EXPERIMENTAL STUDY ON CIRRHOSIS OF THE LIVER

WITH PARTICULAR REFERENCE TO THE INFLUENCE OF THE LIGATION OF THE HEPATIC ARTERY UPON THE PORTAL BLOOD FLOW IN THE DOG WHOSE HEPATIC VEIN HAD BEEN CONSTRICTED

By

Kogo Hosono

From the lst Surgical Division, Kyoto University Medical School
(Director: Prof. Dr. Chisato Araki)
(Received for publication Mar. 6. 1959)

Index

I. INTRODUCTION

Since Rienhoff, Berman and others recently advocated that the ligation of the

hepatic artery was effective for the treatment of cirrhosis of the liver, many investigaters reexamined this problem from various angles. They are, however, of a diversity of opinions about this procedure.

Author intended to investigate the effects of the ligation of the hepatic artery upon the blood flow in the portal vein in cases of the liver cirrhosis associated with or without ascites. By constriction of the hepatic veins in dogs, we succeeded to produce the conditions quite similar to those of the liver cirrhosis in human beings. In these dogs, the hepatic artery was ligated and changes in the portal blood flow were studied.

HERRICK in 1907, through his perfusion test of the liver, suggested there was a interrelation between the blood pressure of the hepatic artery and that of the portal vein. Later McINDOE (1926), DOCK (1942) and TAYLOR & ROSENBAUM (1953) also performed the perfusion test of the liver in cases of the portal hypertension particularly of the liver cirrhosis and found an interrelation between the blood pressure of the hepatic artery and that of the portal vein. Also they studied the correlation between the volume of blood flow of the hepatic artery, portal vein and that of the hepatic vein. We, instead of perfusion on the removed liver, carried out similar kind of experiment, in vivo, with the use of "Thermostromuhr".

II. METHOD AND MATERIAL

Mongrel dogs of 7.6-15.0kg body weight were used. These were divided into three groups, i. e. 1) dogs in normal control group, 2) dogs in which the constriction of the hepatic vein was not followed by the development of ascites and 3) dogs in which the marked ascites developed after the constriction of the hepatic vein. Both in group 2) and 3), the animals underwent a reoperation for the determination of the rate of blood flow in the portal vein on the 14th day after the constriction of the hepatic vein.

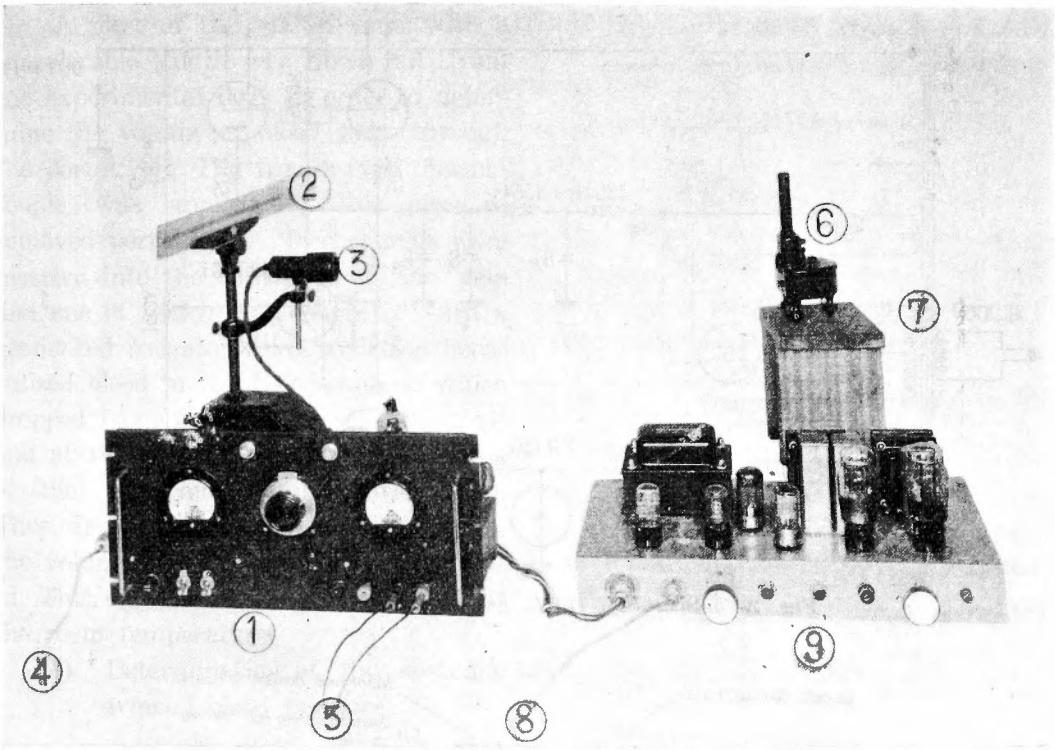
1) Constriction of the hepatic vein in dogs

Prior to the procedure the animal was kept away from food for 24 hours. Under general anesthesia with an intravenous injection of thiopental sodium in dose of 0.04g/kg, laparotomy was carried out with r-subcostal incision. Ligation or constriction of the individual hepatic vein was carried out according to the TSUCHIYA's method. In the present experiment, however, manipulation for the right hepatic veins was slightly simplified, i. e. the right hepatic veins were divided into two groups, superior and inferior, and veins in each group were ligated en masse.

During these procedures a particular care was taken not to constrict the abdominal inferior vena cava. For the middle and left hepatic veins, constriction or ligation of a individual vein was made following the TSUCHIYA's original method.

2) Determination of the rate of blood flow in the portal vein (shown in photograph)

"Thermostromuhr" was used for the determination of the rate of blood flow in the portal vein. "Thermostromuhr" consists of high frequency current generator, galvanometer and lampscale and trough type thermo-couple.



① High frequency current generator
② Scale
③ Lamp
④ Lead wire to A.C. 110V
⑤ Lead wires to Diathermy terminals
⑥ Galvanometer
⑦ Copper wire (connect with constantan wire)
⑧ Lead wire to A.C. 110V
⑨ B-Source of H.F.C. generator with stabilizer

i) High frequency current generator (Fig. 1, 2)

This apparatus was made under the guidance of Mr. YOSHIFUMI SUNAHARA who is a assistant in the institute of applied physics, faculty of technical engg.

ii) Galvanometer and Lampscale

The galvanometer used in the present study was; resistance of wiring line 803 ohms, critical resistance 66,000 ohms, sensitivity 2.4×10^{-10} amperes, 160×10^{-7} volts, period 7.3 sec.

iii) Trough type thermo-couple

In Fig. 3, the trough type thermo-couple which was used by HERRICK et al., was shown. In our experiment, instead of the electric heater, a diathermy electrode was used and this was connected with the diathermy generator which is believed to be ideal for warming the blood. Also 110V A. C. was used instead of the battery, and the rubber plate was used in place of the bakelite plate in order to provide a better approximation to the wall of the blood vessel.

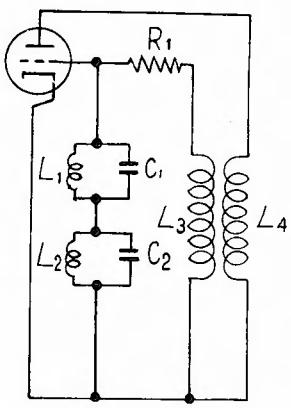


Fig. 1 High frequency current generator

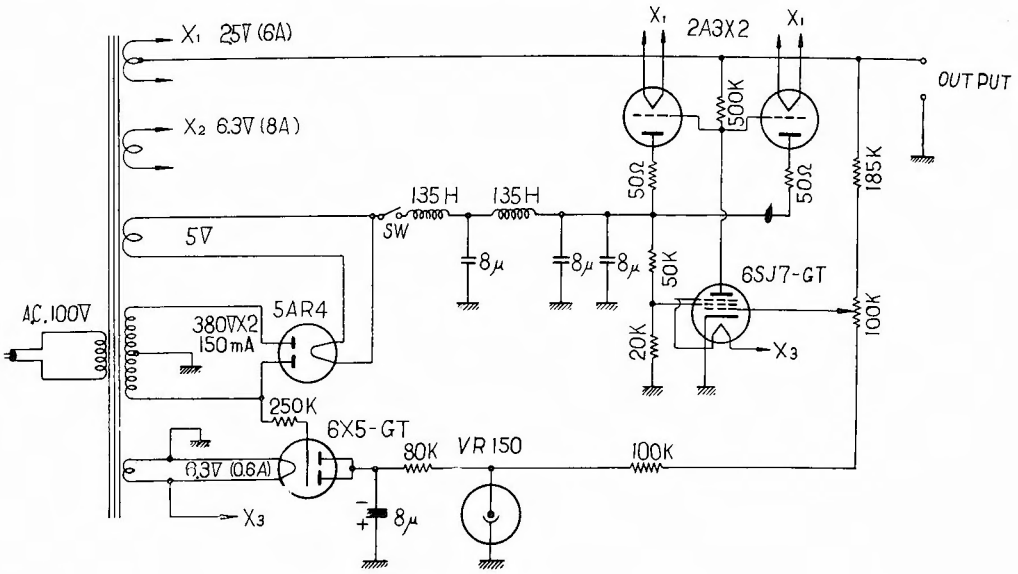


Fig. 2 B-Source of H.F.C. generator with stabilizer.

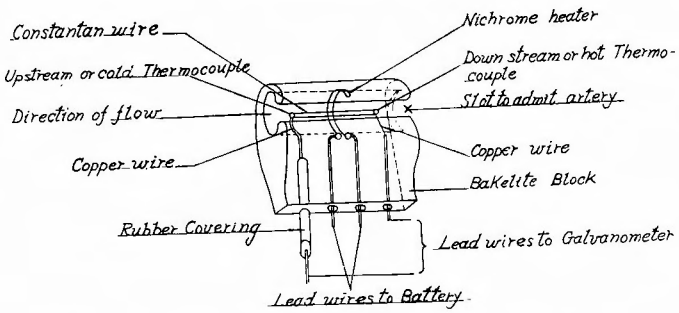


Fig. 3 Thermostromuhr used by BALDES and HERRICK.

iv) Use of the "Thermostromuhr"

The dog was anesthetized with thiopental-sodium and laparotomy was carried out with upper midline incision. The portal vein was dissected from the surrounding tissue. Distally from the bifurcation with the splenic vein and as close as possible to the liver, the trough type thermo-couple was applied to the wall of the portal vein, thus the rate of blood flow in the portal vein was measured. To minimize the errors in measurment by the manipulation of ligating the artery as much as possible, silk thread was wrapped previously around the artery as shown in Fig. 4. Then, blood through the portal vein was warmed with the use of diathermy. Scale of the galvanometer at a time when the blood through the portal vein was thus warmed and before the hepatic artery was ligated, was set at 0 point. Change in scale after the quick-ligation of the hepatic artery by the silk thread previously wrapped around the artery, was read and recorded.

3) Determination of the volume of blood flow in the portal vein

A piece of the portal vein with a considerable length was taken out from the experimental dogs in order to determine the volume of blood flow through the portal vein. The trough type thermocouple was applied to this piece of removed portal vein. Two canules were inserted into the both ends of the vein and one of which was connected with a graduated irrigator filled with the heparinized blood in it. Blood volume which dropped from the irrigator was measured and at the same time change in scale of the "Thermostromuhr" was read. Thus, from these two measured values, the volume of blood flow was determined. This experiment was performed at the room temperature.

Anatomy of the hepatic artery and its branches (═) showing the sites of ligation

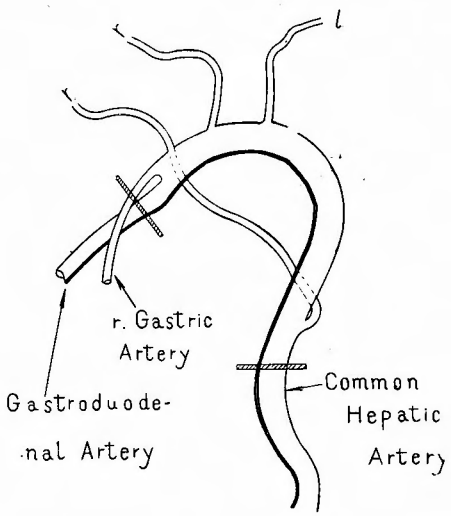


Fig. 4

4) Determination of the systemic arterial blood pressure

Systemic blood pressure was determined with the mercury manometor at the femoral artery.

III. RESULTS

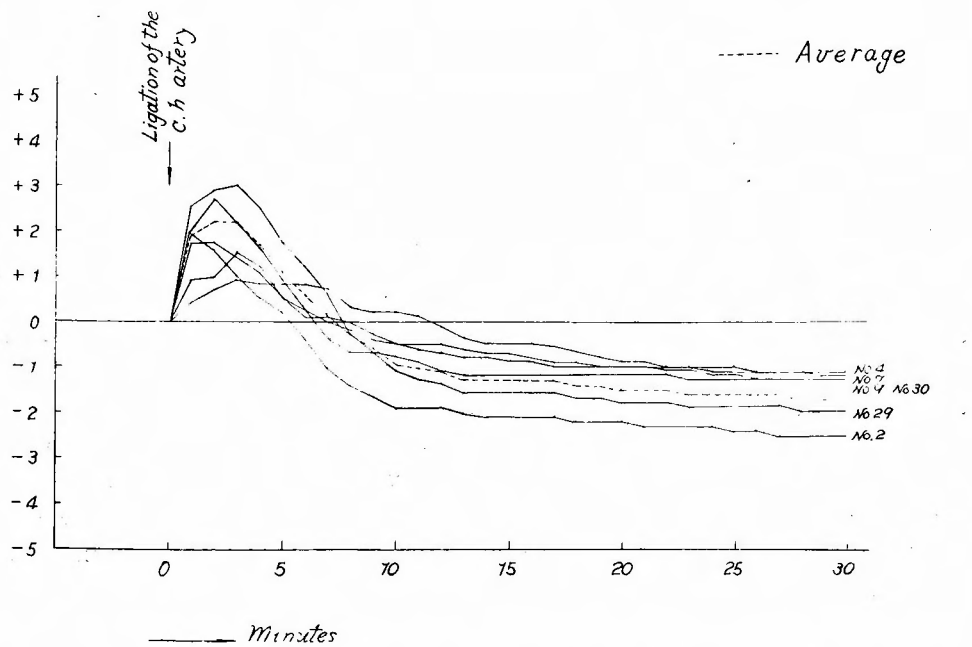


Fig. 5 Changes before and after ligation of the common hapatic artery on normal dogs.

1) Changes in the rate of the portal blood flow after the ligation of the hepatic artery

Since it was difficult from various reasons to observe the animals for long period after the ligation of the hepatic artery, the experiments were limited within a period of 30 minutes. The interruption of the blood flow through the hepatic artery was carried out either by the ligation of common hepatic artery alone or the ligation of the three major arteries (common hepatic, gastroduodenal, and right gastric artery) in one time.

i) In dogs of the control group

As illustrated in Figs 5 & 6, right after the ligation of the common hepatic

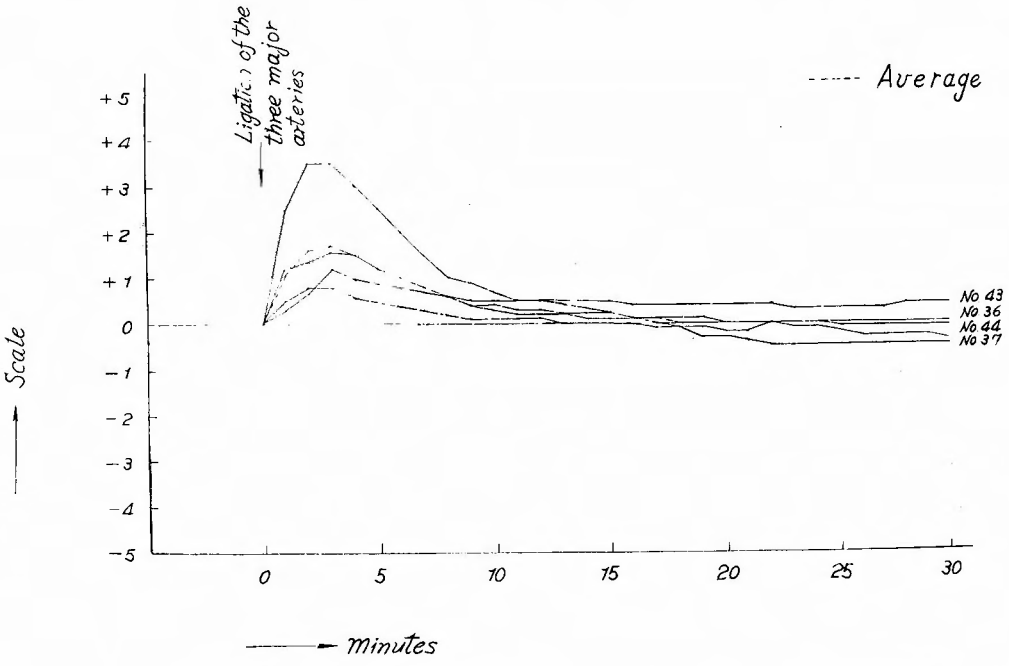


Fig. 6 Changes before and after ligation of the three major arteries on normal dogs.

artery or ligations of three major arteries, the rate of blood flow in the portal vein increased markedly. Within 5 to 20 minutes, however, it returned to the pre-ligation level, then gradually decreased. It was found that the time required the rate of blood flow to return to the pre-ligation level was longer, in the case of the ligation of three major arteries than that of the common hepatic artery alone. Converting these values into the volume of blood flow, as shown in Tab. 1, similar increase or decrease in the volume of blood flow in the portal vein were noticed. The average value of the volume of blood flow through the portal vein in the normal dogs was 208cc minute.

ii) In dogs in which the constriction of the hepatic vein was not followed by the development of ascites

Table 1. Portal blood flow (cc. per minute.)

	Dog No.	Body weight Kg.	before Ligation	after ligation 1 min.	5 min.	10 min.	15 min.	20 min.	25 min.	30 min.	35 min.
Ligation of the common hepatic artery on normal dogs	2	12.5	200	260	206	143	137	134	128	125	
	4	11.5	280	322	303	257	247	233	229	229	
	7	9.5	260	278	296	269	238	220	216	207	
	9	8.5	210	260	225	195	184	181	175	172	
	30	7.6	190	220	203	178	172	172	171	171	
	29	8.2	180	222	208	162	153	150	148	147	
	Average	9.6	220	260	240	201	189	182	178	175	
Ligation of the three major arteries on normal dogs	36	9.2	170	195	195	175	170	160	170	170	
	37	9.6	90	126	126	100	93	86	83	83	
	43	8.7	180	190	210	197	197	193	190	193	
	44	8.4	320	350	350	328	323	320	315	310	
	Average	9.0	190	215	220	200	196	190	190	189	
Ligation of the common hepatic artery on non ascitic dogs	41	9.0	220	243	249	169	163	231	231	226	
	42	8.9	250	287	270	250	244	250	242	236	
	Average	9.0	235	265	260	210	204	241	237	231	
Ligation of the three major arteries on non ascitic dogs	35	7.9	150	165	174	171	159	150	141	144	156
	45	10.5	220	255	255	245	240	235	220	215	220
	Average	9.2	185	210	215	208	200	193	181	180	188
Ligation of the common hepatic artery on ascitic dogs	14	9.5	150	183	193	193	170	149	143	149	159
	18	12.5	180	196	220	180	174	190	206	210	212
	24	10.5	200	240	248	236	210	195	186	200	214
	Average	10.8	177	206	220	203	185	178	178	186	195
Ligation of the three major arteries on ascitic dogs	34	9.0	130	144	180	171	157	153	141	139	144
	40	15.0	180	197	219	236	234	206	206	208	244
	Average	12.0	155	171	200	204	196	180	174	174	194

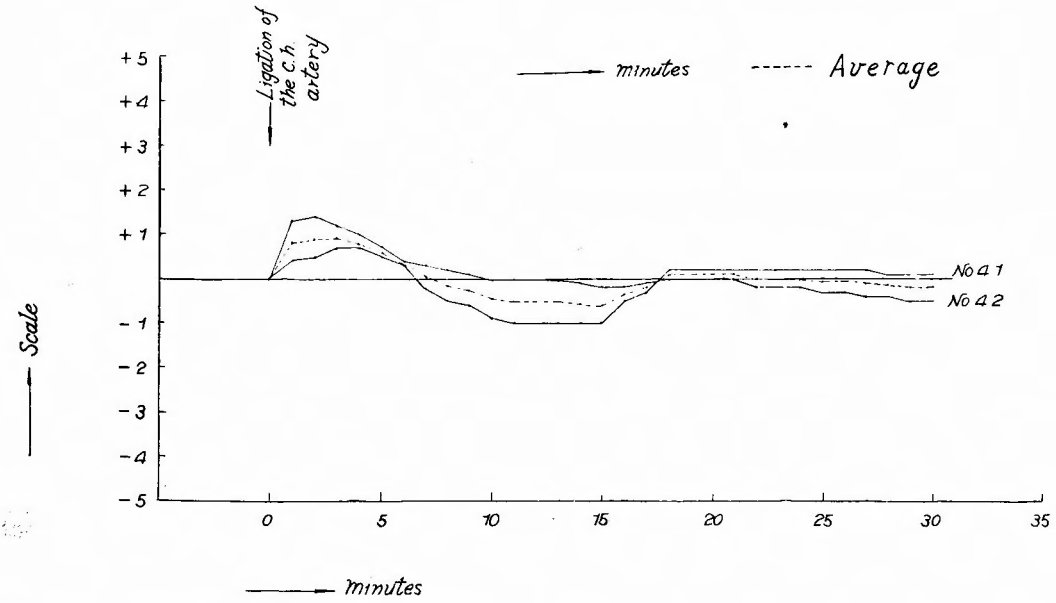


Fig. 7 Changes before and after ligation of the common hepatic artery on non ascitic dogs.

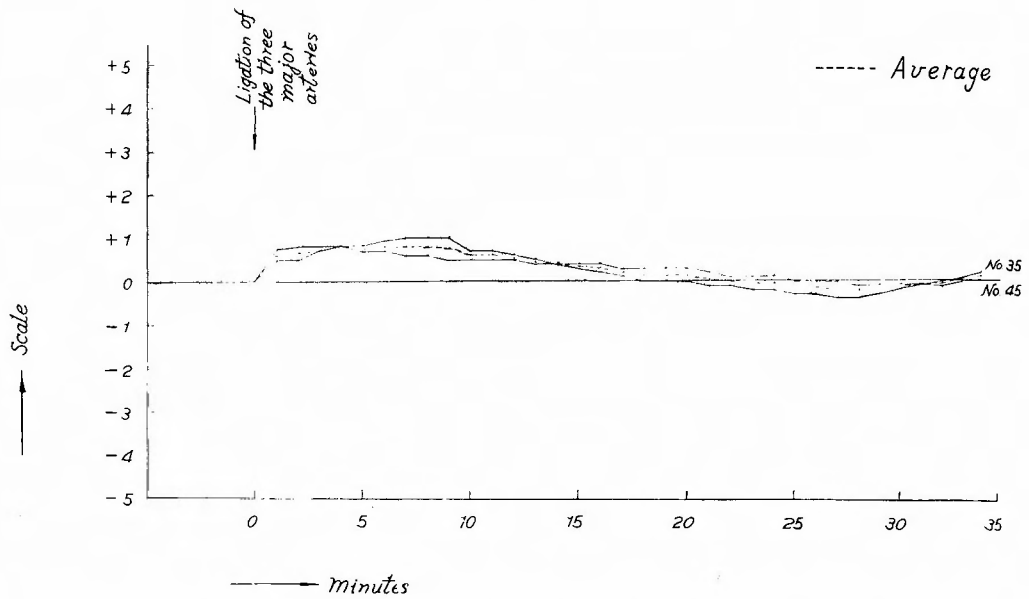


Fig. 8 Changes before and after ligation of the three major arteries on non ascitic dogs.

As illustrated in Figs 7 & 8, in some cases, it took longer time the increased rate of blood flow after the hepatic artery ligation to return to the pre-ligation level, compared with that in control animals, or in other cases, after the rate of blood flow decreased beyond the pre-ligation level, it increased again, so the curve directed upwards. These results were equally obtained either in case of the ligation

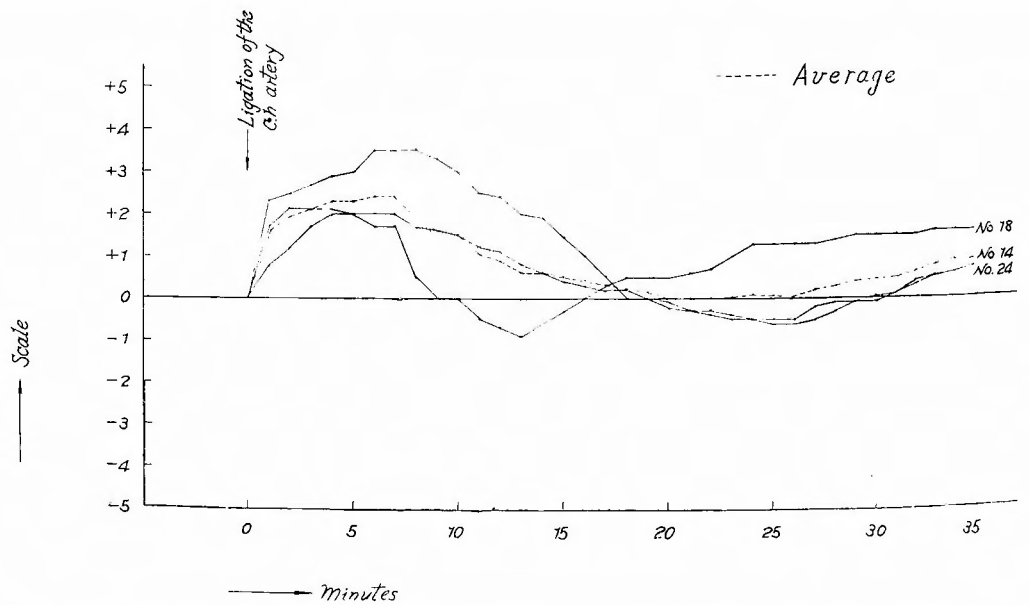


Fig. 9 Change before and after ligation of the common hepatic artery on ascitic dogs.

of the common hepatic artery alone or that of three major arteries. In dogs of this group, the average volume of blood flow through the portal vein before the ligation of the hepatic artery was 210cc/minute (Tab. 1).

iii) In dogs in which the marked ascites developed after the constriction of the hepatic vein

As shown in Figs 9 & 10, the increased rate in blood flow after the hepatic

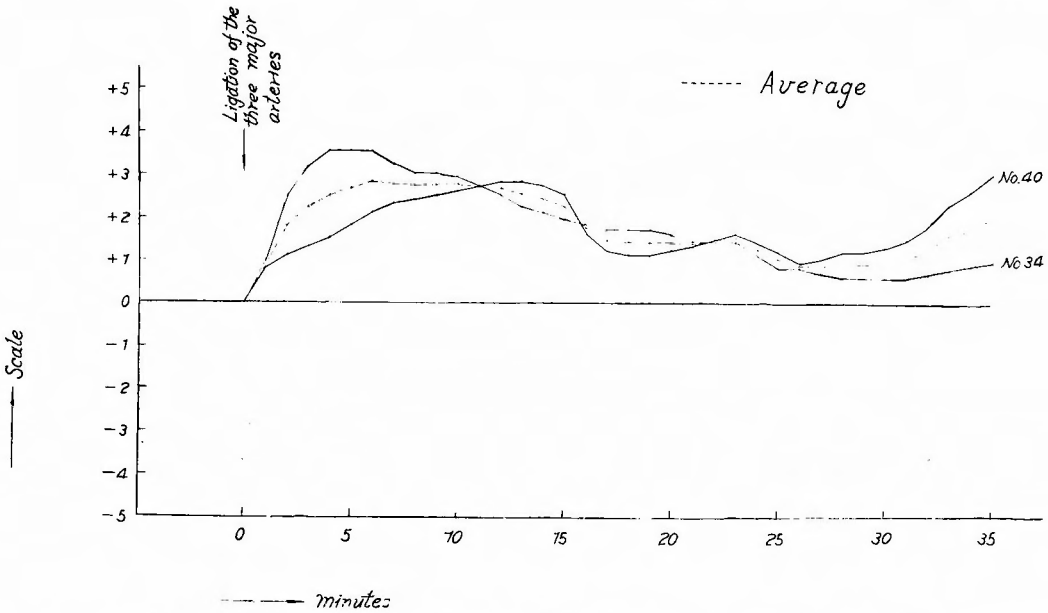


Fig. 10 Changes before and after ligation of the three major arteries on ascitic dogs.

artery ligation, though there was slight fluctuation, did not return to the pre-ligation level and this increase in the rate of blood flow through the portal vein was kept continued. This tendency was especially marked in dogs whose three major arteries were ligated. Average value of the volume of blood flow through the portal vein in dogs of this group was 168cc/minute (Tab. 1).

iv) Comments

As shown in Fig. 11, the increase in the rate of blood flow was most obvious in dogs in which the constriction of the hepatic vein had been followed by the development of the marked ascites, and was the second in dogs in which ascites did not develop after the hepatic vein constriction and was the least obvious in dogs of the control group. In the latter two groups, once increased rate of the blood flow dropped beyond the pre-ligation level as the time elapsed. In the former, on the other hand, the increase in the rate of blood flow continued and never returned to the pre-ligation level.

2) Cganges in the volume of the portal blood flow per 100g of the liver after the ligation of the hepatic artery

Results were shown in Fig. 12 and Tab. 2.

In the normal dogs average value of the blood flow volume through the portal vein before the ligation was 72cc per minute per 100g of liver. Whilst, in dogs

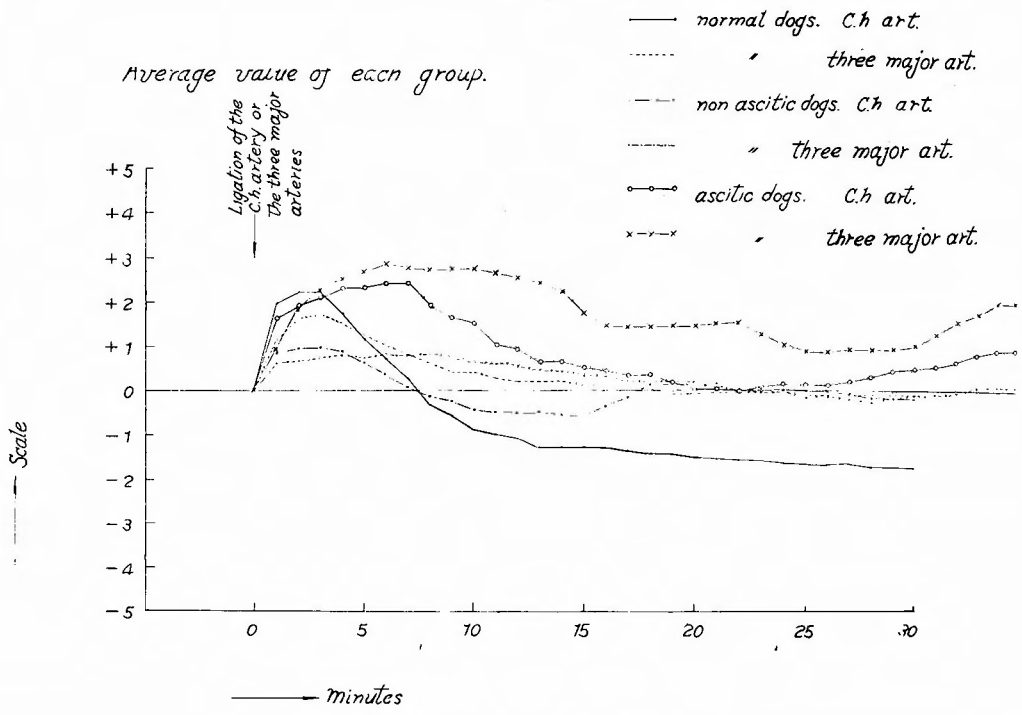


Fig 11 Average value of each group.

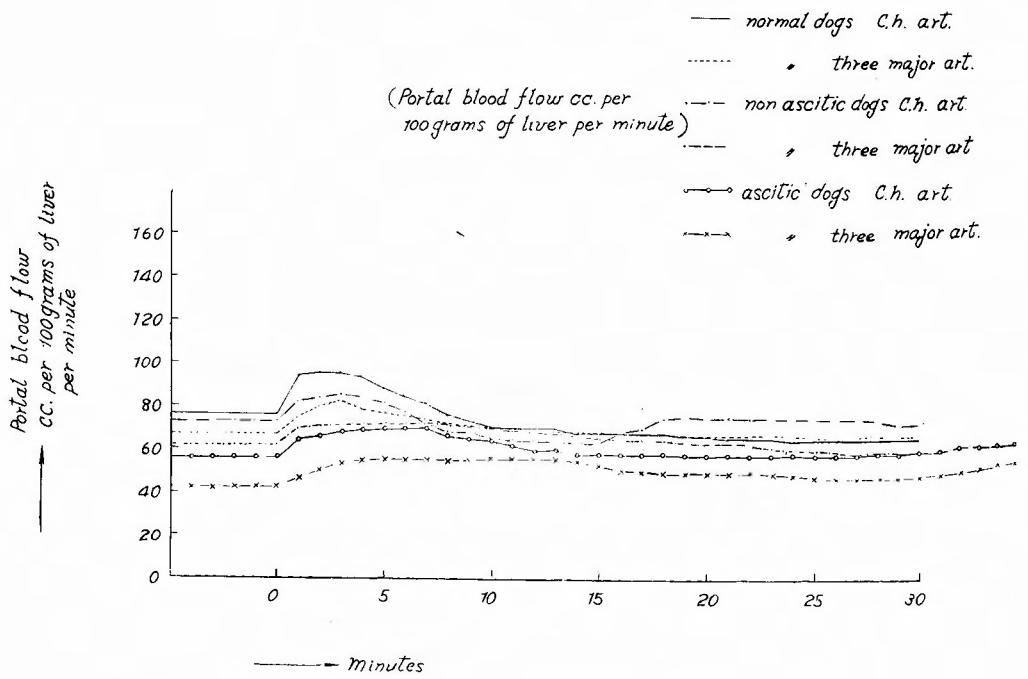


Fig. 12 Average value of each group.

Table 2 Portal blood flow (cc per 100 grams of liver per minute)

	Dog No.	Liver weight	before Ligation	after ligation 1 min.	5 min.	10 min	15 min	20 min	25 min	30 min	35 min
		grams	cc	cc.	cc.	cc.	cc.	cc.	cc.	cc.	cc.
Ligation of the common hepatic artery on normal dogs	2	290	68.9	89.5	70.9	49.3	47.2	46.2	44.1	43.1	
	4	365	76.7	88.2	83.0	70.4	67.8	64.0	62.7	62.7	
	7	330	78.7	84.0	89.4	81.3	72.0	66.6	65.3	62.6	
	9	290	72.4	89.6	77.4	67.4	63.3	62.3	60.3	59.3	
	30	240	79.1	91.4	84.6	74.2	71.7	71.7	71.1	71.1	
	29	220	81.8	100.7	94.6	73.5	69.7	68.2	67.5	66.7	
	Average	289.2	76.3	90.6	83.3	69.4	65.3	63.2	61.8	60.9	
Ligation of the three major arteries on normal dogs	36	250	68.0	78.0	78.0	70.0	68.0	64.0	68.0	68.0	
	37	280	32.1	44.8	44.8	35.6	33.1	30.6	29.6	29.6	
	43	430	41.8	44.1	48.7	45.6	45.6	44.9	44.1	44.9	
	44	250	128.0	140.0	140.0	137.0	129.0	128.0	126.0	124.0	
	Average	302.5	67.5	76.7	77.9	70.6	68.9	66.9	66.9	66.6	
Ligation of the common hepatic artery on non ascitic dogs	41	320	68.8	75.8	77.6	52.7	50.9	72.2	72.2	70.4	
	42	320	78.1	89.7	84.3	78.1	76.4	78.1	75.5	73.7	
	Average	320	73.5	82.8	81.0	65.4	63.7	75.2	73.9	72.1	
Ligation of the three major arteries on non ascitic dogs	35	250	60.0	66.0	69.6	68.4	63.6	60.0	56.4	57.6	
	45	350	62.8	72.8	72.8	69.9	68.5	67.0	62.8	61.4	
	Average	300	61.4	69.4	71.2	69.2	66.1	63.5	59.6	59.5	
Ligation of the common hepatic artery on ascitic dogs	14	310	48.3	58.8	62.1	62.1	54.7	47.9	46.0	47.9	51.0
	18	270	66.6	72.5	81.4	66.6	64.4	70.3	76.2	77.7	78.4
	24	370	54.0	64.9	66.8	63.6	56.5	52.8	50.2	54.0	57.8
	Average	316	56.3	65.4	70.1	64.1	58.5	57.0	57.5	59.9	62.4
Ligation of the three major arteries on ascitic dogs	34	290	44.8	49.7	62.0	59.0	54.1	52.6	48.7	47.7	49.7
	40	460	39.1	42.8	47.4	51.2	50.7	44.6	44.6	45.0	53.0
	Average	375	42.0	46.3	54.7	55.1	52.4	48.6	46.7	46.4	51.4

which had the hepatic veins constricted and without ascites it was 68cc/m/100g of liver, and in dogs with ascites after the hepatic vein constriction it was 49cc/m/100g of liver. As previously mentioned, the volume of blood flow in the portal vein per minute itself did not show any significant difference between in the normal control dogs and in dogs without ascites after the hepatic vein constriction. But calculating it in volume per minute per 100g of the liver tissue, the volume of the portal blood flow in the dogs without ascites after constriction was smaller than that in the normal dogs. Furthermore, comparing the volume in normal dogs with that in dogs which had the hepatic vein constricted and with a development of ascites, the difference became more significant, i. e. it reached as large as 23cc/m/100g of liver.

3) Balance of the increase and decrease in the volume of the portal blood flow at 30 minutes after the ligation of the hepatic artery

After the ligation of the hepatic artery, the volume of blood flow in the portal vein was measured at every one minute for 30 minutes. Comparing these values to that of pre-ligation level, the difference between them, i. e. the values of increase or decrease of the volume of blood flow were calculated at every minute after the ligation. Now, these values of difference, either positive or negative, were arithm-

etically added to obtain the balance for the period of 30 minutes. As shown in Tab. 3, this balance was negative in dogs of the control group and in dogs without ascites after the hepatic veins constriction and in both of which the common hepatic artery alone was ligated. Whilst, it was positive in dogs of the control group and in dogs without ascites of the hepatic vein constriction, and in both of which three major arteries were ligated. It was also positive in dogs with ascites after the hepatic vein constriction, and in which either the common hepatic artery alone or three major arteries were ligated. Among these, however, the positive balance was most markedly observed in dogs which had marked ascites after the hepatic vein constriction and later underwent the ligations of the three major arteries. In these animals an increase in the volume of the portal blood flow for 30 minutes reached as large as 1,000 cc.

Table 3 Changes of the portal blood flow during 30 minutes after hepatic artery ligation (cc)

	Normal dogs		Non ascitic dogs		Ascitic dogs	
Lapset time	Ligation of the common hepatic artery	Ligation of the three major arteries	Ligation of the common hepatic artery	Ligation of the three major arteries	Ligation of the common hepatic artery	Ligation of the three major arteries
minutes	cc	cc	cc	cc	cc	cc
1	40.1	25.1	29.9	25.0	30.4	15.6
2	43.9	37.0	34.2	27.5	37.2	29.6
3	43.9	42.5	37.1	30.5	41.5	36.8
4	34.0	35.9	34.2	32.0	44.4	41.0
5	20.1	30.1	24.2	29.5	44.1	44.2
6	9.4	25.0	14.2	31.0	44.5	47.5
7	1.6	19.9	−1.5	30.0	44.5	47.5
8	−8.3	14.7	−11.4	30.0	34.1	47.1
9	−15.0	11.1	−15.7	27.5	29.3	48.2
10	−19.4	9.7	−25.7	23.0	26.9	48.6
11	−21.4	8.2	−28.6	23.0	19.7	48.2
12	−24.2	8.4	−28.6	21.5	16.1	47.9
13	−28.9	6.0	−28.6	17.5	10.5	52.0
14	−31.0	5.0	−30.0	16.0	9.9	43.9
15	−31.5	5.4	−31.4	14.5	8.5	40.3
16	−32.2	4.3	−17.1	13.0	7.6	34.0
17	−34.2	2.9	−10.0	9.0	6.6	24.9
18	−35.8	2.3	5.7	7.5	5.5	23.8
19	−37.3	1.6	5.7	7.5	4.0	23.8
20	−38.3	−0.3	5.7	7.5	1.9	24.2
21	−38.8	−0.6	5.7	3.5	0.9	23.9
22	−40.0	−0.3	2.8	1.0	0.7	26.0
23	−40.6	−0	2.8	−0.5	1.4	27.5
24	−41.8	−0	2.8	−0.5	3.0	22.9
25	−42.3	−0.6	1.4	−4.5	2.2	18.6
26	−43.5	−1.2	1.4	−4.8	2.2	15.3
27	−44.0	−1.2	0	−6.0	4.4	15.6
28	−44.3	−0.4	−2.9	−8.5	7.1	17.1
29	−45.1	−0.4	−4.3	−7.0	9.4	17.1
30	−45.1	−1.0	−4.3	−5.5	10.2	18.2
Total	−590.0	290.9	−32.3	390.5	507.6	967.2

This fact, as will be discussed later, may suggest that the blood flow of the hepatic artery is working hemodynamically as a resistance upon the blood flow in the portal vein, especially it is true in dogs with ascites after the hepatic vein constriction. The values of increase and decrease shown in Tab. 3, were average

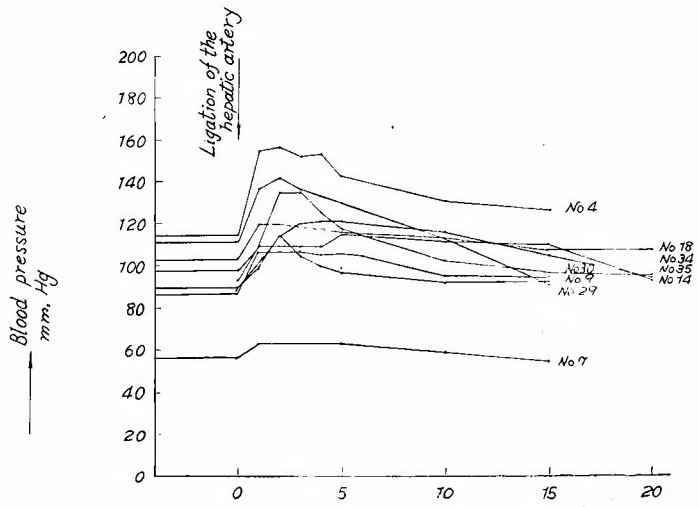


Fig. 13 Changes of systemic blood pressure influenced by hepatic artery ligation

values from many animals.

4) Changes in the systemic arterial blood pressure after the ligation of the hepatic artery

Arterial blood pressure was determined at the femoral artery before and after the hepatic artery ligation with the use of mercury manometer. Results were shown

Table 4. Changes of systemic blood pressure influenced by hepatic artery ligation.

			after ligation							
	Dog No	before ligation	1 min.	2 min.	3 min	4 min	5 min.	10 min.	15 min.	20min.
		mm.Hg.	mm.Hg.	mm.Hg.	mm.Hg.	mm.Hg.	mm.Hg.	mm.Hg	mm.Hg.	mm.Hg.
Normal dogs	4	120~130	150~160	155~160	150~155	150~155	140~146	128~135	125~130	
	median	115	155	158	153	153	143	132	128	
	9	85~95	95~105	110~120	100~110	95~105	95~100	90~95		
	median	90	100	115	105	100	98	93		
	29	110~115	130~145	135~150	130~145	128~140	125~135	110~116	90~95	
	median	113	138	143	138	134	130	113	93	
	30	85~90	100~115	100~116	100~112	100~112	100~110	93~98	92~98	90~95
	median	88	108	108	106	106	105	96	96	93
	7	55~58	62~64	62~64	62~64	62~64	62~64	58~60	53~56	
	median	57	68	63	63	63	63	59	55	
Hepatic vein constricted dogs	14	95~100	105~112	105~112	105~112	105~112	110~119	109~114	107~113	91~95
	median	98	109	109	109	109	116	112	110	93
	24	100~105	115~125	115~125	?	?	112~120	110~115	105~110	105~110
	median	103	120	120			116	113	108	108
	18	110~115	119~125	127~136	124~130	118~123	110~116	105~110	105~109	105~109
	median	113	122	132	127	121	113	108	107	107
	35	86~92	110~119	117~123	118~123	118~123	118~123	114~117	103~106	94~96
	median	89	115	120	121	121	121	116	105	95
	34	90~95	104~115	130~140	130~140	122~130	115~120	100~103	96~98	95~96
	median	93	110	135	135	126	118	102	97	96

in Fig. 13 and Tab. 4. Actually in all dogs, i. e. in dogs in which either the common hepatic artery alone or three major arteries were ligated, or in dogs either in the control group or those with constricted hepatic vein, the systemic arterial blood pressure rose 10-40mm Hg, within 1-2 minutes after the ligation of the hepatic artery and it continued to rise for approximately 10 minutes. This rise in blood pressure seemed to be due to the neuroreflectoric mechanism, (BURTON, OPITZ) and also it quite corresponded in time factor to the transient increase of the portal blood flow soon after the ligation of the hepatic artery. Thus, these two phenomena might have some interrelation with each other.

5) Long-term observation of the changes in the portal blood flow after the ligation of the hepatic artery in the normal dogs

As illustrated in Fig. 14, the simultaneous ligation of three major arteries in the normal dogs, was followed by the marked increase in the rate of blood flow within 1-2 minutes. It, however, decreased rapidly, and the rate which was registered at approximately one hour after the ligation did continue for 8 hours, thereafter, it further decreased gradually. This last decrease was considered naturally to be due to the general weakness by the operation, though the particular care was taken for the maintenance of the body temperature or the relaxation of the legs

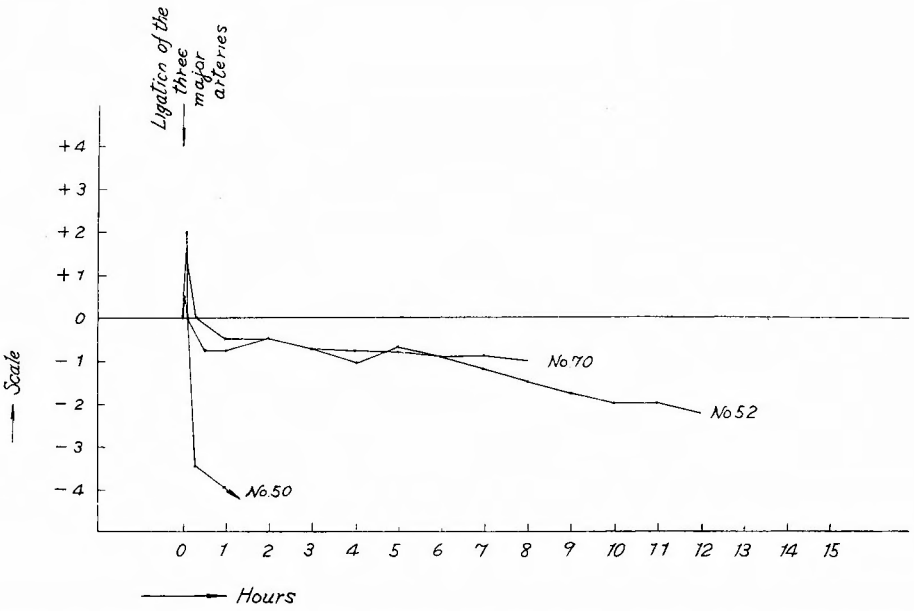


Fig. 14 Changes of portal blood velocity influenced by ligation of the three major arteries on normal dogs.

etc. Exceptionally, as seen in No. 50, very marked decrease in blood flow was observed within an hour.

IV. STUDY WITH BUBBLE-FLOWMETER

For the determination of the volume of blood flow in the peripheral organs, so many different methods have been used. These, however, can be roughly divided into two, i. e. direct and indirect methods. In the present study, in order to confirm the results obtained by the "Thermostromuhr", the bubble flowmeter which is rather primitive in principle but fairly accurate, was also used. This flowmeter was used for the first time by Soskin et al. in 1934 for the determination of the volume of

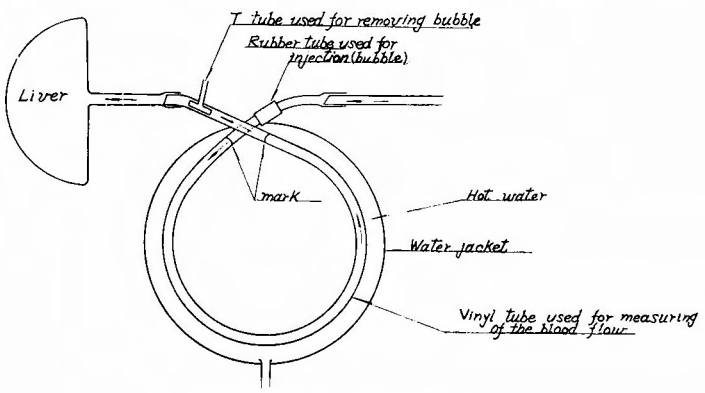


Fig. 15 Bubble Flow Meter

blood flow.

We, as shown in Fig. 15, used a vinyl tube with 5mm of inner diameter, 7mm of external diameter and with 15 cc of inner capacity. This tube was again surrounded with vinyl water jacket. At the distal portion of this tube, i. e. close to the liver, a T-tube was set so that the bubble injected could escape through it. The flowmeter we used was the one of spiral type with one circuit which was believed to be of the least resistance. The tube of this flowmeter was placed on the same level as that of the portal vein. In using this flowmeter particular cares were taken for the following matters; use of anticoagulant drugs, cleanness of the apparatus and use of water jackets for warming the irrigated blood etc.

1) Method

The volume of blood flow through the portal vein was measured before and after the ligation of three major arteries in normal dogs. Animals were kept away from food for 24 hours before measurement. Under a general anesthesia with intravenous injection of thiopental-sodium, a laparotomy was carried out with right subcostal incision. The portal vein was dissected from the surrounding tissue and the splenic vein was ligated and cut for convenience of the manipulation. Heparin was injected through the mesenteric vein, the portal vein was interrupted transiently, the vinyl tube was inserted and the portal vein was reopened. From the proximal part of the tube approximately 0.1-0.2 cc of air bubble was injected and the time which was required for the bubble to pass between two points of the tube. These two points were previously marked, so as the inner capacity of the tube between these two points to be 15 cc. Thus, the volume of the portal blood flow was calculated.

2) Results

This method was adopted, as previously mentioned, to re-examine the data obtained by the "Thermostromuhr" from the different angle. By this method, the volume of the portal blood flow was determined before and after the ligation of

Table 5. Changes of the portal blood flow before and after ligation of the three major arteries, measured by the Bubble Flow Meter.

Dog No.	Portal blood flow cc per minute	Liver weight	Portal blood flow before ligation cc. per 100grams of liver per min.							Portal blood flow after ligation cc per 100grams of liver per min.							
Extra		grams	7min.	6min.	5min	4min.	3min.	2min.	1min	1min	2min.	3min.	4min.	5min.	6min.	7min.	8min.
13	577	210			28	29	28	23	23	31	31	25	23	28			
27	60.6	215	33	32	30	29	28	27	26	34	36	36	34	35			
28	43.0	250	13	14	16	15	14	14	13	13	14	14				12	
29	47.0	350					13	13	13	16	16	15	15	15	15	16	
34	58	170				37	35	32	31	37	56	61	57	50	45	40	30
37	38	255			15	15	15	15	14	17	20	17	15				
61	80	270				26	26	26	26	47	33	30	29	26			
Average	54.9	245.7	23	23	223	25.2	22.7	21.4	20.8	27.8	29.6	28.3	28.8	30.8	30	24	30

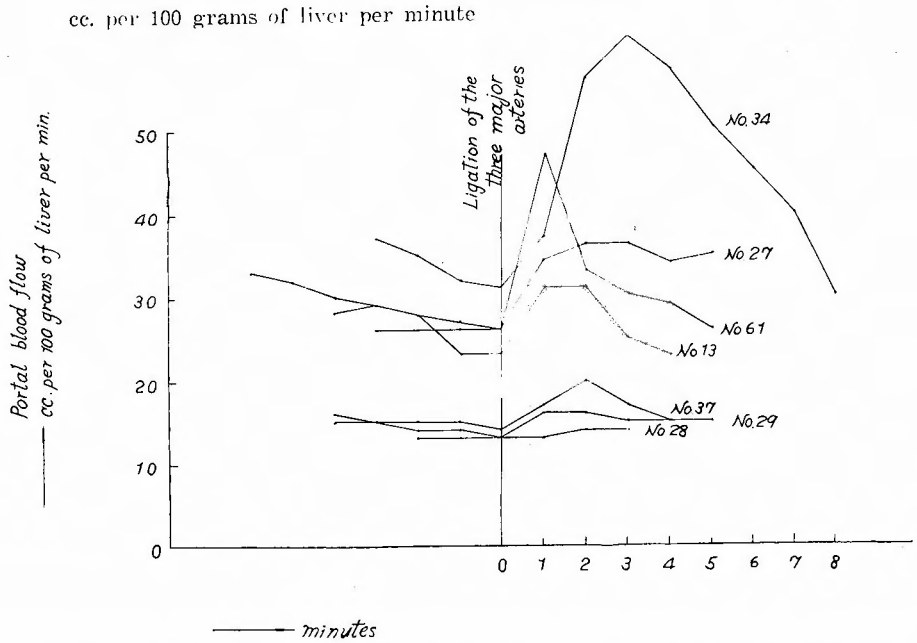


Fig. 16 Changes of the portal blood flow before and after ligation of the three major arteries measured by the Bubble Flow Meter.

three major arteries in the normal dogs. The values of measurement were, as shown in Fig. 16 and Tab. 5, essentially equal to those obtained by "Thermostromuhr". That is, within 1-2 minutes after the ligation of three major arteries the volume of blood flow through the portal vein increased (at maximum 10cc/m/100g of liver compared to the pre-ligation value), and returned to pre-ligation level, and continued to decrease gradually thereafter.

V. DISCUSSION

In 1949, RIENHOFF performed the ligation of the hepatic artery to a patient of liver cirrhosis, and concluded that this procedure was worthwhile to try for the treatment of liver cirrhosis particularly with ascites. In 1951, BERMAN et al. also reported excellent results of this procedure for the treatment of liver cirrhosis with ascites.

TSUCHIYA, in our laboratory, performed the constriction of the hepatic vein in dogs and could produce in them the conditions quite similar to those in human cases of liver cirrhosis. In these animals the common hepatic, gastroduodenal and right gastric arteries were ligated. He made it clear that in dogs which tolerated the procedure and survived for long, the blood pressure of the portal vein markedly decreased. From my study, it was confirmed that when the common hepatic, gastroduodenal and right gastric artery were simultaneously ligated in dogs with ascites, a continuous increase in the volume of the portal blood flow resulted. Also in case of the ligation of the hepatic artery alone, similar increase in the volume of

the portal blood flow, though it was less marked, was observed.

Concerning the mechanisms of the development of ascites, there are many different opinions. Among those, a theory that due to the anomalies of the intrahepatic vascular bed the venous congestion may take place, this, in turn, gives rise to the transdation of the liver lymph into the intraabdominal cavity to become ascites, is believed to be most reasonable (RIENHOFF, MADDEN).

In 1873 GAD reported that the blood flow in the hepatic artery slowed down the blood flow in the portal vein, following his experiments on rabbits. In 1907, HERRICK advocated that the hepatic artery worked as a resistance upon the portal vein, through his perfusion test on the human liver. Further, he found this was most markedly seen in the cirrhotic liver. In 1928, MCINDOE also pointed out that there was a difinite relationship between the blood pressure of the hepatic artery and that of the portal vein.

Thus, it can be easily imagined that the ligation of the hepatic artery will be effective in reducing ascites even when we think of only one factor that this procedure can mitigate the congestive state of the liver. In this view point, our experimental data that the hepatic artery ligation resulted in increase in the volume of the portal blood flow, is quite understandable, since in the case of liver cirrhosis with ascites the blood flow of the hepatic artery acts as a more obstacle upon the portal blood flow than in the normal liver.

Thus, we are of the opinion that the increase in the volume of the portal blood flow will serve to improve the liver function of the ascitic dogs with liver cirrhosis.

VI. SUMMARY

In 29 mongrel adult dogs the hepatic veins were constricted and ascites was produced experimentally. In these animals the effects of the ligation of the common hepatic, gastroduodenal and right gastric arteries upon the flow of the portal vein and upon the systemic arterial blood pressure were observed for 30 minutes.

Results obtained were as follows;

1) In dogs whose hepatic vein was constricted and ascites did not develop, the volume of blood flow in the portal vein did not essentially differ from that in normal dogs.

2) In dogs which had ascites after the hepatic vein constriction, on the other hand, the volume of the portal blood flow reduced markedly.

3) The volume of the portal blood flow increased markedly within 1-2 minutes after the hepatic artery ligation either in normal dogs or in dogs which had the hepatic veins ligated.

4) After the hepatic artery ligation in dogs whose hepatic vein had previously been constricted, the most marked and continuous increase of the portal blood flow was obtained in dogs which had ascites and in which the common hepatic, gastroduodenal and right gastric arteries were all ligated, and similar increase was seen, though in the lesser degree, in dogs of same group and in which the common hepatic artery alone was ligated.

5) In dogs of two other groups, i. e. dogs in the control group and those which did not have ascites, the ligation of the hepatic artery was not followed by a significant change in the volume of the portal blood flow.

6) Data obtained with the use of bubble flowmeter were essentially the same as those obtained by "Thermostromuhr".

I do wish to express my deep appreciation to Prof. Dr. CHISATO ARAKI for his guidance and for his correcting paper. Also I am greatly indebted to Assistant Prof. Dr. ICHIO. HONJŌ for his kind and extended directions throughout the period of this experimentation.

REFERENCES

1) Berman, J. K., H. Koenig and W. K. Saint: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertention. Quart. Bull., **12**, 99, 1950.
2) Berman, J. K.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension. Summary of Experimental Studies and Report of a Case Treated by this Procedure. Arch. Surg., **62**, 810, 1951.
3) Berman, J. K., L. P. Muller, C. Fisch and W. Mortz: Ligation of the Hepatic and Splenic Arteries in a Patient with Atrophic Cirrhosis of the Liver. Arch. Surg., **63**, 5, 1951.
4) Berman, J. K., H. Koenig and L. Muller: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension due to Atrophic Cirrhosis of the Liver. Arch. Surg., **63**, 379, 1951.
5) Berman, J. K. and J. E. Hull: Ascites - Its Experimental Production and Control. Surgery, **32**, 67, 1952.
6) Berman, J. K. and J. E. Hull: Ligation of the Hepatic Splenic and Left Gastric Arteries in Patients with Advanced Portal Cirrhosis. Arch. Surg., **65**, 37, 1952.
7) Berman, J. K. and Hull, J. E.: Circulation in the Normal and Cirrhotic Liver. Ann. Surg. **137**, 3, 1953.
8) Burton-Opitz, Russell: The Vascularity of the Liver. The Magnitude of the Portal Inflow. J. Exper. Physiol., **4**, 113, 1911.
9) Bruner, H. D.: Bubble flowmeter; Method in Medical Research. Vol. **1**,80-86, The Yr. BK. Publ., Chicago 1948.
10) Child, C. G. and Others: Pancreaticoduodenectomy with Resektion of the Portal Vein in the Macaca Mulatta Monkey and in Man. Surg. Gynec. & Obst., **94**, 31, 1952.
11) Davis, L., C. Tanturi and J. Tarkington: The Effect of Reduced Blood Flow to the Liver in Renal Hypertension. Surg. Gynec. & Obst., **89**, 360, 1949.
12) Desforge, G. and Others: Hepatic Artery Ligation for Portal Hypertension. Ann. Surg. **137**, 4, 1953.
13) Douglas, T. C. and Others: Attempts at the Experimental Production of Portal Hypertension. Arch. Surg., **62**, 785, 1951.
14) Fraser, D., A. M. Rappaport and Others: Effect of the Ligation of Hepatic Arteries in Dogs. Surgery, **30**, 624, 1951.
15) Grab, W., Janssen S. und Rein H: Über die Grösse der Leberdurchblutung. Zeitschrift f. Biologie, **89**, 324-331, 1929.
16) Grindlay, J. H., Herrick, J. F. and Mann, F. C.: Measurement of the Blood Flow of the Liver. Am. J. Physiolog., **132**, 489, 1941.
17) Herrick, F. C.: An Experimental Study into the Cause of Increased Portal Pressure in Portal Cirrhosis. J. Exper. Med., **9**, 93, 1907.
18) Harumi Hisatsune: Hemodynamic Studies on the Hepatic Circulation of Experimental Ascites. The Japanese Journal of Gastro-enterology, **55**, 1, 1958.
19) Tokuo Kagitani: Study on Hepatic Circulation in Surgery of Portal System. J. J. S. S. ("Nihongekagakkai-Zasshi" in Jap.), **55**, 2, 1954.
20) T. Kajitani, et al.: Report of a Case who survived after the Hepatic Artery Ligation. Clinical Surgery ("Rinshōgeka" in Jap.), **9**, 2, 1954.
21) MacLeod, J. J. R. and R. G. Pearce: The Outflow of Blood from the Liver as Effected by

Variations in the Condition of the Portal Vein and the Hepatic Artery. Am. J. Physiol., **35**, 87, 1914.
22) Madden, J. L., et al.: The Pathogenesis of Ascites and a Consideration of its Treatment. Surg. Gynec. Obst., **99**, 385, 1954.
23) McIndoe, A. H.: Vascular Lesion of Portal Cirrhosis. Arch. Path. & Lab. Med., **5**, 23, 1928.
24) Markowitz, J. and A. M. Rappaport: The Hepatic Artery. Physiol. Rev., **31**, 188, 1951.
25) Markowitz, J., A. Rappaport and A. C. Scott: Prevention of Liver Necrosis Following Ligation of Hepatic Artery. Proc. Soc. Exper. Biol. & Med., **70**, 305, 1949.
26) T. Misao et al.: Medical Electronics.
27) K. Motokawa: Experimental Electronics. 4th Ed.
28) Rein, H.: Die Thermostromuhr. Zeitshrift f. Biologie, **89**, 195–201, 1929.
29) Rienhoff, W. F.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension with a Report of Six Cases. Bull. Johns Hopkins Hosp., **88**, 368, 1951.
30) R. Soejima, et al.: Variation in the Portal Circulation after Hepatectomy in Dogs (Experimental Study). J. J. S. S. ("Nihongekagakkai-Zasshi" in Jap.), **56**, 8, 1955.
31) Taylor, F. W. Rosenbaum. D.. The Case Against Hepatic Artery Ligation in Portal Hypertension. J. A. M. A., **14**, 4, 187, 1953.
32) M. Urabe, et al.: Measurement of Organ Blood Flow. ("Sōgōigaku" in Jap.), **11**, 10, 1954.
33) Wakim, K. G. and F. C. Mann: The Intrahepatic Circulation of Blood. Anat. Rec., **82**, 233, 1942.

和 文 抄 録

肝 硬 変 症 の 実 験 的 研 究

——特に肝静脈狭窄犬における肝動脈結紮の門脈流に及ぼす影響について——

京都大学医学部外科学教室第1講座 (指導：荒木千里教授)

細 野 幸 吾

最近 Rienhoff, Berman 等が肝硬変症の治療に肝動脈結紮が有効であることを提唱して以来，諸家により本法は種々追試検討されてきたが，いまだ定説を得ない現状である．著者は肝硬変症の場合に，特に腹水の有無と関連して肝動脈結紮が門脈血流に対して如何様に働くかを確めるため，犬の肝静脈を狭窄し肝硬変類似の状態を作成し，これら肝静脈狭窄犬に肝動脈血流遮断をおこない，門脈流に対する影響を "Thermostromuhr" 及び Bubble Flowmeter を使用して検索した．

実験動物には7.6kg～15.0kgの雑犬を使用し正常犬群，肝静脈狭窄犬で腹水の貯溜をきたさなかつた犬群及び肝静脈狭窄犬で腹水の貯溜をきたした犬群にわかち，肝静脈狭窄犬は腹水の有無にかゝわらず肝静脈狭窄後14日目に再開腹し，門脈血流速度測定を実施した．肝静脈狭窄犬の作成には大略教室の土屋が行つた方法を採用した．

"Termostromuhr" 測定装置のうち，樋状熱電対は Herrick 等の使用したものと大差はないが，ベークライト板には，よりよく血管に接着させるためゴム板を，又血液加熱には高周波発生装置を使用した．樋状熱電対の門脈への装着は脾静脈流入部より肝臓側でおこなつた．門脈血流速度の判明した実験犬について門脈血流量の測定には犬の剔出門脈片及び同一個体より採集したヘパリン加血液を使用した．全身動脈圧測定には，便宜上股動脈圧を水銀マノメーターで測定した．

実 験 成 績

1) 肝動脈結紮後の門脈血流速度の変動

肝動脈血流遮断には総肝動脈単独結紮と，三大動脈

（総肝動脈，胃十二指腸動脈，右胃動脈）同時結紮との両者を実施した．

i 正常犬群

総肝動脈又は三大動脈結紮直後，門脈血流速度は著明に増加するが5分～20分で結紮前の速度に迄戻り，以後徐々に速度は低下する．門脈血流量に換算しても同様の増減を認めるのは当然で，正常犬の門脈血流量は平均208cc/分である．

ii 肝静脈狭窄犬で腹水の貯溜をきたさなかつた犬群

正常犬群のそれと比較すると肝動脈結紮直後上昇した血流速度は結紮前値に戻る迄の時間が延長したり，又一時結紮前値以下の速度に下降した曲線が再び上昇する傾向を示す症例もある．この犬群の肝動脈結紮前の門脈血流量は平均210cc/分である．

iii 肝静脈狭窄犬で腹水の貯溜をきたした犬群

肝動脈結紮後上昇した血流速度は多少の増減はあるが結紮前値迄減少することなく，速度増加を示したまゝで推移する．この傾向は三大動脈結紮の場合に特に著明であつた．この犬群の門脈血流量は平均168cc/分である．

2） 肝動脈結紮後30分間における各犬群の門脈血流量増減総和について

各犬群について肝動脈結紮前門脈血流量に対して結紮後各分毎の増減量を加減した値を30分間で区切つて総計を求めると，正常犬及び肝静脈狭窄犬で腹水の貯溜をきたさなかつた犬群の総肝動脈結紮例では負の値を示し，他方正常犬及び肝静脈狭窄犬で腹水の貯溜をきたさなかつた犬群の3大動脈結紮例，及び肝静脈狭窄犬で腹水の貯溜をきたした犬群では総肝動脈のみの結紮例でも，3大動脈結紮例でも共に正の値を示し，殊に肝静脈狭窄犬で腹水の貯溜をきたした犬群の3大動脈結紮例では30分間に約1000ccの門脈血流量増加を示す．

3） 全身動脈圧の変動

総肝動脈のみの結紮でも3大動脈の結紮でも，又正常犬でも肝静脈狭窄犬でも結紮後1分～2分で10mmHg～40mmHg上昇し10分前後持続する．この肝動脈遮断後の一時的動脈圧上昇と門脈流の一時的増加とは時間的によく一致する．

4） 肝動脈結紮による門脈流変動を長時間観察したが，結紮後大略1時間前後の血流速度を約8時間保つた．その後実験犬の全身衰弱等により漸次減少した．

5） 空泡流量計による検討

正常犬群について3大動脈結紮前後の門脈血流量を測定した．測定値は“Thermostromuhr”で測定した値と大略同様であることを確め得た．