

THE EFFECTS OF INTERRUPTION OF THE HEPATIC ARTERY ON THE OXYGEN CONTENT OF THE PORTAL BLOOD IN ASCITIC DOGS

by

KAZUYASU ADACHI

From the 1st Surgical Division, Kyoto University Medical School

(Director : Prof. Dr. CHISATO ARAKI)

(Received for publication Aug. 10, 1959)

- I. Introduction
- II. Methods and materials
 - 1. Production of portal hypertension in dogs
 - a) Constriction of the hepatic vein
 - b) Constriction of the inferior vena cava
 - 2. Determination of volume percentage of oxygen content of the portal blood
 - a) Reagents
 - b) Extraction of blood gas
 - c) Absorption of CO₂-gas
 - d) Absorption of O₂-gas
- III. Results
 - 1. Interruption of the hepatic artery in normal dogs
 - a) Group given antibiotics
 - b) Group not given antibiotics
 - 2. Portal hypertension dogs
 - a) Ascitic dogs produced by constriction of the inferior vena cava
 - b) Dogs who showed marked accumulation of ascites after constriction of the hepatic vein
 - c) Dogs in whom constriction of the hepatic vein was not followed by accumulation of ascites
- 3. Comments
- IV. Clinical cases of liver cirrhosis with marked accumulation of ascites
 - 1. Changes in volume percentage of oxygen content of the portal blood after interruption of the hepatic artery
 - 2. Changes in liver color after interruption of the hepatic artery
- V. Discussion
- VI. Summary

1. INTRODUCTION

Since RIENHOFF, BERMAN and others advocated that ligation of the hepatic artery was effective for the treatment of liver cirrhosis in which marked ascites developed, many investigators have reexamined this problem from various angles. They are, however, of a diversity of opinions about this procedure.

Author intended to investigate the effects of ligation of the hepatic artery upon the blood oxygen content in the portal vein in cases of liver cirrhosis associated with or without ascites. By the method of TSUCHIYA of our clinic, that is, constriction of the hepatic vein in dogs, we succeeded in producing conditions quite similar to those of liver cirrhosis in human beings. In these dogs the hepatic artery was ligated and changes in the blood oxygen content were studied. This method, however, could not always develop ascites. I modified the method of MCKEE by fixing a cellophane band around the inferior vena cava in the thorax with the purpose of its constriction and succeeded in producing ascitic dogs in high percentage. Then I performed the interruption of

the hepatic arterial flow to these dogs to examine changes in the oxygen content of the portal blood, and, at the same time, to determine that of the arterial blood. On patients with highly developed ascites, I performed the interruption of the hepatic artery, and measured the changes in the oxygen content of the portal blood, comparing these values with those of experimental dogs.

II. METHODS AND MATERIALS

1. Production of portal hypertension in dogs

With the purpose of development of ascites author devised the following method

a) Constriction of the hepatic vein

Mongrel dogs 7.6–15 kg in weight were used. Author applied the method of TSUCHIYA of our clinic, that is the constriction of the hepatic vein. Prior to this procedure, the animal was kept away from food for 24 hours. Under general anesthesia with an intravenous injection of Pentobarbital Sodium by Abbott's 'Nembutal' in dose of 0.5 cc/per kg in body weight, laparotomy was carried out with right-subcostal incision. Ligation or constriction of individual branches of the hepatic vein was done according to TSUCHIYA's method. In the present experiment, however, the method of HOSONO was sometimes adopted, since by this method manipulation for the right hepatic vein was slightly simplified, i.e. the branches of the right hepatic vein were divided into two groups, superior and inferior, and veins in each group were ligated on masse.

During these procedures a particular care was taken not constrict the abdominal vena cava. As for the middle and the left hepatic vein, constriction or ligation of an individual vein was done by TSUCHIYA's method.

b) Constriction of the inferior vena cava

Under basal narcosis with an intravenous injection of 'Nembutal' in dose of 0.5cc/kg, endotracheal anesthesia with an artificial respirator was applied, and the thorax opened in the right VI intercostal space. Then the inferior vena cava was somewhat constricted by a cellophane band of 12×2 cm. After operation, Penicillin amounting to 100,000 units was administered in the thorax cavity. Thus, the marked accumulation of ascites developed 2 to 14 days after the operation. By this method I could produce ascitic dog in higher percentage than by the method of constriction of the hepatic vein, than by the method of constriction of the hepatic vein, and obtained over 1,000 cc ascites as a rule.

2. Determination of volume percentage of oxygen content in the portal blood

Portal blood was taken directly from the portal trunk at the time of laparotomy. The subjects examined were kept in supine position and horizontally under the narcosis with intravenous injection of 'Nembutal' of 0.5 cc per kg in body weight, and they were away from feeding prior to

the examination. In taking the blood specimen, the femoral artery was substituted for the hepatic artery.

The wall of the dried sterilized pump was moistured with hepalin solution to keep air away from blood. To prevent coagulation of blood in pointed glass, I added 0.2 mg/cc neutral kalium oxalate per 1 cc of blood, and then 1 mg/cc NaF per 1 cc of blood was added to the glass to prevent the formation of lactic acid through the decomposition of sugar. This means that 5 g of NaF and 10 g Kalium oxalate were dissolved in 100 cc of water. 0.02 cc of this solution per 1 cc of blood was put in the pointed glass moistening its wall evenly and then dried. To this blood taken from the portal vein or the artery was put under fluid paraffin.

a) Reagents

i) Reagents used in extraction of blood gas

32 g of $K_3Fe(CN)_6$ and 8 g of Saponin were dissolved in 1,000 cc of water successively. 8 cc of concentrated lactic acid which has 1.2 of specific gravity was diluted to 1,000 cc of its solution by adding water.

ii) Reagents used in absorption of CO_2 gas

The solution of NaOH of 1-n from which gas was extracted was put in a pointed glass under fluid paraffin.

iii) Reagents used in absorption of O_2 gas

5 g of $Na_2S_2O_4 \cdot 2H_2O$, and 0.5 g of Anthrachinon- β -Sulfonacid Natrium were mixed with 25 g of 1-n-NaOH in a beaker. After shaking these reagents a few minutes, they were rapidly filtered through cotton, and air was extracted from them. Then, they were put under fluid paraffin of over 1cm of thickness. This procedure was done as rapidly as possible to prevent oxydation in the air. Extraction of gas from the reagents described i) and ii) was done on every test. As the reagents iii) could be preserved only for a very short time, they were prepared newly on every test and the extraction of gas was done at the same time. Determination was made by VANSLYKE-NEIL manometer.

b) Extraction of blood gas

7.5 cc of $K_3Fe(CN)_6$ -Saponin solution added by one drop of Kaprylalcohol was put into the VANSLYKE-NEIL manometer. After extraction of gas, its 1.5 cc was left in the manometer. To this, 1 cc of blood sample was added with Ostwald-Differential-Pipette and shaken under the reduced pressure for 3 minutes, and thus the blood gas was extracted from the blood sample.

c) Absorption of CO_2 -gas

0.5 cc of NaOH solution stated above was dropped within 1 minute.

d) Absorption of O_2 -gas

1 cc of $Na_2S_2O_4 \cdot 2H_2O$ and Anthrachinon- β -Sulfonacid Natrium

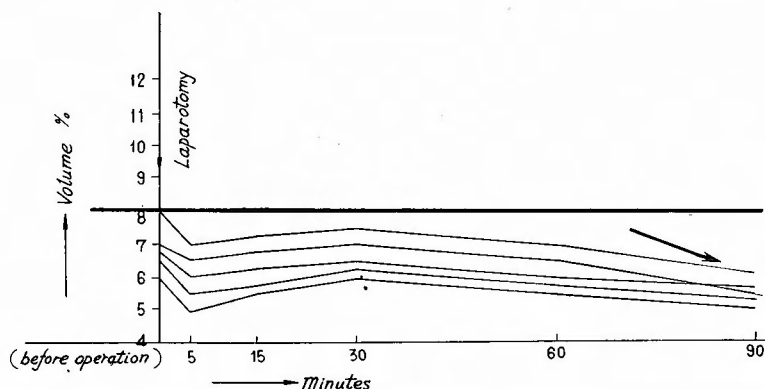
mentioned above was dropped within 1 minute. When extraction of gas was finished, volumes of CO_2 and O_2 could be determined by reading the volumes of manometer and calculating by the table attached to this manometer.

III. EXPERIMENTAL RESULTS

1. Interruption of the hepatic artery in normal dogs

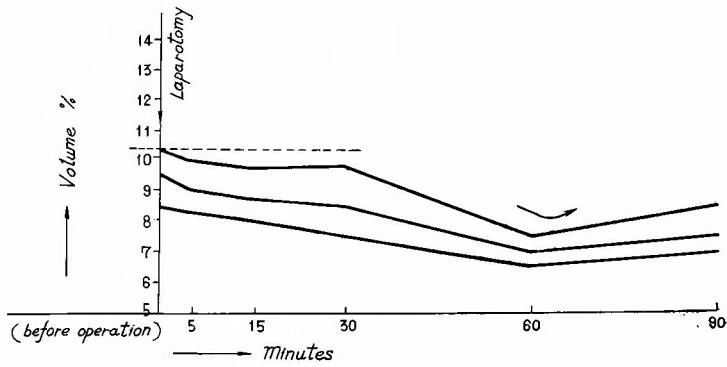
In the first place, I examined the influence of laparotomy on the oxygen content of the portal blood. Mongrel dogs weighing about 10 kg were used in 5 cases. No antibiotic substance was used. Under general anesthesia with intravenous injection of Nembutal (0.5 cc per kg in body weight), I performed laparotomy without doing any other surgical procedure, and took a blood specimen from the portal vein. Its volume percentage of oxygen content was determined. As shown in Fig. 1, it

Fig. 1 Changes of the oxygen content of the portal blood (Vol %) Laparotomy on normal dogs. (no administration of penicillin)



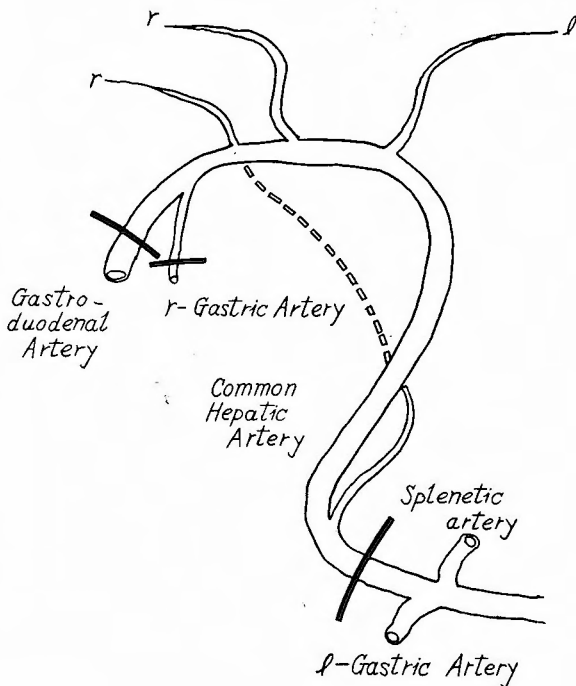
continued to decrease immediately after laparotomy, returning almost to its initial level 30 minutes later, but never exceeding it. In another three cases, in which intramuscular injection of 300,000 units of procaine Penicillin G in aqueous suspension was done prior to the laparotomy, the volume percentage of oxygen content in the portal blood, as shown in Fig. 2, decreased gradually until 60 minutes after the operation when it began to increase, but not reaching the initial level. Considering these results, it could be said that there was no evident change to be noted in the oxygen content of the portal blood after laparotomy, irrespective of Penicillin administration. During this experiment no changes in oxygen content of the arterial blood was demonstrated.

Fig. 2 Changes of the oxygen content of the portal vein (Vol %) Laparotomy on normal dogs. (under administration of penicillin)



Next, determination was made as to oxygen-volume percentage of the portal vein and the hepatic artery blood after ligation of the hepatic artery. These dogs were divided into two groups, one was given antibiotics, and the other not. As shown in Fig. 3, ligation of the common hepatic artery, the gastroduodenal artery and right gastric artery was done. Since it was difficult for various reasons to observe the animals for a long time without closing the abdominal cavity after the ligation of the hepatic artery, experiments were limited within the period of 90 minutes while I determined oxygen Vol. % of the portal vein blood.

Fig. 3. Anatomy of the hepatic artery and its branches (—) showing the sites of ligation.



a) Group not given antibiotics

As shown in Fig. 4, & Table 1, the average value of oxygen volume

Fig. 4 Changes in O_2 Volume % of the portal vein blood before and after interruption of the three major arteries on normal dogs.
(26 Cases Average)

(Group not given penicillin)

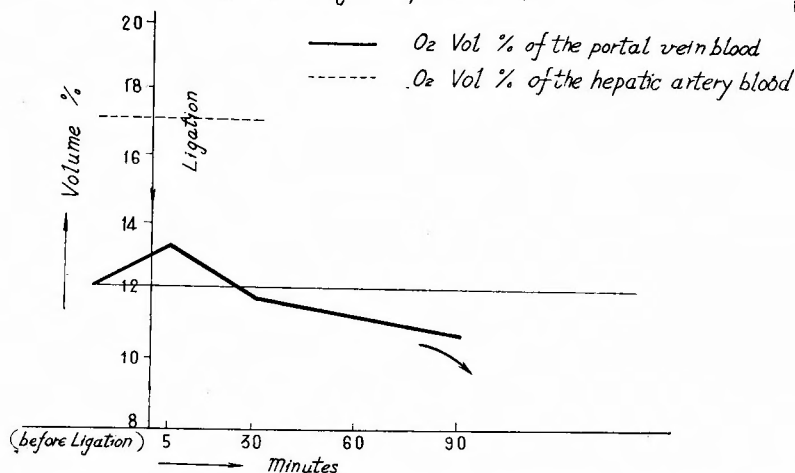


Table 1 Changes in the O_2 Vol % of the portal vein, and hepatic artery blood before and after ligation of the three major arteries on normal dogs.
(non penicillin injection cases 26)

O_2 Volume %				O_2 Volume %				Artery-Portal	
Portal vein				Hepatic artery				O_2 -Difference	
before Ligation	after Ligation			before Ligation	after Ligation			before	after
	5 min.	30 min.	90 min.		5 min.	30 min.	90 min.	Ligation	Ligation
12.00	13.50	12.50	10.30	16.80		16.80		4.80	4.30
15.90	17.10	16.00	12.60	21.60		21.60		5.70	5.60
10.26	13.00	10.90	9.40	15.80		15.80		5.54	4.90
11.34	13.77	12.00	9.50	17.91		17.91		6.57	5.91
17.01	18.63	17.00	16.00	23.22		23.22		6.21	6.22
14.80	14.58	14.00	13.70	16.47		16.47		1.62	2.47
14.85	15.00	14.80	14.20	17.01		17.01		2.16	2.21
12.41	13.79	10.52	10.00	14.91		14.91		2.50	4.39
13.36	13.55	12.71	12.30	20.52		20.52		7.16	7.81
13.90	13.99	13.20	11.80	15.32		15.32	15.32	1.42	2.12
15.59	15.80	13.00	12.40	19.58		19.58		3.99	6.58
13.30	14.70	13.20	12.60	18.00		18.00	18.00	4.70	4.80
15.60	15.75	15.50	14.50	20.01		20.01		4.41	4.51
11.00	12.08	10.90	10.60	20.09		20.09		9.09	9.19
13.25	15.02	13.02	12.00	18.75		18.75		5.50	5.73
11.00	12.08	10.80	7.80	18.25		18.25		7.25	7.45
10.32	11.98	10.05	9.45	12.48		12.48		2.16	2.43
11.28	12.40	11.09	10.59	15.60	15.60	15.60	15.60	4.32	4.51
11.76	12.92	10.98	10.40	14.64		14.64		2.88	3.66
12.95	13.68	10.64	9.55	15.50	15.50	15.50	15.55	2.55	4.86
8.64	9.12	8.64	7.88	13.40		13.40		4.76	4.76
6.52	8.50	6.30	6.00	12.72		12.72		6.20	6.42
9.60	12.00	11.24	10.61	13.27		13.27		3.67	2.03
8.64	9.84	7.80	6.50	12.09		12.09		3.45	4.29
11.41	12.63	11.07	10.05	14.43		14.43		3.22	3.36
11.49	13.33	12.19	10.01	15.43		15.43		3.94	3.24
Average	12.24	13.41	11.93	10.97	16.68		16.68	4.44	4.75

percentage of the portal vein blood in 26 cases was 12.24 before ligation and was 13.41 5 minutes after ligation showing an increase of 1.17, and 11.93 30 minutes after ligation and 10.79 90 minutes after ligation

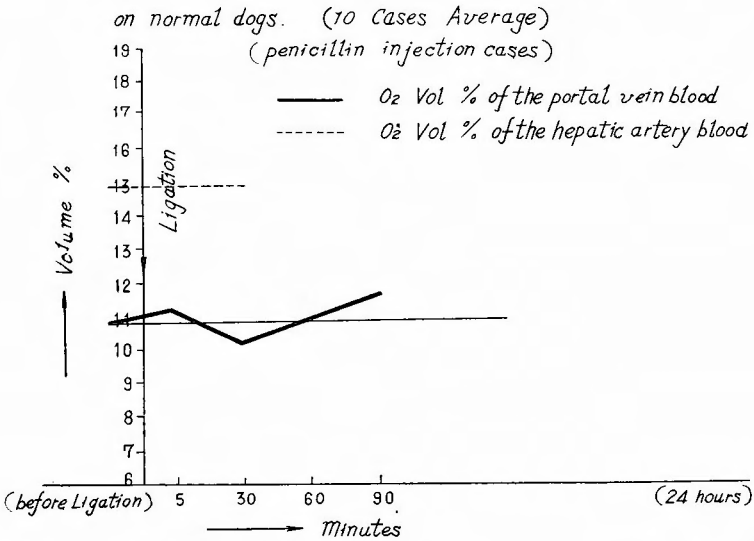
demonstrating a gradual decrease. It is interesting to note that these findings were quite in parallel with those of HOSONO of our clinic who had observed the initial rise of the velocity of the portal vein flow after the ligation of the hepatic artery.

The average value of O_2 vol. % of the arterial blood was 16.68 before ligation, and was the same 30 minutes after ligation. The value of O_2 vol. % difference between arterial and portal vein blood was 4.44 before ligation in average, and was 4.75 30 minutes after ligation showing increase a slight.

b) Group given antibiotics

As shown in Fig. 5, & Table 2, dogs were injected intramuscularly

Fig. 5 Changes in the O_2 Volume % of the portal vein blood before and after interruption of the three major arteries



with 300,000 units of penicillin G in aqueous solution 3 hours before operation and the day before operation, and also were injected intraabdominally 100,000 units of procaine Penicillin G in aqueous solution after the operation. The average value of O_2 Vol. % the portal vein blood was 10.86 before ligation, 11.22 5 minutes after ligation showing an increase of 0.36, and 10.26 30 minutes after ligation demonstrating a lower value than before ligation, again increased to 11.67 90 minutes after ligation exceeding the value before ligation. These fluctuations were, however, considered to be insignificant because they were limited in a small range.

The average value of O_2 Vol. % of the artery blood was on the equal level being 14.92 Vol. % 30 minutes before and after ligation respectively. The artery portal blood O_2 difference was 4.06 Vol. % before ligation and was 4.66 Vol. % 30 minutes after ligation showing

Table 2. Changes in the O₂ Vol % of the portal vein and hepatic artery blood before and after ligation of the three major arteries on normal dogs. (penicillin injection cases 10)

O ₂ Volume %				O ₂ Volume %				Portal-Artery		
Portal Vein				Hepatic artery				O ₂ Difference		
after Ligation				after Ligation						
before Ligation	5 min.	30 min.	90 min.	before Ligation	5 min.	30 min.	90 min.	before Ligation	after Ligation 30 min.	
12.00	12.50	11.50	13.00	16.78	16.78	16.78	16.78	4.78	5.28	
11.75	12.25	11.25	12.50	16.55	16.55	16.56	16.56	4.80	5.31	
11.50	12.00	11.00	12.00	15.96	15.90	15.88	15.89	4.40	4.88	
10.80	11.25	10.25	12.50	14.20	14.20	14.21	14.20	3.40	3.96	
10.75	11.00	10.00	11.75	15.10	15.09	15.11	15.14	4.35	5.11	
10.50	10.75	9.75	11.50	14.30	14.28	14.31	14.32	3.80	4.56	
10.25	10.50	9.60	10.90	13.99	13.99	13.99	13.99	3.74	4.39	
10.00	10.25	9.25	10.80	13.68	13.67	13.68	13.69	3.68	4.43	
9.80	10.20	9.20	10.50	12.98	12.99	12.98	12.98	3.18	3.78	
11.25	11.50	10.80	11.25	15.70	15.69	15.71	15.71	4.45	4.91	
Average	10.86	11.22	10.26	11.67	14.92	14.91	14.92	14.93	4.06	4.66

a higher value than before ligation. In discussing an increase of O₂ Vol. % of the portal vein blood, I could not attribute much importance to Penicillin.

2. Portal hypertension dogs (These are hereafter referred to as P. H. dogs)

P. H. dogs were divided into three groups.

- Ascitic dogs produced by constriction of the inferior vena cava.
- Dogs who showed marked accumulation of ascites after constriction of the hepatic vein.
- Dogs in whom constriction of the hepatic vein was not followed by accumulation of ascites.

20 dogs in total (ten of a-group, four of b-group, six of c-group) were examined without administration of Penicillin.

- Ascitic dogs produced by constriction of the inferior vena cava.

We used them 14 days after constriction of the inferior vena cava, and ligated the hepatic artery. The oxygen content in Vol. % of the portal vein blood was measured before ligation, and 5 minutes, 30 minutes, 60 minutes and 90 minutes after ligation. These measurements were done under basal narcosis of 0.5cc per kg in body weight of Nembutal.

As shown in Fig. 6, & Tab. 3, the average value of O₂ Vol. % of the portal vein blood was 9.17 and was found to be 11.00 5 minutes after ligation showing an marked increase 15 minutes after ligation it was 10.30 Vol. % showing a decrease somewhat, but this decrease continued for only a short period and again it increased to 12.22 Vol. % exceeding the initial value by more than 3 Vol. %. After that, although

Fig. 6 Changes in the O₂ Volume % of the portal vein blood before and after interruption of the three major arteries on ascitic dogs in whom constriction of the inferior vena cava was done. (no penicillin given)

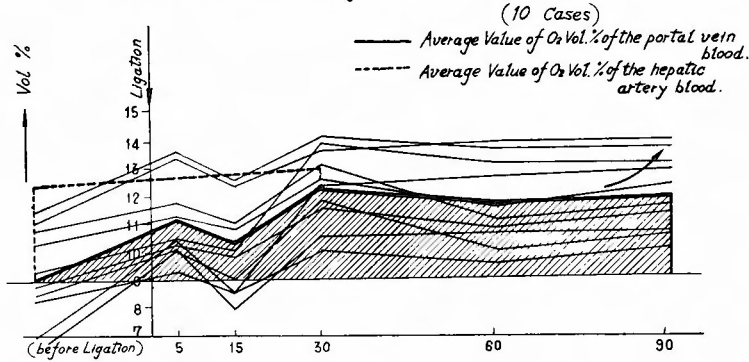


Table 3. Changes in the O₂ Vol % of the portal vein and hepatic artery blood before and after ligation of the three major arteries on ascitic dogs in whom constriction of the inferior vena cava was done. (10 cases)

Dogs No.	O ₂ Volume %						Portery-Portal	
	Portal vein				Hepatic artery		O ₂ -Difference	
	before Ligation	after Ligation			before Ligation	after Ligation		
		5 min.	30 min.	90 min.			before Ligation	after Ligation
84	11.40	13.50	14.00	13.50	14.09	15.00	2.69	1.00
110	6.50	10.00	11.70	10.50	11.50	12.00	5.00	0.30
115	10.70	11.65	13.00	11.50	13.20	13.50	2.50	0.50
114	8.25	9.25	10.00	10.00	10.75	11.50	2.50	1.50
103	11.00	13.25	13.50	13.75	14.30	14.30	3.30	0.80
82	8.45	10.10	10.50	10.60	10.95	11.50	2.50	1.00
95	7.00	10.40	12.25	12.75	11.00	12.50	4.00	0.25
104	9.30	10.45	13.25	13.00	12.50	13.90	3.20	0.65
120	10.30	11.20	12.50	12.20	13.07	13.20	2.77	0.70
119	8.75	10.20	11.50	11.20	11.15	11.80	2.40	0.30
Average	9.17	11.00	12.22	11.90	12.25	12.92	3.08	0.70

some fluctuations were observed, it continued to keep high values. The average value of O₂ Vol. % of the arterial blood was 12.25 before ligation and 12.95 30 minutes after ligation. As shown in Fig. 7, oxygen difference between the arterial and the portal venous blood was only 0.7 Vol. % after ligation, while that before ligation was 3.8 Vol. %. At autopsy, however, there was no trace of liver necrosis 24 hours after ligation in all cases.

Fig. 7 Artery-portal O₂ difference of the normal dogs and ascitic dogs before and after interruption of the hepatic artery.

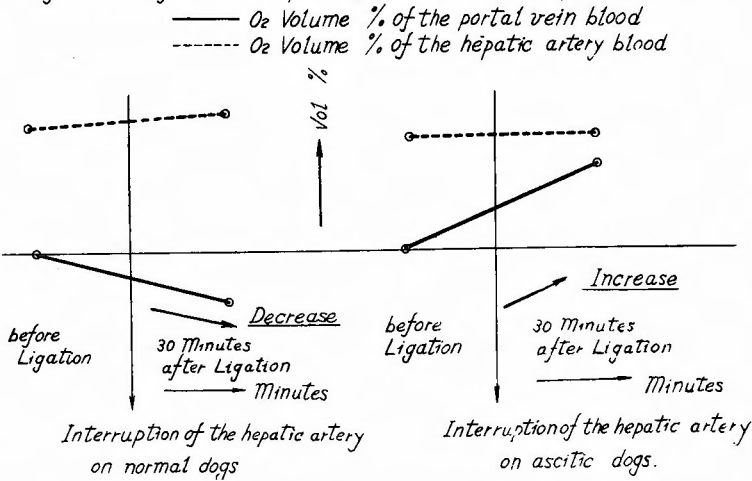


Fig. 8 Changes in the O₂ Volume % of the portal vein blood before and after interruption of the three major arteries on ascitic dogs in whom constriction of the hepatic vein was performed.

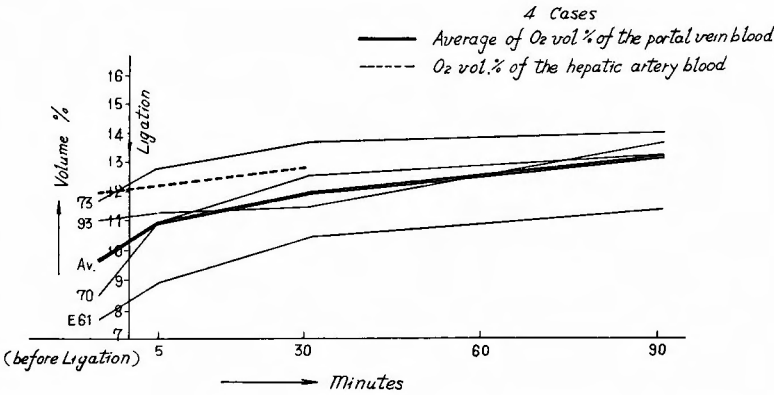


Table 4. Changes in the O₂ Vol % of the portal vein and hepatic artery blood before and after ligation of the three major arteries on ascitic dogs in whom constriction of the hepatic veins was done.

(4 cases)

Dogs No.	O ₂ Volume %						Artery-Portal	
	Portal vein			Hepatic artery		O ₂ -Difference		
	before Ligation	after Ligation		before Ligation	after Ligation			
		5 min.	30 min.	90 min.		30 min.	before Ligation	after Ligation 30 min.
73	11.75	12.75	13.75	13.96	12.15	12.67	2.40	0.92
93	11.00	11.25	11.50	13.75	11.75	12.00	0.75	0.50
70	8.50	11.00	12.50	13.25	12.45	12.63	3.95	0.13
E 61	7.65	8.92	10.41	11.40	10.20	11.80	2.55	1.39
Average	9.72	10.98	12.04	13.33	12.14	12.77	2.32	0.73

b) Dogs who showed marked ascumulation of ascites after constriction of the hepatic vein

14 days after constriction of the hepatic vein, the ligation of the hepatic artery was done. In Fig. 8, and Tab. 4, the average value of O_2 Vol. % of the portal vein blood was 9.72 before ligation, and was 10.78, 12.04 and 13.33 respectively 5 minutes, 30 minutes, and 90 minutes after ligation. An increase of 3.5 Vol. % or more was demonstrated after ligation. This result was quite the same as that in the dogs in whom the constriction of the inferior vena cava was performed.

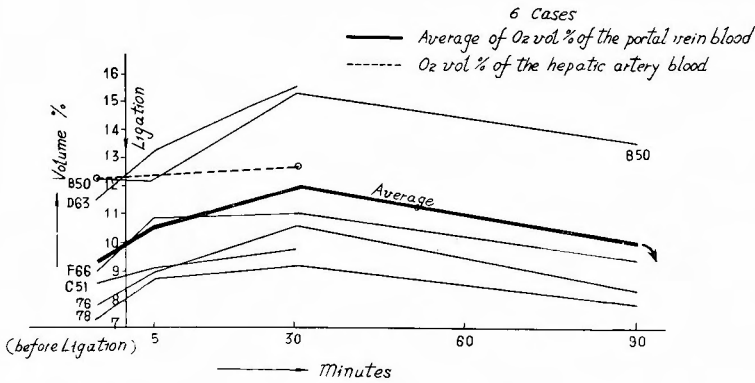
The average value of O_2 Vol. % of the arterial blood was 12.14 before ligation and 12.77 after ligation showing only an increase of 0.6. The oxygen difference between the arterial and the portal venous blood was 2.32 Vol. % before ligation, and 0.73 Vol. % after ligation.

c) Dogs in whom constriction of the hepatic vein was not followed by accumulation of ascites.

In six dogs, the constriction of the hepatic vein was not followed by development of ascites. 14 days after the constriction of the hepatic vein, the ligation of the hepatic artery was done in order to mensure the oxygen volume percentage of the portal vein blood.

As shown in Fig. 9, & Tab. 5, the average value of oxygen Vol. %

Fig. 9 Changes in the O_2 Volume % of the portal vein blood before and after interruption of the three major arteries on non ascitic dogs in whom constriction of the hepatic vein was done.



of the portal vein blood was 9.38 before ligation, and was 10.56, 11.99 and 10.02 respectively 5 minutes, 30 minutes and 90 minutes after ligation showing a tendency to decrease, although it was yet somewhat higher than the value before ligation. The average value of O_2 Vol. % of the arterial blood was 12.30 before ligation. The average value of O_2 Vol. % of the arterial blood was 12.30 before ligation and was 12.80 30 minutes after ligation. In this group dogs died in a few days after ligation, and most of them showed a finding of liver necrosis at autopsy.

Table 5 Changes in the O_2 Vol % of the portal vein and hepatic artery blood before and after ligation of the three major arteries on non ascitic dogs in whom constriction of the hepatic veins was done.

(6 cases)

Dogs No.	O ₂ Volume %							Artery-portal	
	Portal vein				Hepatic artery			O ₂ -Difference	
	after Ligation				after Ligation				
	before Ligation	5 min.	30 min.	90 min.	before Ligation	5 min	30 min.	before Ligation	after Ligation 30 min.
B 50	1225	1225	1536	1372	1536	1520	1580	311	044
C 51	858	907	980		1008	1002	1020	150	040
D 63	1150	1330	1568		1421	1520	1598	271	030
F 66	896	1096	1121	971	1180	1160	1190	284	069
76	775	900	1065	855	1290		1310	515	245
78	725	875	926	810	950		990	225	064
Average	938	1056	1199	1002	1231		1281	293	082

3. Comments

- 1) In normal dogs whose hepatic artery was interrupted, a few minutes after interruption it was followed by remarkable increase of the oxygen content of the portal vein blood. It, however, decreased, gradually irrespective of the administration of antibiotics.
- 2) In the case of interruption of hepatic artery in normal dogs, the administration of Penicillin exerted no influence on the oxygen content of the portal vein blood as far as the findings obtained within 90 minutes after interruption was concerned.
- 3) In the case of development of ascites in either dogs produced by the constriction of the inferior vena cava or those produced by the constriction of hepatic vein, after the interruption of the hepatic artery, there was a remarkable and continuous increase of the oxygen content of the portal vein blood. In other words, the oxygen difference between the blood of the portal vein and that of the hepatic artery was diminished in the ascitic dogs after the interruption of the hepatic artery. Concerning the blood oxygen content, the blood of the portal vein comes near to that of the hepatic artery. To the contrary, in normal dogs, the portal-artery blood O_2 -difference increased after the ligation.

In dogs in which the constriction of the hepatic vein was not followed by accumulation of ascites, the oxygen content of the portal blood showed temporary increase at first after the interruption of the hepatic artery, but then revealed gradually the constant decrease, even if these dogs had portal hypertension.

IV. CLINICAL CASES OF LIVER CIRRHOSIS WITH MARKED ACCUMULATION OF ASCITES

1. Changes in volume percentage of oxygen content of the portal vein blood after interruption of the hepatic artery

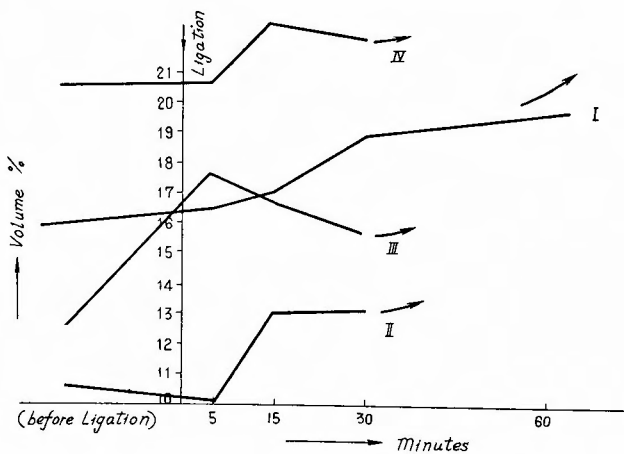
After laparotomy under general anesthesia, the portal vein blood was taken by a vinyl tube inserted into the portal stem and its oxygen content was measured before ligation of the hepatic artery, and also the measurement was done 5 minutes, 15 minutes and 30 minutes after the ligation successively.

The blood of the femoral artery was measured before laparotomy and after ligation of the hepatic artery.

Case 1, KITAKAWA 倉

In this case, the common hepatic, the gastroduodenal, the right gastric, the proper hepatic and the splenic arteries were simultaneously ligated. As illustrated in Fig. 10, value of oxygen Vol. % of the portal blood is

Fig. 10 Changes in the O₂ Volume % of the portal vein blood before and after interruption of the three major arteries on the patients with liver cirrhosis accompanied by a marked ascites.



15.75 before ligation, and was 16.50, 18.75, and 19.50 respectively 5 minutes, 30 minutes 60 minutes after ligation showing so markedly high values.

In measuring these values, there was no need of taking the influence of oxygen gas into consideration, because the dose of oxygen gas inhaled was kept constant throughout the operative course.

Case 2, FUJII 藤井

we ligated the common hepatic, the gastroduodenal, the right gastric and the proper hepatic arteries. The value of the O₂ Vol. % of the portal vein blood was 10.75 before ligation, and was 10.00, 13.00 and 13.00

respectively 5 minutes, 15 minutes and 30 minutes after ligation. The value of O_2 Vol. % of the arterial blood was 11.25 before ligation and was 13.05 30 minutes after ligation.

Case 3, TAJIMA ♂

We ligated the common hepatic, the gastroduodenal, the right gastric and the proper hepatic arteries. The value of oxygen Vol. % of portal blood was 12.50 before ligation, and was 17.75 and 16.50, 17.00 respectively 5 minutes, 15 minutes, 30 minutes after ligation.

Case 4, KASHIHARA ♂

The ligation of artery was done in the same method as in 2 and 3 cases.

The value of oxygen Vol. % of the portal blood was 20.75 before ligation, and was 20.75, 22.50 and 22.00 respectively 5 minutes, 15 minutes, 30 minutes after ligation and thus some increase was observed.

The value of O_2 Vol. % of the arterial blood was 22.25 before ligation, and was 22.00 30 minutes after ligation.

2. Changes in liver color after interruption of the hepatic artery

In one case of metastatic liver cancer, I tried to interrupt temporally the blood flow of the hepatic artery. Soon after the interruption, however, there was a change of color into dark blue on some parts of the liver surface. But, when interruption was removed, it returned to the original color.

On the other hand, it was ascertained that, in the case of liver cirrhosis with marked accumulation of ascites, the change of color on the liver surface did not occur even if the hepatic arterial flow was completely interrupted. In one case of liver cancer, the oxygen Vol. % of the portal blood was decreased from 12.25 to 9.24 soon after the ligation of the hepatic artery.

V. DISCUSSION

The liver is very sensitive to fluctuations in its content of oxygen, because it performs various biochemical reactions which need oxygen. Oxygen deficiency brings about the lowering of the hepatic function and damages the hepatic tissue. It is generally accepted that the hepatic artery is an alimentary vessel giving oxygen to the tissues and the portal vein is a functional one playing its role in metabolism.

POPPER and others have understood that the function of the portal vein is the drainage of the splanchnic system, and the liver does not require portal vein blood for its basal functions.

In 1905, HABERER demonstrated that the ligation of the hepatic artery, was followed by death within 1 to 3 days after operation in dogs, cats, and rabbits. Thereafter, it has been believed that liver necrosis after ligation of the hepatic

artery is invariably followed by death.

In 1937, HUGGINS and POST likewise confirmed the fact ligation of the hepatic artery and its largest collaterals, the gastroduodenal and the right gastric, in one stage was always fatal in dogs, death beeing due to liver autolysis and occurring within 72 hours.

URABE in our clinic demonstrated that the hepatic artery and its collaterals usually took a definite course and that when the common hepatic, the right gastric and the gastroduodenal arteries were ligated simultaneously, interruption of the arterial flow via the hepatic hilus might be said to be almost complete.

In may study also, interruption of these three main arteries were followed by death in almost all cases. In human beings, there were reported some cases which the hepatic artery was severed by mistake during surgical operations with the result that rearly half of these cases died of liver necrosis.

On the other hand, in 1947, MARKOWITZ demonstrated that administration of large dose of Penicillin greatly reduced the mortality rate from 100 % to 30 % in dogs after ligation of hepatic artery. Moreover, CHILD ascertained that Macaca Mulatta Monkey could survive the interruption of the hepatic arterial flow.

In 1959, HONJO in our clinic reported that development of livernecrosis after ligation of the hepatic artery might be due to the disturbance of portal circulation brought about by interruption of hepatic arterial flow, and emphasized that the effectiveness of antibiotics could be explained by the mechanism which prevented the reversible disturbance of portal circulation from changing into irreversible.

Moreover, HONJO, TSUCHIYA and others succeeded in producing the state similar to liver cirrhosis in dogs by constriction of the hepatic vein, and thus marking marked ascites in these dogs. They found that the ascitic dogs were much stronger in resistance against ligation of the hepatic artery than normal dogs and that in these dogs liver necrosis never happened.

NAKASE in our clinic in the same year showed that the ferritin content of the ascitic dogs was smaller than those of normal dogs. He remarked that although the disturbance of portal circulation mentioned above diminished gradually in its extent, there remained several areas where the portal circulation yet disturbed, and that from these areas ferritin was mobilized into the blood stream, incurring the lowering of activites of vessels in general including those of the portal vein and thus making a circulus vidiosus until at last anearobes furst out to grow owing to an high degree of oxygen deficiency.

The reason why liver necrosis seldom occur after ligation of the hepatic artery in ascitic dogs may partly be explained by the fact that the ferritin content of the liver is small in these dogs.

I noticed the fact that the change of color was not observed on the surface of the liver of ascitic dogs after ligation of the hepatic artery while the change of color into dark blue was shown in the normal dogs. Thereupon, I determined the oxygen content of the portal blood after ligation of the hepatic artery with the results that in the ascitic dogs produced by constriction of either the hepatic

vein or the superior vena cava, the oxygen content of the portal blood increased markedly, as far as the 90 minutes, determination was concerned, despite some decrease in normal dogs. From this determination, it was believed that the reason why the color of the liver did not change after ligation of the hepatic artery could partly be explained.

In 1947, for the first time, RIENHOFF and in 1950, BERMAN and others performed the interruption of the hepatic artery on patient with liver cirrhosis accompanied by portal hypertension. From these cases, it was learned that this method of therapy was efficacious in the cases of liver cirrhosis with marked ascites reducing its amount and restoring the hepatic function.

On our four clinical cases, in which marked ascites due to liver cirrhosis developed, ligation of the hepatic artery was performed, and the oxygen content of the portal blood was determined with the results that its content increased so much that the portal blood came near to the arterial blood so far as oxygen was concerned.

In these cases, moreover, signs of liver necrosis were not found at all, while the reduction of ascites was recognized more or less.

I believe that the reason why the ligation of the hepatic artery, both experimentally and clinically, brought about the reduction of ascites and the restoration of hepatic function, instead of developing liver necrosis, could partly be explained by the results obtained above.

VI SUMMARY AND CONCLUSION

1. Irrespective of Penicillin administration, the oxygen content of the portal vein blood in normal dogs increases temporarily within a few minutes after ligation of the hepatic artery, and soon afterwards shows a tendency to decrease.
2. In ascitic dogs produced by constriction of the hepatic vein, the oxygen content of the portal vein blood shows marked increase and continues to keep high values after ligation of the hepatic artery, while in non-ascitic dogs it does not show so marked increase, but rather gradual lowering with the elapse of time postoperatively.
3. In ascitic dogs produced by constriction of the vena cava, the oxygen content of the portal vein blood continues to show remarkable increase after the ligation of the hepatic artery, coming near to that of the arterial blood.
4. In four cases of atrophic liver cirrhosis with a high degree of ascites, complete interruption of the hepatic artery excised at the hilus of the liver showed an evident increase in the oxygen content of the portal vein blood without exception.

Acknowledgement

I do wish to express my deep appreciation to Prof. Dr. CHISATO ARAKI for his kind guidance

and for his correcting my papers. Also I am greatly indebted to Assistant Prof. Dr. ICHIO HONJO for his kind and earnest directions throughout the period of this experimentation.

BIBLIOGRAPHY

- 1) Baret, A. C. and Fitts, W. T. : Ligation of the Hepatic Artery in Experimental Cirrhosis of the Liver with Portal Hypertension. *Surg. Gynec. & Obst.*, **100**, 33, 1955.
- 2) Berman, J. K. and Hull, J. E. : Circulation in the Normal and Cirrhotic Liver. *Ann. surg.*, **137**, 3, 1959.
- 3) Bradley, S. E. : The Effect of a Portal Shunt on Estimated Hepatic Blood Flow and Oxygen uptake in Cirrhosis. *J. Clin. Invest.*, **34**, 525, 1953.
- 4) Buecherl, E. : Experimentelle untersuchungen uber O₂-Saettigung und Druck in der V. portae nach Ligatur der A. Hepatica. *Langen beck Arch. u. Deut : Zschr Chir.*, **278**, 239, 1954.
- 5) Child, C. G. and Others : Pancreaticoduodenectomy with Ressection of the Portal Vein in the Macaca Mulatta Monkey and in Man. *Surg. Gynec. & Obst.*, **94**, 31, 1952.
- 6) Huggins, C. : Experimental subtotal Ligation of the arteries supplying the Liver. *Arch. of Surg.*, **37**, 879, 1930.
- 7) Haberer, H. : Experimental Ligation of the Hepatic Artery. *Arch. of Klin. Chir.*, **78**, 557, 1906.
- 8) Hosono, Kogo : Experimental Study on Cirrhosis of Liver. *Archiv Für Japanische Chirurgie* ("Nihongekahokan in Jap."), **28**, 4, 1127, 1959.
- 9) Kagitani, Tokuo : Study on Hepatic Circulation in Surgery of Portal System. *J. J. S. S.* ("Nihongekagakkai-Zasshi in Jap."), **55**, 2, 1954.
- 10) Laufman, H. : Graded Hepatic Arterial Ligations in Experimental Ascites. *Surg. Gynec. & Obst.*, **96**, 4, 409, 1953.
- 11) Madden, J. L., et al. : The Pathogenesis of Ascites and a Consideration of its Treatment. *Surg. Gynec. & Obst.*, **99**, 385, 1954.
- 12) Markowitz, J. and Rappaport, A. M. : The Hepatic Artery. *Physiol. Rev.*, **31**, 188, 1951.
- 13) McKee, F. W., Schilling, J. A., Tishkoff, G. H. and Hiatt, R. E. : Experimental Ascites Effects of Sodium Chloride and Protein Intake on Protein Metabolism of Dogs with Constricted Inferior Vena Cava. *Surg. Gynec. & Obst.*, **89**, 529, 1949.
- 14) McMichael, J. : The oxygen Supply of the Liver. *J. Physiol.*, **11**, 73, 1937.
- 15) Popper, H. L. and Jefferson, N. C. : Survival of the Liver after Gradual Devascularisation. *Am. J. of Physiol.*, **177**, 444, 1954.
- 16) 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.
- 17) Tsuchiya, Ryoichi : Experimental Study of Cirrhosis of the Liver. I, II, *Archiv für Jap. Chir.* ("Nihongekahokan in Jap."), **28**, 4, 1147, 1959.
- 18) Urabe, Hidehiko : The Interruption of the Arterial flow to the Liver an Experimental Study. *Archiv für Japanische Chirurgie.* ("Nihongekahokan in Jap."), **28**, 4, 1112, 1959.
- 19) Van Slyke and Sendroy : Manometric Analysis of Gas Mixtures. *J. Biological Chemistry*, **73**, 127, 1927.

和 文 抄 録

胸部下大静脈狭窄その他の方法による腹水犬に対する
肝動脈遮断の門脈血酸素含有量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 (主任 荒木千里 教授)

足 立 和 保

Rienhoff や Berman が肝動脈遮断が肝硬変症で腹水の貯留著しきものに対して、有効である事を提唱して以来、諸家により本法は種々の追試検討をされて来たが、本法の是非については定説を得ない現状である。私は肝硬変症の場合の門脈血酸素含有量を重視し、門脈血酸素含有量が肝動脈遮断によりどのように影響せられるか検討を加えた。即ち犬で肝静脈狭窄を教室の土屋の方法により行い、肝硬変類似の状態を作成したが、腹水貯留を来す事がすくないので、McKee法に多少の創意工夫を加え、セロハンバンドを胸腔内下空大静脈周囲に装着狭窄した所、非常に高率に腹水犬を作成し得た。

そこで之等の犬に対し肝動脈遮断を行い、門脈血酸素含有量の増減変動を検討し、同時に動脈血酸素含有量をも測定した。次で腹水を高度に貯留せる肝硬変症患者に対し、肝動脈遮断を行つた際の門脈血酸素含有量の変動についても測定を行い、実験成績と比較検討を加えた。なお血中酸素含有量の測定には、Vanslykeのマノメーターを使用した。

実 験 成 績

1) 開腹のみの正常対称犬群

8頭に付き測定し、そのうち抗生物質投与群と無投与群とに分けて観察した所、その各々に有意の変動は認められなかつた。

2) 正常犬群肝動脈遮断

ペニシリン無投与群として26頭を用い、三肝動脈遮断前後の門脈血酸素含有量の変動については、遮断後初期増加を認め、一時的なものである事を知つた。ペニシリン投与群10頭に対して測定した結果、直接門脈血酸素含有量の増加に関係あり、とは云い難い事実を得た。

3) 門脈圧抗進症犬群

a) 下大静脈狭窄腹水犬群

下大静脈狭窄後14日目の腹水犬10頭を使用した。ペニシリンを投与せず、肝動脈を同時に結紮し夫々、結紮前、結紮後5分、15分、30分、60分、90分の門脈血酸素含有量を測定した所、遮断後5分にして、著しい増加を示し漸次持続的増加を認め、術後30分では実に3 Vol %の増加を来し、遮断前より遙かに高値を示す傾向を見出した。同時に測定した動脈血門脈血酸素較差は著明に少となり、正常犬の較差と対照的であつた。

b) 肝静脈狭窄腹水犬群

4頭に付き肝静脈狭窄後14日目に肝動脈遮断を行つた所、遮断後の門脈血酸素含有量の増加は、下大静脈狭窄腹水犬と全く同様傾向を示し、遮断後30分で3 Vol %以上の増加を認めた。

c) 肝静脈狭窄による腹水貯溜なき犬群

6頭を肝静脈狭窄後14日目に、同様肝動脈遮断を行つた所、著明な遮断後の門脈血酸素含有量の増加を認めず、むしろ正常犬と近似した変化を認めた。本群は全例結紮後短時間で死亡しており、その多くに肝壊死像を認めた。

4) 腹水を伴う肝硬変症 (臨床例)

a) 肝動脈遮断後の門脈血酸素含有量の変動

全身麻酔下で開腹後、肝動脈遮断前後の門脈血酸素含有量を測定したところ、4例共遮断後30分乃至90分で著明な増加を示した。尚手術中に用いた酸素吸入量は、全手術期間中を通じて一定の濃度と量を統一して維持せしめた為、すべて酸素吸入の影響は考慮に入れないでよい。

b) 肝動脈遮断後の肝表面の色調の変化

肝硬変患者の肝動脈を徹底的に遮断しても、決して色調の変化を来す事なく、むしろ明るさを増す事実を知つた。尚肝癌の一例では肝動脈血流停止を行なうと肝表面の処々に藍色の色調の変化を来すことを経験した。

む す び

1) 正常犬の肝動脈遮断後の門脈血酸素含有量は、遮断直後数分内に一時増加するが、間もなく減少し、その後漸減の傾向を示す。

ペニシリンを投与した場合も、遮断後90分迄の測定値では特別の影響は認められない。

2) 肝静脈狭窄後、腹水の発生を来した犬では、肝動脈遮断後門脈血酸素含有量は著明な持続的の増加を示した。腹水の貯溜を来さざる犬では、肝動脈遮断

後、門脈血酸素含有量は著明な増加を示さず、むしろ時間の経過と共に減少の傾向が認められる。

3) 下大静脈狭窄後、腹水を発生した犬では、肝動脈遮断後、門脈血酸素含有量の著明な持続的増加を来し、動脈血に近付く。

4) 腹水を高度に伴う、萎縮性肝硬変症患者4例に対し、肝門部に於ける徹底的の肝動脈血流遮断を行つたところ、全例に門脈血酸素含有量の著明な増加を認めた。