portal pressure was measured by using a water manometer which was connected to a vinyl tube inserted through a mesenteric vein to a portal vein.

CHAPTER II RESULTS

§ 1 Omentum volume (oncograph of omentum)

1. Normal case (control)

The omentum volume showed a pulsation synchronously with heart beat. No change in the omentum volume was observed for a period of an hour after onset

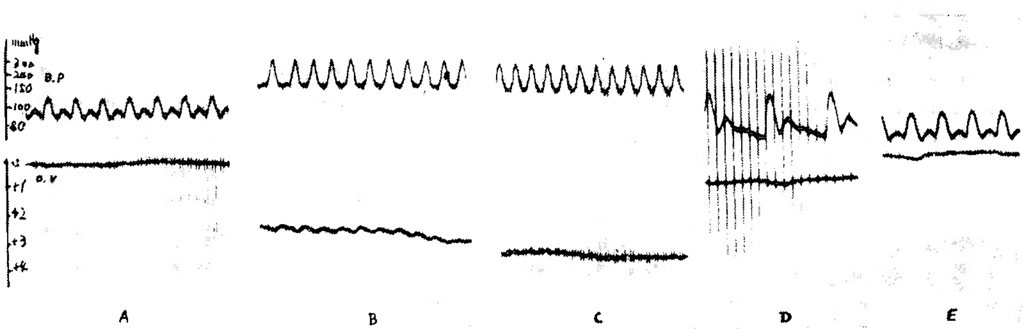


Fig. 7 Change of blood pressure and omentum volume by injection of epinephrine hydrochloride.

A : before
B : immediately after injection of epinephrine HCl 0.25×10^{-7} g per Kg of body weight.
C : 30 second after injection of epinephrine HCl 0.25×10^{-7} g per Kg of body weight.
D : 1 minute after injection of epinephrine HCl 0.25×10^{-7} g per Kg of body weight.
E : 5 minutes after injection of epinephrine HCl 0.25×10^{-7} g per Kg of body weight.

of the perfusion, if temperature in the instrument was kept constant. However, it showed very sharp response to the autonomic nerve stimulating drugs. When epinephrine hydrochloride 0.25×10^{-7} g per kg of body weight was injected intravenously, the omentum volume increased as blood pressure rose and then decreased slightly after several minutes. When acetylcholin 0.05 mg per kg of body weight was injected intravenously, omentum volume decreased with a concomitant lowering of blood pressure only transiently, and the volume resumed the original value immediately.

2. Extracorporeal circulation

As shown in Fig. 8. 9., immediately after starting the total body perfusion, temporary changes in the omentum volume were observed in both groups. However, 10-15 minutes after the onset, it came back to the preperfusion level and remained at this level without remarkable changes in the pulsatile flow groups. On the contrary, in the non-pulsatile flow groups, 15 minutes after the onset, the omentum volume showed a general tendency to increase and a remarkable contrast to the pulsatile flow groups was observed hereafter.

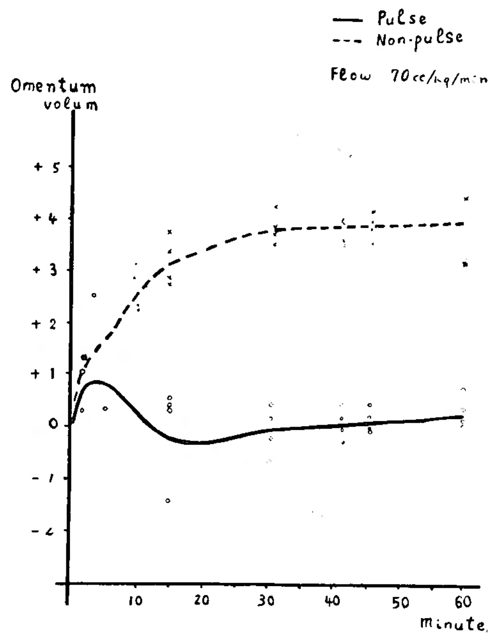


Fig. 8 Curve showes the change of omentum volume under extracorporealcirculation.

In order to analyze the relationship between the omentum volume and the flow rate, experiments were conducted with three groups of test animals i. e. high flow group, middle flow group and low flow group.

As shown in Table 1. 2., the changes of the omentum volume were smallest in the pulsatile high flow group, and next smaller was the pulsatile middle flow group.

In the non-pulsatile flow, the omentum volume increased in both the high and the middle flow group.

In the low flow group, at the beginning of the extracorporeal circulation the omentum volume decreased but 10～15 minutes after the onset of the total body by-pass, they showed a tendency to increase in both the pulsatile and the nonpulsatile group.

§ 2 Microscopic observation of omentum capillary

1. Normal case

The arterioles, metarterioles, precapillaries, true capillaries, collecting veins and venules could be observed in a single field of vision.

Table 1 This table showes arterial & venous pressure and change of omentum volume during extracorporealcirculation using pulsatile flow

Pulsatile flow

High flow 100cc/kg/min

No.	Time	A.P (mean)	V.P	O.V
	M	mmHg	mmHg	
17	1	95	1.7	0
	15	102	4.8	−0.2
	30	70	6.6	−0.3
	60	85	4.6	+0.3
20	1	105	2.7	+0.3
	15	70	3.2	+0.1
	30	80	4.8	+1.3
	60	85	4.6	−1.3
36	1	70	3.3	0.
	15	77	1.2	+1.0
	30	68	1.4	+2.0
	60	82	1.2	+1.0

Moderate flow 80～70cc/kg/min

No.	Time	A.P	V.P	O.V
	M	mmHg	mmHg	
11	1	85	2.6	+0.2
	15	85	3.2	+0.5
	30	60	5.0	+0.3
	60	80	3.0	+0.1
21	1	80	4.0	+2.5
	15	85	5.0	−1.5
	30	75	5.0	−0.3
	60	80	6.0	−0.1
31	1	80	0	+0.2
	15	75	2.6	+0.5
	30	73	5.9	+0.4
	60	95	7.0	+0.2
34	1	60	4.9	+1.0
	15	90	4.0	+0.2
	30	60	6.0	−0.6
	60	95	6.4	+0.4

Low flow 50cc/kg/min

No.	Time	A.P	V.P	O.V
	M	mmHg	mmHg	
41	1	80	0.9	−2.0
	15	75	1.0	−4.0
	30	50	2.0	−4.5
	60	55	1.0	+3.0

A. P : Femoral atrery pressure.
V. P : Venous pressure.
O. V : Change of omentum volume.

Table 2 This table showes arterial & venous pressure and change of omentum volume during extracorporealcirculation using non-pulsatile flow.

Non-pulsatile flow

High flow 100cc/kg/min

No.	Time	A.P	V.P	O.V
	M	mmHg	mmHg	
16	1	85	2.0	+2.0
	15	70	8.6	+4.5
	30	80	5.5	+4.3
	60	85	7.8	+4.6
33	1	98	4.0	−0.6
	15	75	7.7	+1.2
	30	58	7.7	+3.3
	60	55	8.9	+3.2
29	1	70	2.4	+1.5
	15	65	5.0	+1.8
	30	45	5.0	+1.5
	60	30	2.5	+2.0

Moderate flow 80～70cc/kg/min

No.	Time	A.P	V.P	O.V
	M	mmHg	mmHg	
15	1	70	0	−1.3
	15	80	0	+2.6
	30	75	0	+3.4
	60	70	0.8	+2.9
22	1	90	3.5	+1.0
	15	77	16.0	+3.3
	30	60	7.5	+3.7
	60	40	6.0	+3.1
25	1	90	4.3	+1.0
	15	84	3.4	+2.4
	30	64	3.8	+3.6
	60	76	2.9	+2.9
37	1	82	4.4	−0.2
	15	75	6.6	+3.6
	30	75	6.8	+4.1
	60	70	5.9	+1.1

Low flow 50cc/kg/min

No.	Time	A.P	V.P	O.V
	M	mmHg	mmHg	
18	1	70	1.0	−1.2
	15	43	0.8	+2.4
	30	32	1.0	+3.4
	60	28	0.8	+4.7

A. P : Femoral artery pressure.
V. P : Venous pressure.
O. V : Change of omentum volume.

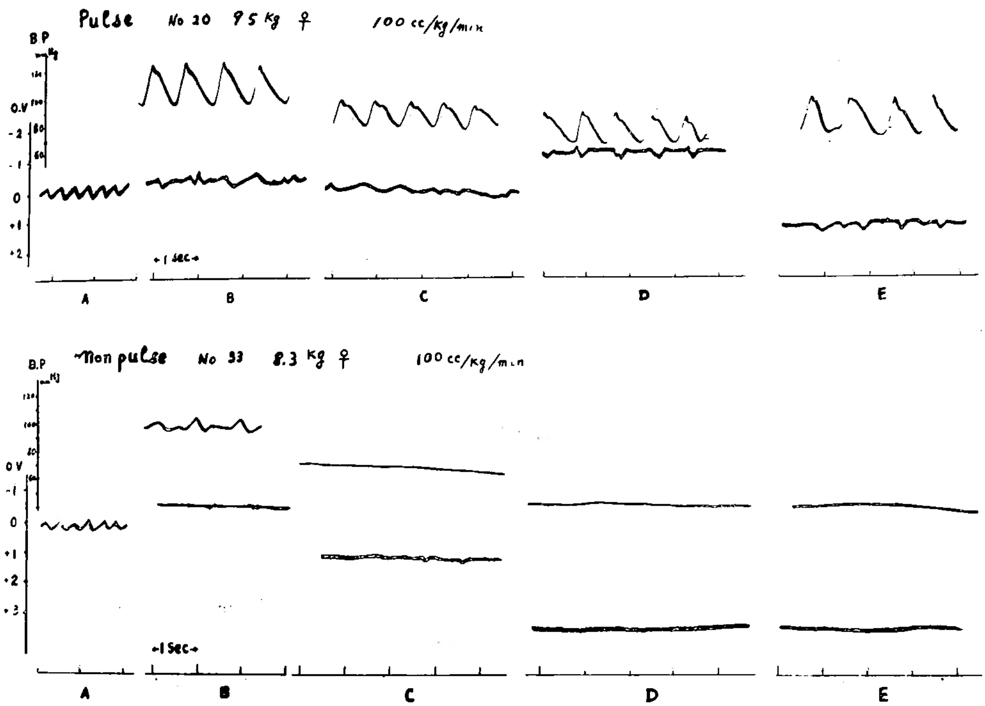


Fig. 9 Relationship between blood pressure and change of omentum voiume.

A : before
B : immediately after onset of extracorporealcirculation.
C : 15 minutes after onset of extracorporealcirculation.
D : 30 minutes after onset of extracorporealcirculation.
E : 60 minutes after onset of extracorporealcirculation.

In the arterioles, metarterioles and venules, it was impossible to distinguish individual blood corpuscles, and blood stream looks like a red belt, and in the center of the blood stream flow rate was more rapid than in the periphery of the blood stream. In the capillaries individual blood corpuscles could be distinguished, and each corpuscle flowed as if it were snapped out. Therefore, the blood stream in the capillaries was not continuous but intermittent, which may be considered as what is called plasma flow.

Not all the true capillaries in the field of vision are filled by blood at the same time. At a given moment one true capillary may be filled by blood, another can be unfilled.

In order to estimate the sensitivity of the capillary, local epinephrine threshold test was performed.

The minimal effective concentration necessary to stop blood stream in the metarteriole and precapillary was shown in Table 3. The values fell between $1/4 \times 10^{-8}$g and $1/8 \times 10^{-8}$g and did not change for 30 minutes after the onset of the experiment. These results were compatible with those reported by a number of investigators[20)55)56)].

2. Extracorporeal circulation

Table 3 This table showes the minimal effective concentration to stop blood stream in metarteriole & precapillary of normal dogs.

Dog No.	adrenalin (Bosmin) threshold	adrenalin threshold after 30 minute
19	$1/4\times10^{-6}$	1×10^{-6}
23	$1/8\times10^{-6}$	$1/8\times10^{-5}$
24	$1/8\times10^{-6}$	
26	$1/2\times10^{-6}$	$1/4\times10^{-6}$
28	1×10^{-6}	$1/2\times10^{-6}$
30	$1/4\times10^{-6}$	$1/2\times10^{-6}$
35	$1/8\times10^{-6}$	
36	$1/4\times10^{-6}$	$1/2\times10^{-6}$
C_1	$1/8\times10^{-6}$	$1/8\times10^{-6}$
C_2	$1/2\times10^{-6}$	$1/2\times10^{-6}$

a) The pulsatile flow

Although immediately after the onset of the total by-pass, a slowing down of the blood flow in the metarteriole and precapillary was often observed, it resumed a reasonable speed soon and the blood flow in the true capillary was kept more or less constant thereafter (Fig. 10.). Occasionally, the blood flow from precapillary to venule became slower but such a change was transient and soon recovered. Blood flow rate was slightly slower than in the normal cases. A slight change in caliber of the arteriole could be observed.

b) The non-pulsatile flow

When the perfusion was carried out with the non-pulsatile flow a temporary increase in the blood flow rate occured initially. The blood flow in the precapillary venule and true capillaries were maintained at a high level. However, 10～15 minutes after the onset of the total body by-pass, the blood flow in the true capillaries diminished gradually and finally ceased. Under such condition blood flowed mainly through the preferential channel and a-v. anastomosis, and their flow rate was very high.

Increased caliber of the arteriole could always be observed (Fig. 11.).

§ 3 Plethysmograph of hind leg

Omentum was chosen to represent abdominal organs for the observation of blood flow, on the other hand, in order to observe the peripheral blood flow other than that of abdominal organ, plethysmograph of hind leg was performed.

1. Normal case

The blood flow of the hind leg was affected by body motion and depth of anesthesia. When the body motion was removed by intravenous injection of succinylcholine chloride and depth of anesthesia is maintained at a constant level, the plethysmograph showed a more or less constant value during the experiment but it showed a tendency to decrease forward 1 hour after the onset.

2. Extracorporeal circulation

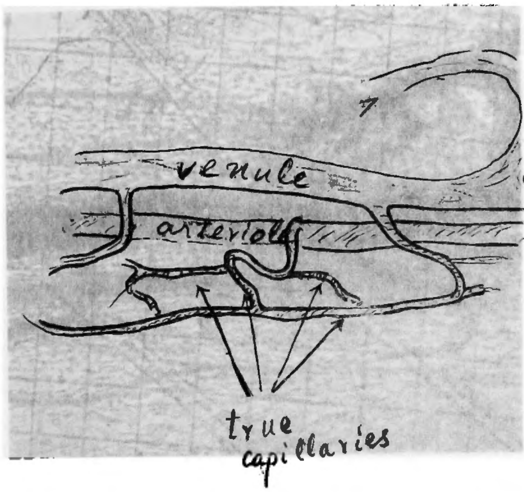
a) The pulsatile group

The plethysmograph showed a slight pulsation which was synchronous with the pulsation produced by the pump, and its changes were parallel to the blood pressure.

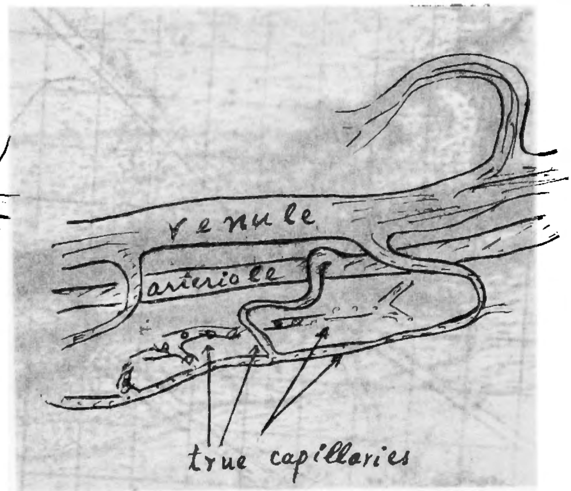
b) The non-pulsatile flow group

The value of plethysmogram showed an increased 20～30 minutes after the onset of the total by-pass, but this increase was lesser than the increase of omentum volume.

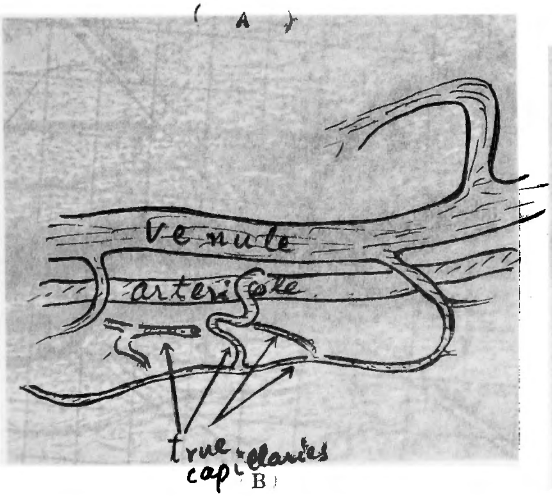
When the flow rate of perfusion was low, the value of plethysmogram decreased



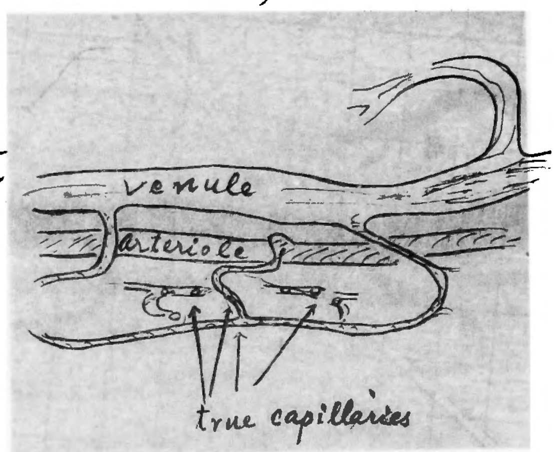
(A)



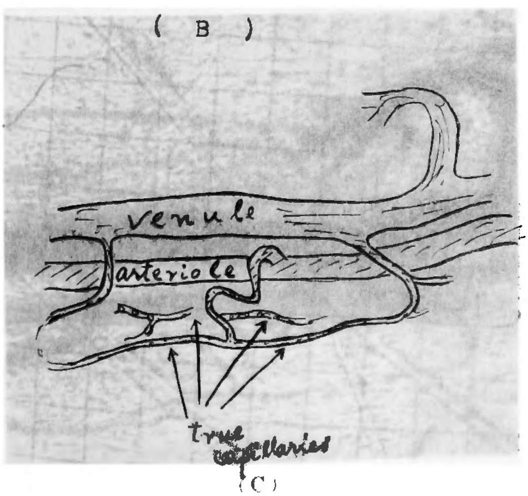
(D)



(B)



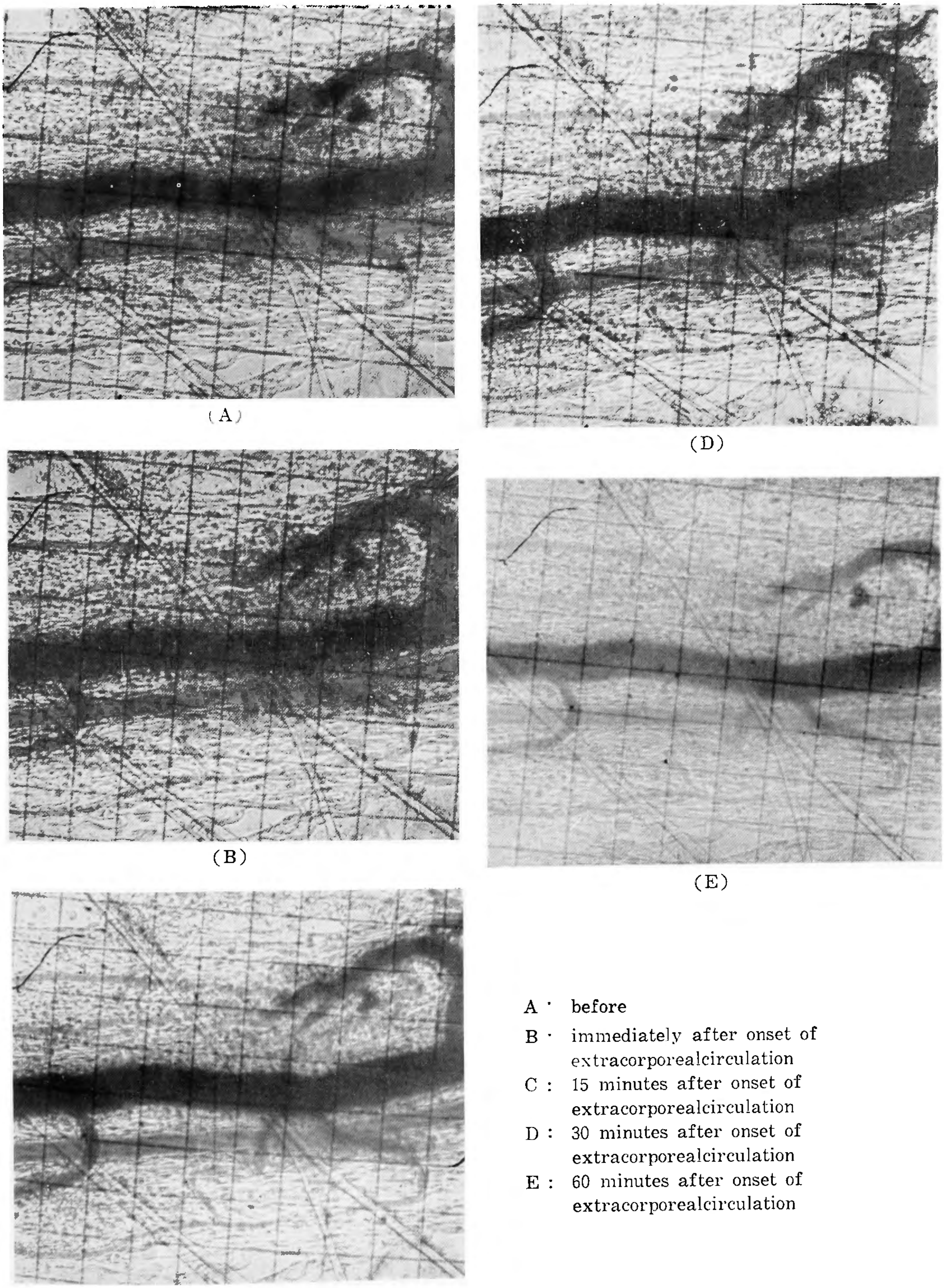
(E)



(C)

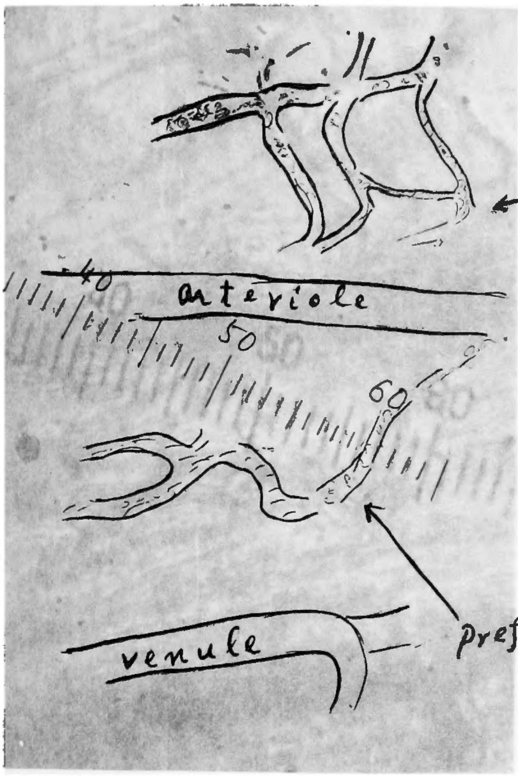
A : before
B : immediately … extracorp…
C : 15 minutes after onset of extracorporeal circulation
D : 30 minutes after onset of extracorporeal circulation
E : 60 minutes after onset of extracorporeal circulation

… roscopic findings of omentum capillaries during extra[illegible] circulation using pulsatile flow. (magnification 100×)

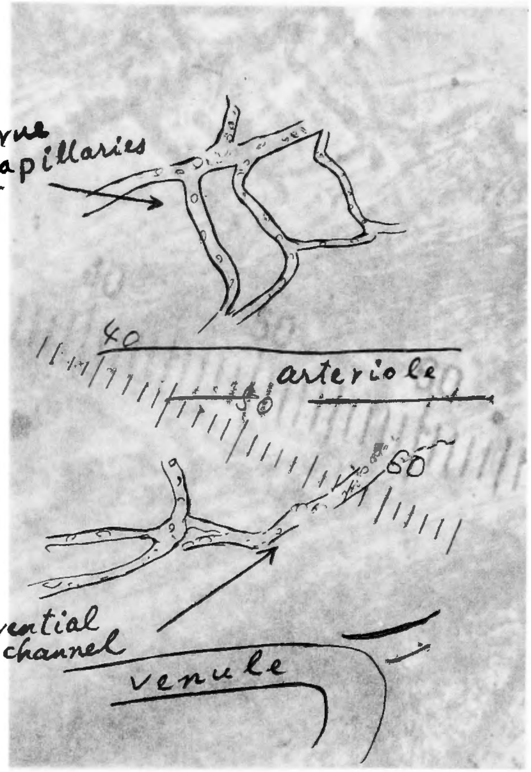


A · before
B · immediately after onset of extracorporealcirculation
C : 15 minutes after onset of extracorporealcirculation
D : 30 minutes after onset of extracorporealcirculation
E : 60 minutes after onset of extracorporealcirculation

Fig. 10 Microscopic findings of omentum capillaries during extracorporeal circulation using pulsatile flow. (magnification 100×)


true
capillaries
40
arteriole
50
60
preferential
channel
venule

(A)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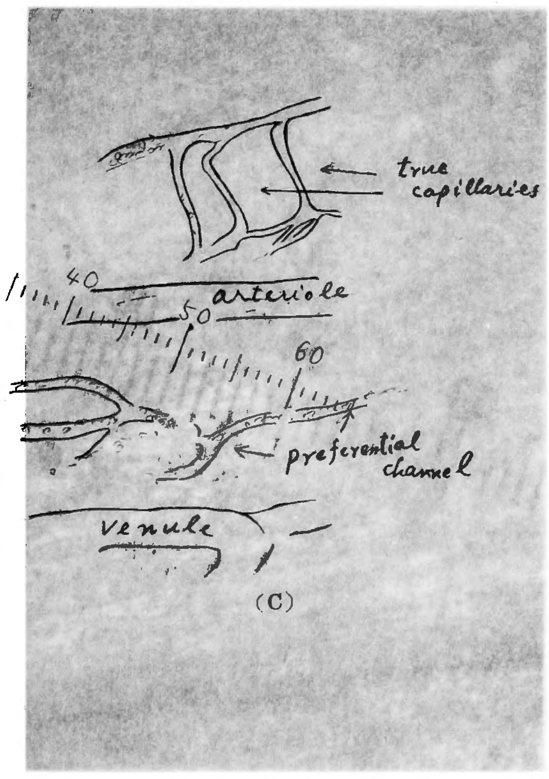
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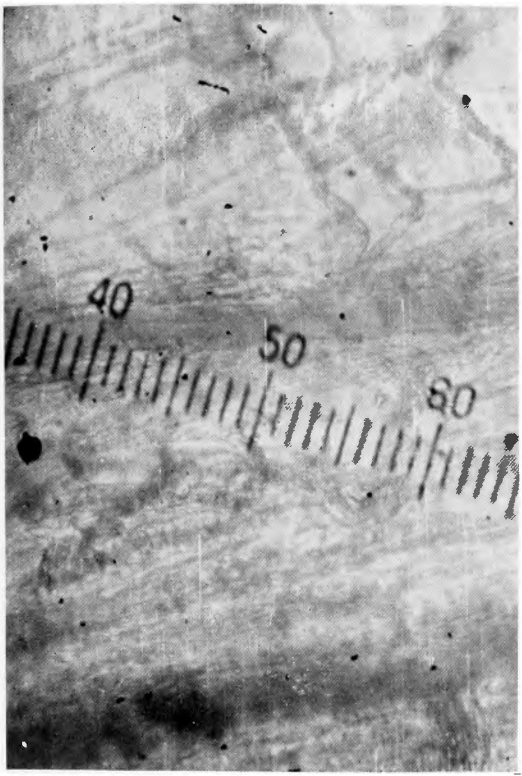
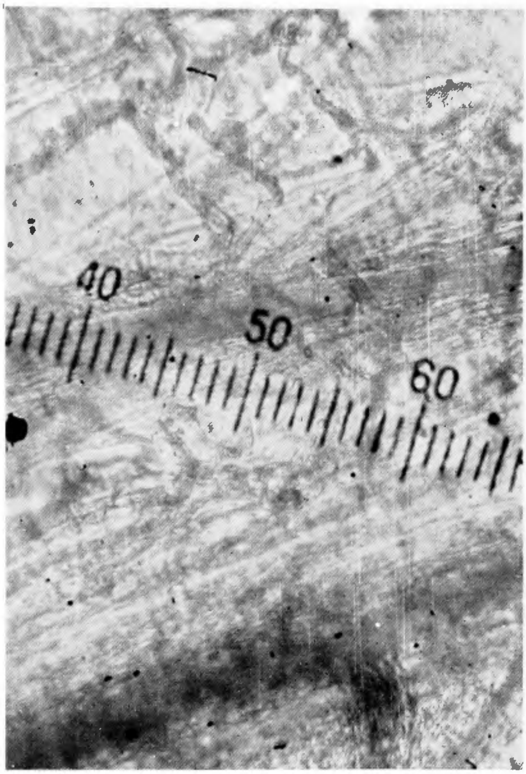


(A)



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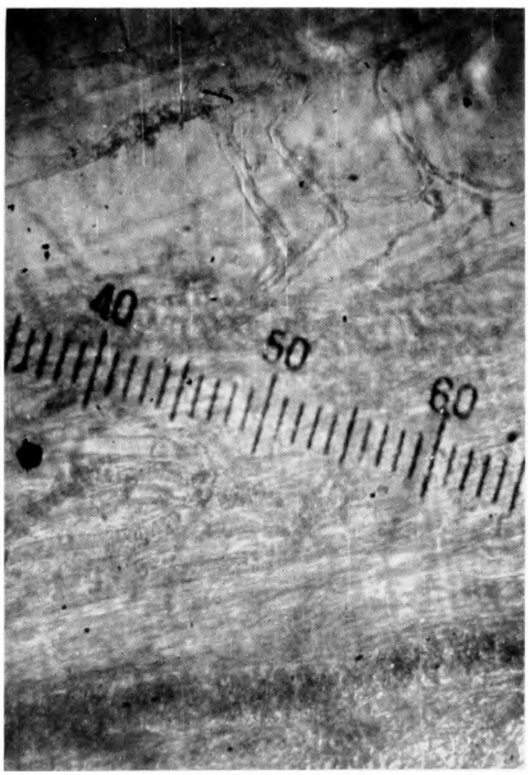
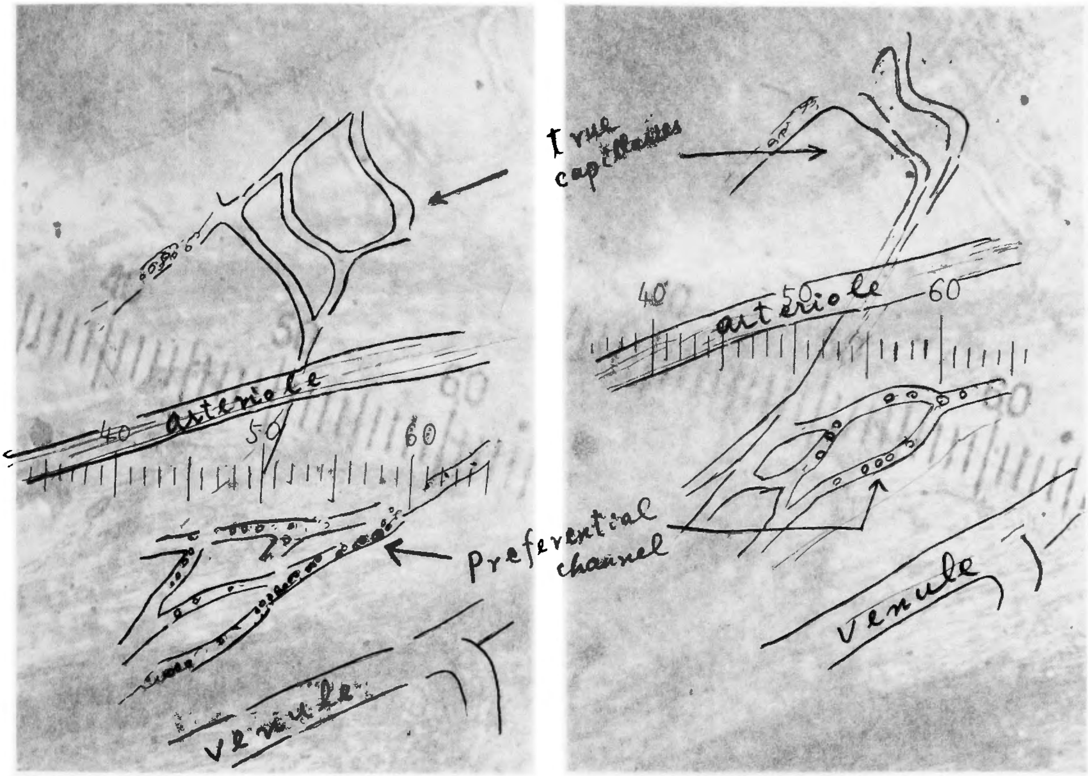


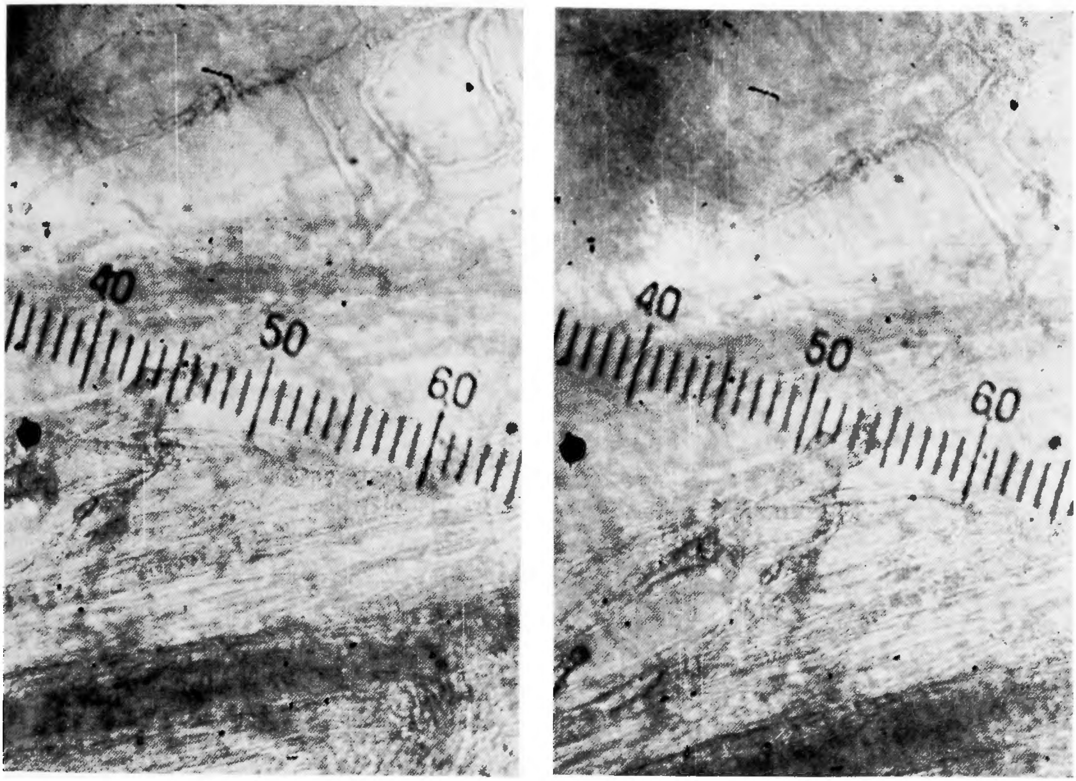
(C)



(D) (E)

A : before
B : immediately after onset of extracorporeal circulation
C : 15 minutes after onset of extracorporeal circulation
D : 30 minutes after onset of extracorporeal circulation
E : 60 minutes after onset of extracorporeal circulation

Fig. 11 Microscopic findings of omentum capillaries during extracorporeal circulation using non-pulsatile flow. (magnification 100 ×)



(D) (E)

A : before
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E : 60 minutes after onset of extracorporealcirculation

Fig. 11 Microscopic findings of omentum capillaries during extracorporeal-circulation using non-pulsatile flow. (magnification 100×)

immediatly after the perfusion in both cases of pulsatile and non-pulsatile flow groups, and showed a tendency of recovery 5～10 minutes later but the preoperative level could not be attained.

§4 Blood pressure

1. Pulsatile flow group

An initial temporary rise of the blood pressure immediately after the start of the perfusion was observed very often but this rise disappeared soon afterward, and in most cases the blood pressure was kept practically constant during the ensuing period of the extracorporeal circulation, although sometimes temporary lowerings of the blood pressure occurred.

The changes in small artery pressure were similar to that in the femoral artery pressure (Fig. 12). The blood pressure rose abruptly upon injection of epirenamine hydrochloride 0.1×10^{-4}g per kg of body weight 1 hour after the start of the perfusion (as shown in Fig. 14. A.).

The small artery pressure rose likewise, and this fact showed that the reactivity of peripheral vessels was maintained.

2. Non-pulsatile flow group

The blood pressure went down gradually 10～15 minutes after switching to non-pulsatile flow, and small artery pressure went down equally. In general, the maintenance of the blood pressure during total by-pass was difficult (Fig. 13.).

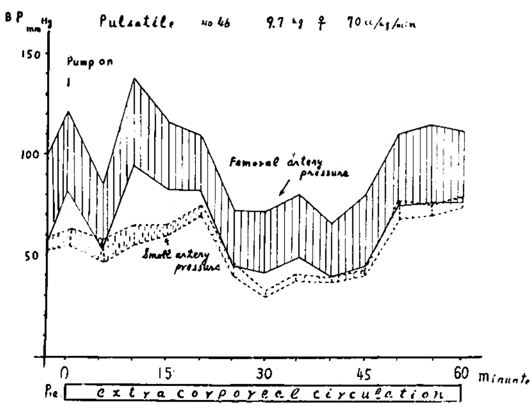


Fig. 12 Curve showes the change of femoral artery and small artery pressure under extracorporealcirculation using pulsatile flow.

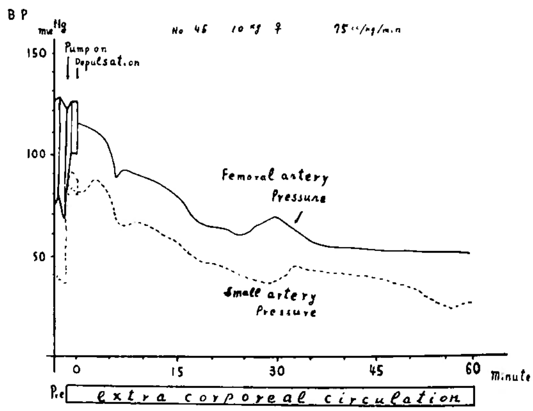
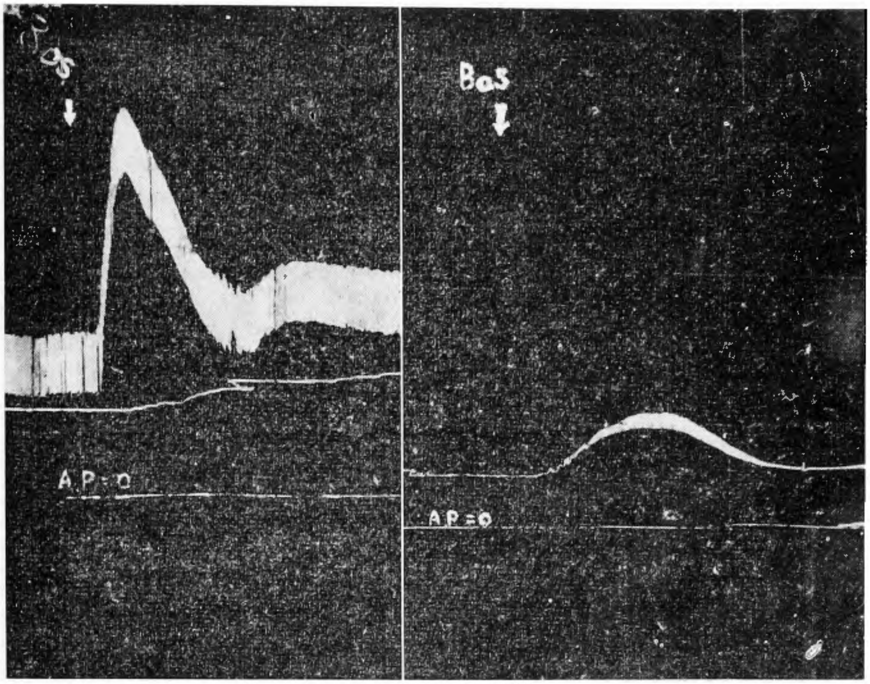


Fig. 13 Curve showes the change of femoral artery and small artery pressure under extracorporealcirculation using non-pulsatile flow.

In case of non-pulsatile flow, rise in blood pressure caused by injection of epirenamine hydrochloride was not steep but drew a gently sloping curve as shown in Fig. 14. B. and its maximum value was lower than that of pulsatile cases.

§5 Central venous pressure

No remarkable difference between pulsatile and non-pulsatile groups could be



A : case of pulsatile flow B : case of non-pulsatile flow

Fig. 14 Change of blood pressure by injection of epirenamine HCl at 1 hour after onset of extracorporealcirculation.

recognized.

The central venous pressure could be maintained at less than 5 cm water by judiciously chosing the diameter of venous canule. This was possible because the venous pressure is determined with diameter of venous canule and reservoir level.

§ 6 Portal pressure

No remarkable difference between pulsatile and non-pulsatile group could be recognized. The portal pressure was often observed to rise abruptly immediately after onset of the perfusion, but about 10 minutes later, it fell down to the preperfusion level and stayed at this level. Sometimes these fluctuations were occurred again 30～40 minutes after the onset of perfusion (Fig. 15.).

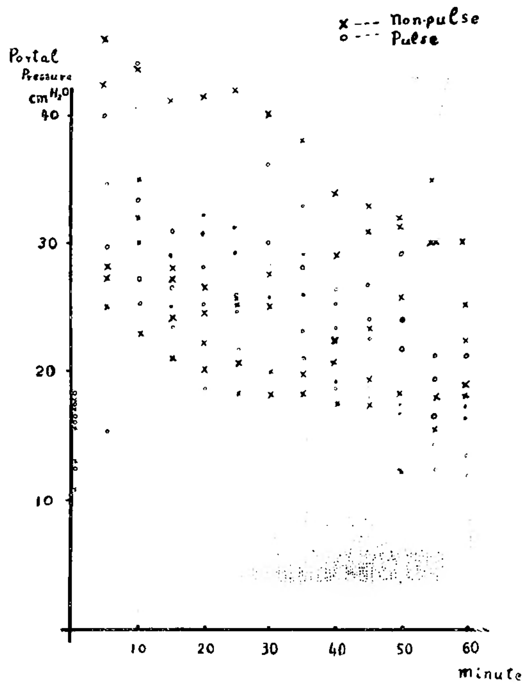


Fig. 15 Change of portal pressure under extracorporealcirculation.

CHAPTER III DISCUSSIONS

In order to clarify pathophysiology of the various diseases, a number of studies on peripheral hemodynamics have arisen a keen interest recently. Methodologically the studies may be divided into two major trends, namely the micro-circulatory study consisted of microscopic observation of the living tissues and the hemodynamic study in which blood circulation is investigated from the hydrodynamic stand point.

Beginning with A. KROGH's[28] work on the blood capillaries in 1921, extensive investigations have been conducted in the United States of America by B. W. ZWEIFACH and R. CHAMBERS et al[7)55)56)]. using frog, rabbit and dogs. As the results, it has been made clear that the blood capillaries are not terminal branchings, but the arterioles branch out to the precapillaries which in turn are eventually connected to the venules via preferential channels, and that true capillaries, originating from precapillaries and preferential channels, unite each other like a net. It has also been found that true capillaries are devoid of muscles, but can be obstructed by precapillary sphincters which are located at the branching point of the true capillaries. Furthermore, the periodicity of alternating dilatations and contractions of blood vessels was discovered, and was named vasomotion, and its significance on the function of blood capillaries has since been recognized. Ever since many investigators have studied peripheral circulation and a number of achievements have been accomplished. It is well known fact that the behavier of peripheral capillaries play an important role in blood circulation at shock state. Also because of the development of hypothermic anesthesia in recent years, the behavior of the peripheral circulation in the hypothermic state has been thoroughly studied. There are but few works, however, have been done, in spite of importance on the peripheral circulation study during cardiopulmonary by-pass, especially the direct microscopic observation of the peripheral blood flow has rarely been documented.

In the field of hemodynamic study, on the other hand, a number of studies have been reported since the POISEUILLE's well known work achieved between 1835 and 47.

Lately these two trends have shown the tendency to be unified and have developed along the line of rheology.

The author has attempted the study on the behavior of the peripheral circulation during extracorporeal circulation from the rheological stand point of view, and investigated the effect of pulsation by comparing the results of experiments with and without pulsation.

So far the pulsation has been considered to have only little effect on the caliber of blood capillaries, but to have some effect on the flow rate (velocity) of blood. The absence of pulsation in the blood stream of venules after passing the blood capillaries has been regarded as the result of cancellation by interference due to randomness in lengths of capillaries. And it had been accepted that blood flows in capillaries do not pulsate normally. However, it has recently been found that the blood flow in pulmonary capillaries is not steady but pulsatile, and that this fact must always be taken into consideration when the gas exchange and metabolism in the lungs are discussed[51].

Furthermore, the study of the effect of pulsation on lymphatic flow by PARSONS et al[39]. showed that the pulsatile flow was essential for the smooth lymphatic circulation, and that the non-pulsatile flow caused edema.

Now let us look at the pulsatile and non-pulsatile flows from a purely physical stand point of view by using hydrodynamics. When a fluid flows inside a rigid straight cylinder with a periodic change of the rate of flow, the coefficient of resistance λ_p is represented by the following equation

$$\lambda_p = \lambda \frac{\int_0^T \omega^{-\frac{11}{4}} dt}{\bar{\omega}^{-\frac{11}{4}} T}$$

where λ is the coefficient of resistance for a steady flow and is expressed as

$$\lambda = 0.3164 \left(\frac{\bar{\omega} d}{\upsilon}\right)^{-\frac{1}{4}} = 0.3164\ R^{-\frac{1}{4}}$$

R is Reynolds number,
T is the period of the pulsation,
ω is the mean rate of flow taken over the cross section of the cylinder,
$\bar{\omega}$ is the time average of ω,
and d is the diameter of cylinder.

When the ratio $\varepsilon = \lambda_p/\lambda$ is considered, its value ranges between 2 and 11 in the case that ω is sign function or step wise periodic function of time, which shows that the coefficient of resistance is larger for the pulsatile flow than for the non-pulsatile one. The above discussion was based on a rigid cylindrical model.

A similar theoretical treatment on the elastic blood vessels of living body, which furthermore are capable of self dilating and self contracting, seems to be almost impossible. In spite of the apparent difficulties EGAMI[12] in 1944 attempted a theoretical analysis of the blood flow in the human blood capillaries and obtained a result which indicates that again in the elastic vessels the effective cross section for the fluid flow is smaller for a pulsatile one than the steady one.

By employing a electro-magnetic flow meter, the author recorded the blood flow continuously during the total by-pass while the pulsatile flow was shifted to the non-pulsatile one.

The result as shown in Fig. 16. indicates, a higher flow rate by 30 % for the steady flow under the same mean blood pressure. As a matter of course, the mean blood pressure was maintained identical for both cases.

In other words, under the same mean blood pressure, the peripheral resistance is less for the non-pulsatile flow, hence more blood can be circulated. Conversely, this means that at the same flow rate the pressure decreases in the non-pulsatile flow.

Although a number of works have been reported on pressure-flow relationship, it still remains a point of contraversy. DONALD[11], READ[41][43] and others maintain a linear relation between the blood pressure and the flow rate, while CLOWES[5][6],

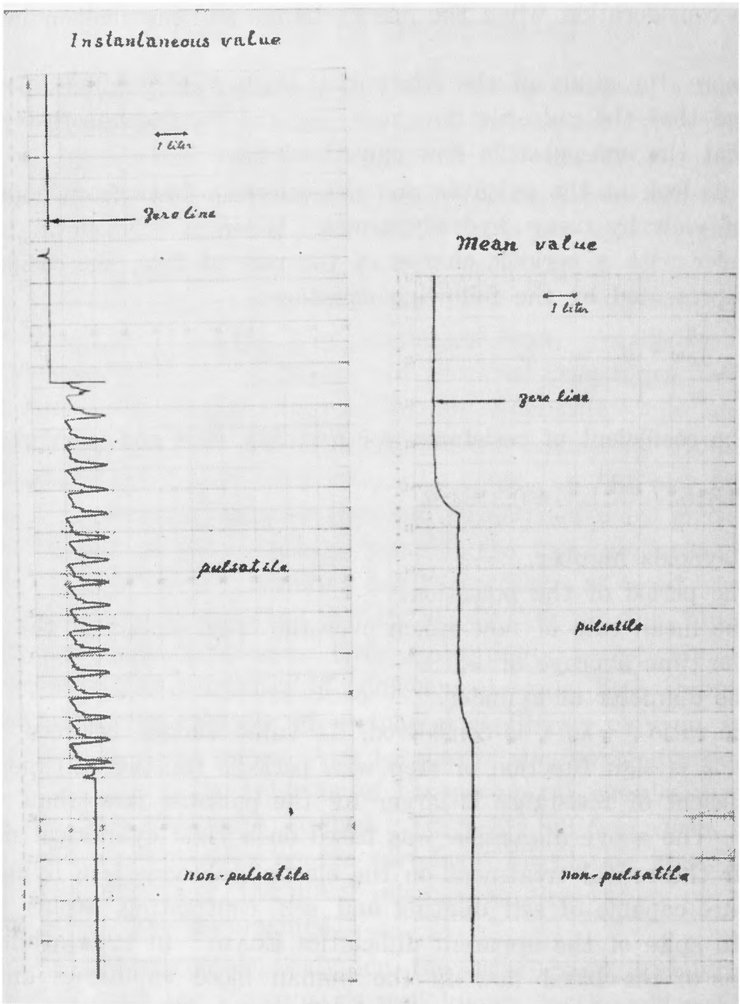


Fig. 16 Electromagnetic pattern of flow rate

GIANELL[16)17)], STARR[44)] and others do not admit the linearity. The third group of investigators like FOLKOW[14)] and others proposed an exponential relationship. Furthermore, Donald and others[10)] reported that even with high flow close to cardiac output, it was impossible to maintain the blood pressure at a normal preoperative level.

At any rate, the maintenance of the blood pressure during the cardiopulmonary by-pass is relatively difficult matter, and the unbalance of vasomotor system have often been attributed to the cause of lowering of blood pressure. Also dilatation of the peripheral blood vessels due to a liberated vasodilator substance has been considered as a cause by some investigators[33)]. DONALD[11)] and DIETTERT[9)], however, observed the increase in total peripheral resistance during total body perfusion above the normal level and infered that it is due to the contraction of peripheral blood vessels. They further mentioned that change in the sympathetic activity might be affected by the tension of sympathetic nerve change in blood composition and effect of reflex mechanism as possible cause for vaso-contraction during total body perfusion.

In our experiments with pulsatile flow the blood pressure could be maintained relatively satisfactorily.

Although, the pressure underwent a temporary dip half an hour after the start of the total body perfusion, it rose up to the original value again. On the contrary, with the non-pulsatile flow the pressure began to lower at about 15 minutes after the start and kept declining steadily, thus making the maintenance difficult.

The total peripheral resistance also could be maintained by the pulsatile flow satisfactorily, while with the non-pulsatile one it showed a tendency to decrease steady with elapse of time.

This last mentioned fact suggests diminution of the tonus of the peripheral blood vessels.

By using the value of small arterial pressure, the femoral artery pressure and venous pressure, the vascular resistance of the blood vessels downstream of the small artery and the resistance upstream of it were compared by the following equations. Since

$$\text{femoral artery pressure} - \text{small artery pressure} = \text{flow} \times \text{upstream resistance}$$

$$\text{small artery pressure} - \text{venous pressure} = \text{flow} \times \text{downstream resistance.}$$

Therefore, by assuming the flow to be constant and the same, the ratio of the upstream resistance to the downtsream resistance is

$$\frac{\text{femoral artery pressure} - \text{small artery pressure}}{\text{small artery pressure} - \text{venous pressure}} = \frac{\text{upstream resistance}}{\text{downstream resistance}}$$

As shown in Fig. 17. the ratio is larger in the case of non-pulsatile flow indicating that the dilatation or decrease in tonus of vessels downstream of the small artery is larger than those of upstream.

We will next consider the significance of change in omentum volume and factors which control it. Among others change in the pressure of vascular system and change in blood volume and tissue fluid can be considered as important factors, though it is not easy to decide which is the true factor. In addition to venous pressure, vascular tonus and permeability of the wall of blood vessels may be involved (in controlling the omentum volume) in a very intricate manner. However, as shown in Fig. 18. 19. the comparison of change in blood pressure and change in omentum volume between pulsatile flow group and non-pulsatile flow group clearly shows an opposite tendency. That is, with pulsatile flow the arterial pressure is decreased and the omentum volume is increased, while with non-pulsatile flow, blood pressure is not decreased nor the omentum volume is increased. On the other hand, although shock is considered to be accompanied by a rise in portal pressure and peripherisation of blood (especially abdominal region), our measurement of the portal pressure could not detect difference between the pulsatile group and the non-pulsatile group except for a transient increase or decrease. On these grounds one may conclude that the increase in the omentum volume was caused by congestion edema or an increased blood flow due to the decrease in peripheral blood vessel resistances.

Microscopic study shows that although in the case of non-pulsatile flow an initial temporary increase in blood flow occurs, after 10 or 15 minutes the flow in true capillaries decreases as described before and blood flows mainly through preferential channels.

These facts together with the failure to observe a conspicuous congestion after the non-pulsatile flow experiment makes it adequate to conclude that the increase in the omentum volume was caused by edema. This conclusion seems to be compatible with the observation made by author's coworker, A. NONOYAMA, that the relative increase in body weight after the experiment with the total body perfusion is larger with the non-pulsatile group than with pulsatile group.

Thus in the case of the non-pulsatile group, in contrast to pulsatile group, the maintenance of the blood pressure is difficult, the tonus of the peripheral blood vessels weakens, the blood flow in true capillaries diminishes or stops in

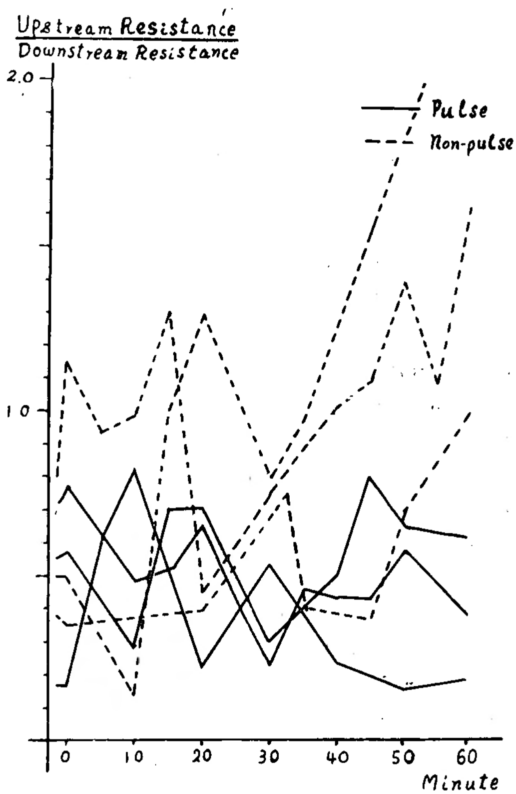


Fig. 17 Change of Up-and-Downstreamresistance ratio during extracorporealcirculation.

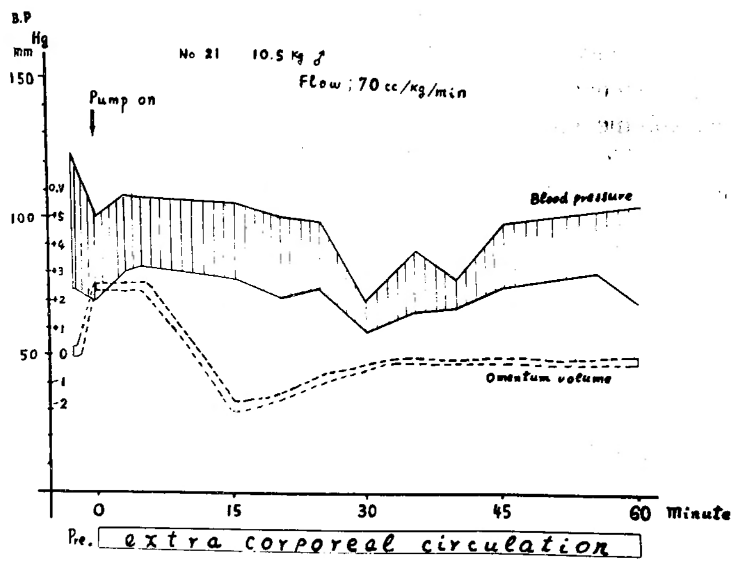


Fig. 18 Relationship beween blood pressure and change of omentum volme under extracorporealcirculation using pulsatil flow.

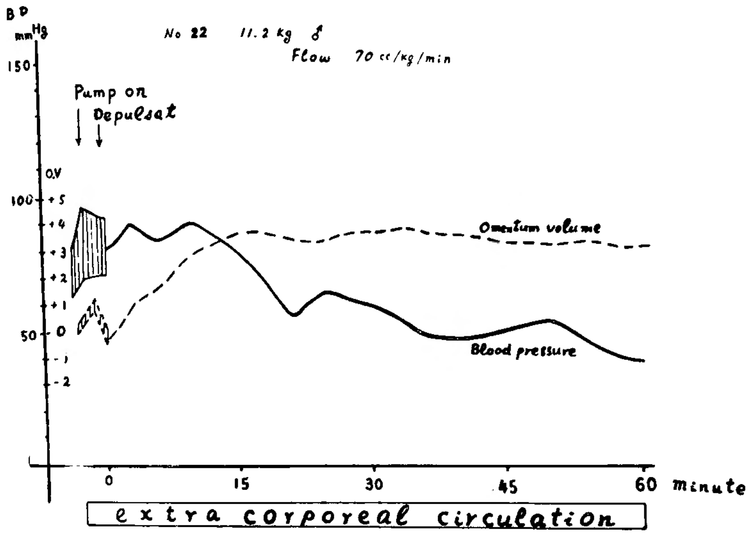


Fig. 19 Relationship between change of blood pressure and change of omentum volume under extracorporealcirculation using non-pulsatile flow.

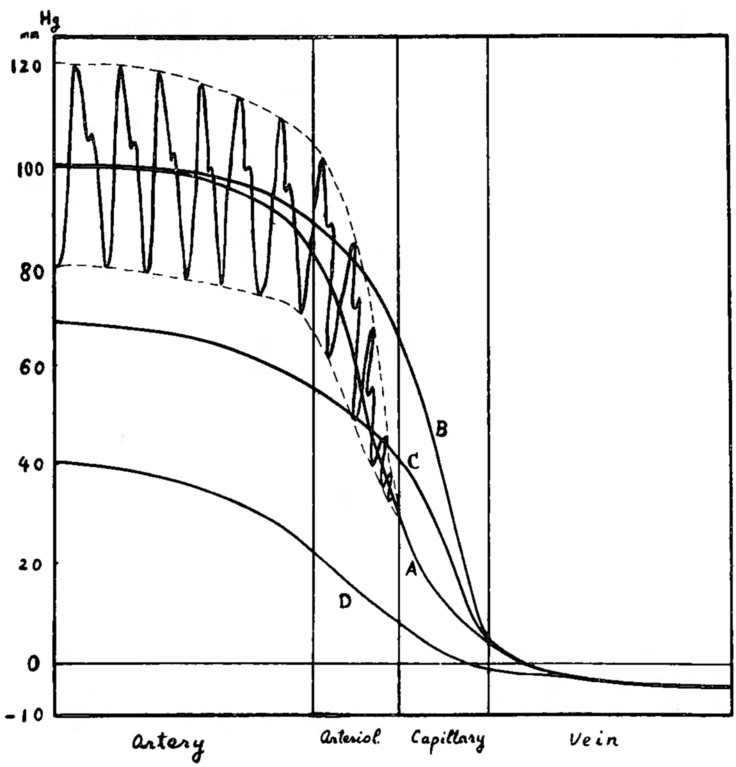


Fig. 20 Schematic illustration of distribution of blood pressure in the vascular system.

the periphery and edema appears in the tissue.

What is the cause of such phenomena? Many answers to the question may be proposed but the following one seems to give the most harmonious explanation.

Along the blood flow, the pressure gradually diminishes from heart to periphery. However, as shown by curve (A) of Fig. 20. the decrease is not uniform over the entire region of the blood vessels, but it is small in the region of arteries of relatively large caliber, gets larger as the caliber decreases after branchings, and finally drops steeply after arterial region to ward blood capillary.

When we try to draw the pressure distribution curve for the non-pulsatile flow by inference, it will be the one as represented by curve (B) because the pressure drop with the non-pulsatile flow is slower and the curve becomes flatter due to the smaller vascular resistance with the non-pulsatile flow as compared to the pulsatile one. On the other hand, however, in our experiments the same rate of flow is applied to both the pulsatile and non-pulsatile flows, hence the pressure of the latter should be lower than the former, accordingly the curve should be as represented by curve (C).

At this point, attention should be called upon the fact that curve (A) and curve (C) intersect in the precapillary region (arteriale region). In other words, it is possible that the pressure with the non-pulsatile flow is higher than that with the pulsatile flow in the precapillary region.

If this possibility is assumed to be the case, all of the above described phenomena can be explained coherently. It is generally recognized that in the peripheral tissues water in serum moves into the tissue by the difference in the capillary pressure of blood and the effective colloidal pressure of tissue fluid. Now when the capillary blood pressure is higher the water in serum will be transported into tissue which will result in edema and an increase in the omentum volume. Immediately after switching to non-pulsatile flow, an increased omentum capillary blood flow has been observed by a biomicroscopic study. This phenomenon can be explained as due to an increase in the pressure difference. In this case an increase in the caliber of arterioles can be detected by photography. Thus when the pressure of the arteriole is higher edema is resulted. On the contrary, when the fluid pressure of tissue gets higher, the blood capillaries are oppressed, and the blood flow into the capillaries are suppressed. This situation naturally leads to hypoxia of the peripheral tissue or further to anoxia of that and eventually by increasing permeability of the blood capillaries facilitate the development of edema. Under such a condition blood flows only through preferential channel or a-v. anastomosis in which the pressure gradient should become steeper, and velocity higher, the situation compatible with the results of biomicroscopic observation. Such conditions will inhibit tissue respiration in the periphery thus will result in a decrease of arterio-venous oxygen difference and an accumulation of metabolic products like lactic acid etc.

These phenomenon have actually been reported by author's coworkers A. Nonoyama, and Y. Ida.

Another experimental fact that a test with epirenamine hydrochloride gave a sharp reaction in the pulsatile group while the reaction was very weak in the non-pulsatile group, seems to render a further support to the above discussion.

Thus in the non-pulsatile group there appear symptoms which suggest failure of vasomotor, which further helps to lower blood pressure.

As the blood pressure lowers further to the state represented by the curve (D) of Fig. 20. the pressure in arteriole should be too low to circulate blood through pre-capillary sphincter. In this state the pressure should be below what BURTON and others[3] call critical closing pressure and the blood would not flow in the true capillaries hence edema does not take place, which can be considered as the state of shock.

Since such a state is still accompanied by some venous return, some investigators do not concur with BURTON's hypothesis. However, the augment can be settled down when the mechanism of shunts like a-v. anastomosis and preferential channel are taken into consideration. On the other hand, it is known that the pulsatile output of blood from left ventricle to aortic arch acts as stimulus to induce an efferential impulse in vagal nerves[4] and vasomotor center located in the medulla oblongata. The possibility may not be excluded that such a reflectory factor plays a role in maintaining the tonus of peripheral vessels.

CONCLUSION

The effectiveness of the pulsatile and the non-pulsatile flow in extracorporeal circulation on peripheral circulation was experimentally studied, and following results were obtained.

1. In the case of non-pulsatile flow, 10～15 minutes after onset of extracorporeal circulation, the flow rate in true capillaries slowed down and finally stopped. Blood flows mainly through preferential channel and a-v. anastomosis in which flow rate is higher than pulsatile cases.
2. In the case of non-pulsatile flow, the edema occurred in the tissue especially abdominal region, after 10～20 minutes of extracorporeal circulation.
3. The maintenance of arterial blood pressure, peripheral vascular tone and normal peripheral circulation were more difficult in the non-pulsatile cases than in the pulsatile cases, because the peripheral vascular tone especially in the downstream of small artery decreased in the non-pulsatile cases.
4. From the present results, the author would like to emphasize the necessity of the pulsatile flow in the extracorporeal circulation for long period of time, because the non-pulsatile flow causes marked changes in the peripheral circulation.

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I wish also to express my gratitude to Drs. OGATA, Kuma, and Hirakawa for their helpful suggestions and kind guidances in the course of exeriment and express my sense of indebtedness to my coworkers, Drs. Y. IDA, A. NONOYAMA and H. SASAKI for their encouragement and assistance.

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Surgery (Oct. 1959), at the 8th Kinki Block meeting of Japanese Circulation Society (Oct. 1959), and at the 9th Kinki Block meeting of Japanese Circulation Society (June 1960).

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和文抄録

体外循環の実験的研究，特に脈動の有無が末梢循環に及ぼす影響について

京都大学医学部外科学教室第２講座（指導：青柳安誠教授）

武 田 惇

最近頓に発展して来た心臓外科，特に長時間に汎る直視下心臓内手術は，人工心肺装置の理想的な運用によつてはじめて安全に行いうるものである．併し人工心肺装置による体外循環は生体にとつてはあくまで異常なものであり，生理的状態にはほど遠いものであると考えなければならない．而もこの様な異常な状態下における血行動態，病態生理については既に種々の点から研究されているがその末梢循環についてはなお不明の点が多く，その究明は体外循環の運用に貢献するところが多いと思われる．

現在，体外循環を行う場合に論議される問題の１つに脈動流の問題がある．即ち体外循環を行う場合に脈動を有する流れで環流した方がよいのか，それとも無脈動の定常流でよいのかと云う問題であり，そしてこれは1955年 Wesolowski の研究発表により一応無脈動流でもよいと結論されたかの様にもみえるが，彼の研究は主として試獣犬の生死を指標として論ずるにとどまり，末梢における循環状態の詳細な検討は行われていない．一方生体にとつて脈動流を，全然脈動のない定常流に切替えた場合，母体に何らかの変化が現われるであろうことは想像に難くないが，私は体外循環の実験に際して末梢循環の立場から脈動の有無が生体にどのような影響を及ぼすかを検討した．即ち，平均体重10kgの雑種成犬を用い，京大工学部神元教授の御指導によつて作製した独自の脈動式ポンプを使用し，脈動流で環流したもの（脈動流群）と air chamber を用いた Depulsator によつて脈動を消失させ定常流で環流したもの（無脈動流群）の２群について夫々１時間乃至１時間半の完全体外循環を行い，同一流量下における成績を比較検討した．

まず股動脈圧，伏在動脈圧（小動脈圧），中心静脈圧，大網容積，下肢容積，門脈圧，流量等を比較測定し，更に大網を用いて末梢毛細管の血流状態を直接顕微鏡下に観察した．その結果，

1. 無脈動流では環流開始約15分を経過すると真性毛細管の血流は緩かとなり，遂には停止し，血流は主に選択毛細管（preferential channel）又は a-v. Anastomosis のみを流れ，この間を流れる速度は脈動流の時よりも速い．併し脈動流群では以上の様な変化は一切みられない．
2. 無脈動流で環流すると環流開始後10～20分で末梢組織（特に腹部内臓器）に浮腫が発生する．
3. 無脈動流では末梢血管トーヌス及び末梢血管抵抗，特に小動脈以下の末梢血管トーヌスの著しい減弱によつて全身血圧の維持及び正常な末梢循環の維持は脈動流群に比べて困難となる．
4. 以上即ち，無脈動流は末梢循環に非常な悪影響を及ぼすものであるから，特に『長時間の体外循環には脈動流が必要である』ということを強調したい．
5. また以上の諸現象を説明するために，流体力学的所見を考慮して，心臓から末梢に至る脈管系各域に於ける血圧分布曲線を，脈動流，無脈動流の２群について想定し解説を試みた．