THE INTERRUPTION OF THE ARTERIAL FLOW TO THE LIVER—AN EXPERIMENTAL STUDY

by

HIDEHIKO URABE

From the Ist Surgical Division, Kyoto University Medical School
(Director: Prof. Dr. CHISATO ARAKI)
(Received for publication Mar. 24. 1959)

In 1947, RIENHOFF[33] undertook the treatment of cirrhosis of the liver by ligation of the hepatic artery. Previously it was commonly assumed that ligation of this vessel would result in liver necrosis and death. Therefore, it is a surprising fact when considered from the traditional surgical and physiological commonsense that this operation reduced the amount of ascites and improved some clinical signs. However, ligation of the hepatic artery in man gives us dangerous impression.

In 1905, HABERER[16] already demonstrated that ligation of the hepatic artery at the celiac axis can be accomplished without any fear of liver necrosis, but ligation beyond the right gastric or the gastroduodenal arteries may lead to hepatic necrosis and death. Thereafter, it was convinced that liver necrosis after ligation of the hepatic artery is invariably followed by death. However, in 1949, MARKOWITZ, RAPPAPORT & SCOTT[23,24,25] stated that administration of penicillin prevented liver necrosis following the ligation of the hepatic artery in a dog. They concluded from this work that the hepatic necrosis which developed after ligation of the hepatic artery was primarily caused by the proliferation of anaerobes normally present in the liver of dogs.

On the other hand, GRINDLAY, MANN & BOLLMAN[15] stated, although penicillin therapy greatly reduces the mortality following the ligation of the hepatic artery, administration of antibiotics is not always safe as an ischemic hepatic necrosis may occur postoperatively. Moreover, FRASER[14] observed that while the antibiotic therapy reduces the mortality rate after ligation of the hepatic artery from 90% to 35%, both bacterial proliferation and reduced arterial blood supply are important factors in causing hepatic necrosis and death following the hepatic artery ligation.

Now, whether survival or not after ligation of the hepatic artery even if antibiotics was administered in human remains undetermined. Whether such anaerobes regularly exist in human liver tissue can hardly be settled yet.

TUCHIYA, in our laboratory, constricted the hepatic vein under the diaphragm and produced a state similar to liver cirrhosis in dogs and ligated their hepatic artery. As a result of his work, he stated that the hepatic necrosis after ligation of the hepatic artery in dogs with ascites is hard to occur as compared with those having no ascites.

HOSONO in our laboratory reported the influence of the portal circulating blood volume by ligation of the hepatic artery in ascitic dogs.

The purpose of this research was to study the effect of interruption of the arterial flow to the liver and on the mechanism of necrosis of the liver in a normal dog.

EXPERIMENTAL METHOD

Experiments were carried out on healthy normal dogs weighing 8 to 14 kg and were operated upon aseptically under intravenous isomital sodium anesthesia.

EXPERIMENT I

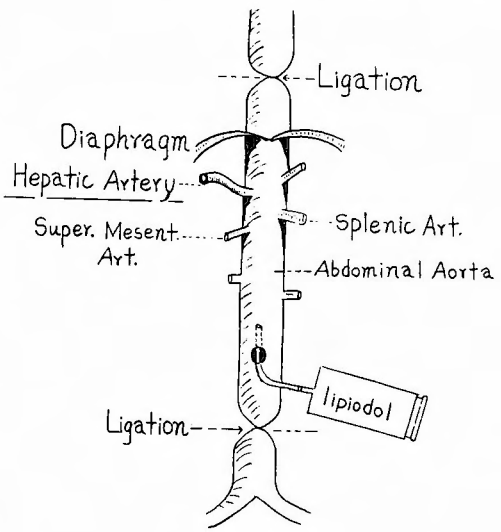
ANATOMICAL, ROENTOGENOLOGICAL STUDIES OF THE EXTRAHEPATIC ARTERY SYSTEM

In order to understand the influence of hepatic artery ligation on the liver, it is necessary to make clear the position of ligation and anatomy of the extrahepatic artery. For this purpose, the next experiment was undertaken.

METHOD

The abdomen was opened and gross observations of the extrahepatic artery was done along the course of the hepatic artery from the celiac axis. On the other hand, the thoracic aorta was ligated completely about 4 cm above the diaphragm and, at the same time, ligation of the abdominalaorta was done directly above the origin of the common iliac artery, and then a roentogenogram was taken after the injection of Lipiodol (5%, 5-10 cc) through the vinyl tube inserted into the abdominal aorta (Fig. 1).

Fig. 1 Method of Roentogenologic Examination of the Extrahepatic Artery



RESULT

It was observed that the extrahepatic artery almost showed a uniform course in 27 healthy dogs. The arterial flow to the liver will be interrupted completely when ligation was done as shown in Fig. 2 and 3.

In order to interrupt completely the arterial flow to the liver, the common hepatic, the right gastric and the gastroduodenal arteries must be ligated at the same time.

Some variations was observed in a few cases. For this reason, its abnormalities must be attended to usually at surgery. In this study, variations of the hepatic artery were classified into 3 kinds as shown in Fig. 4.

EXPREIMENT II
EFFECTS OF ANTIBIOTICS ON LIGATION OF THE HEPATIC ARTERY IN DOGS

Fig. 2 Standard Pattern of the Extra-hepatic Artery of a Dog

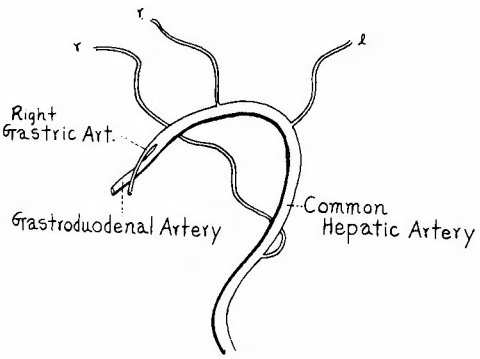


Fig. 3 The Sites of Ligation of the Hepatic Artery

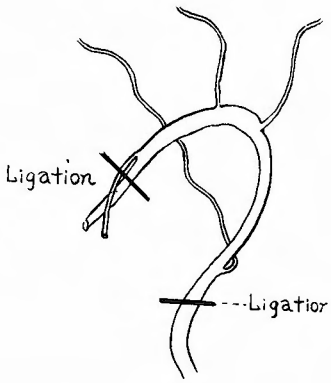
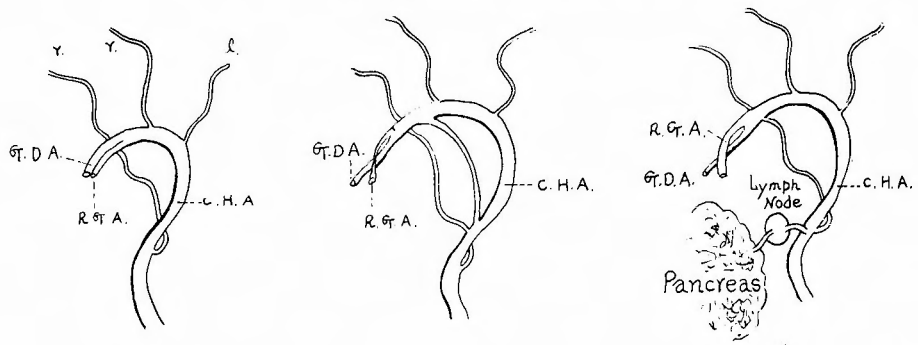


Fig. 4 Abnormalities of the Hepatic Artery



SKetch 1 SKetch 2 SKetch 3

G. D. A. : Gastroduodenal Artery R. G. A. : Right Gastric Art.
C. H. A. : Common Hepatic Art.

This experiment was undertaken to investigate the effect of antibiotics on the mortality rate after ligation of the hepatic artery.

Except in the cases of accidental death due to over-dosage of narcotic, bleeding during the operation and the unknown cause, the mortality rate was calculated 2 weeks after ligation of the hepatic artery as standard. Thirtyeight dogs were used and were divided into the following groups.

METHOD

The hepatic artery was ligated in all dogs.

In the first group, no antibiotics was given after the operation. The second group received only a single dose of 100,000 units of penicillin intraperitoneally immediately after the operation.

The third group received 300,000 units of penicillin intramuscularly. This dosage was repeated once a day for 9 days (5 days before and 4 days after the operation).

The fourth group received 1.0g of dihydro-streptomycin intraperitonearly immediately after the operation.

RESULT

Of the dogs in the antibiotics treated groups only 8 of the 27 died while all of the 11 control dogs died within 48 hours postoperatively. In the dead cases, a massive liver necrosis was observed despite antibiotic treatment. The results in this group are summarized in Table 1.

Table 1. Effects of Antibiotics on Ligation of the Hepatic Artery

Group	Cases	Postoperative Day of Death										Mortality Rate (%)
		1	2	3	4	5	6	7	8	9	10	
I	11	7	2	1							1	100
II	11						2				1	28
III	10				1			2				30
IV	6			1	1							33

In group I, one died on the 3rd postoperative day, another died on the 10th day and in the latter perforation in the gall bladder was observed.

Another 9 dogs died within 2 days after the operation. A massive liver necrosis was observed in all these dogs. In group II, 2 dogs died on the 6th day, one died on the 10th day, and in the latter perforation in the gall bladder was observed. In group III, one died on the 4th day, 2 dogs died on the 7th day. However, no perforation in the gall bladder was observed. In group IV, one died on the 3rd day, another died on the 4th day after the operation.

EXPERIMENT III

In this experiment, I tried to investigate the effect of a single dose of antibiotics which was given at later periods after ligation of the hepatic artery.

METHOD

Six dogs were divided into 2 groups and the dogs of both groups received 100,000 units of penicillin respectively intramuscularly 6 hours (the first group), and 15 hours (the second group) after the operation.

RESULT

The mortality rate was 40% respectively, and all dogs were living 15 hours after ligation of the hepatic artery.

COMMENT

In a group of dogs which did not receive antibiotics after ligation of the hepatic artery, the mortality rate was remarkably different from those which received antibiotics. Although antibiotic treatment was shown to reduce greatly mortality

following ligation of the hepatic artery, I comfirmed the fact that in a group of dogs which received antibiotics before and after the operation the mortality rate did not differ from that of the dogs receiving a single dose of 100,000 units of penicillin. Furthermore, it became evident that all dogs could maintain their livers about 15 hours after ligation fo the hepatic artery. This result may show the fact that dogs could tolerate ischmia and anoxia in the liver within 15 hours after ligation of the hepatic artery; moreover, it must be considered that the necrosis of the liver developed rapidly after 15 hours postoperatively from the fact that the dogs died at the average of 27 hours after ligation of the hepatic artery with no antibiotics.

EXPERIMENT IV

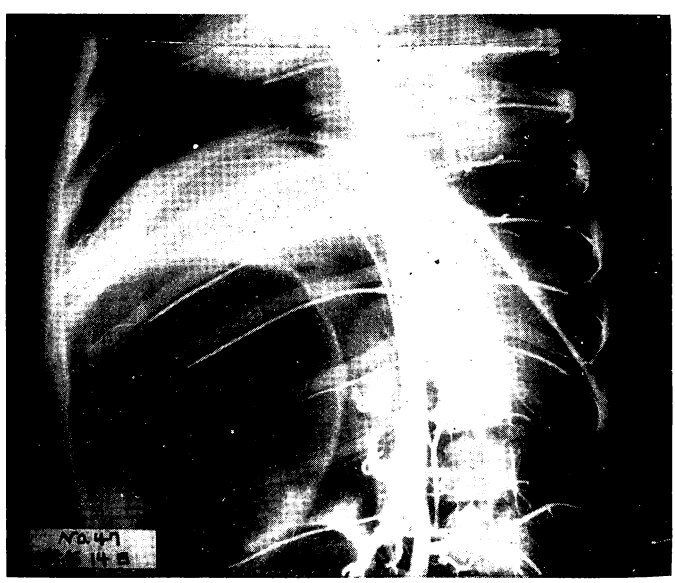
STUDIES ON THE COLLATERAL ARTERIAL CIRCURATION OF THE LIVER AFTER LIGATION OF THE HEPATIC ARTERY

Of great importance is the question of why the dogs survive after penicillin has been discontinued. Someone doubt that a sufficient number of arterial collaterls have developed in the very short period of time. On the other hand, others believe that it is entirely a matter of rapid development of collateral arterial blood supply.

METHOD

In order to determine the presence or absence of the collateral arterial circulation to the liver, 8 living dogs and 6 dead ones after hepatic artery ligation (with or without administration of antibiotics) were used. The study was carried out with the same method as shown in Fig. 1 using Lipiodol.

Fig. 5



No collateral arterial vessels other than the hepatic artery was demostrated within 2 weeks after the hepatic artery ligation.

RESULT

As a result of this work, any arterial vessels other than the hepatic artery could not be found in all animals within 2 weeks after the operation. Moreover, in a group of dogs that survived the operation no arterial collateral circulation was found to account for their survival (Fig. 5).

EXPERIMENT V
EFFECTS OF THE CHOLECYSTECTOMY ON LIGATION OF THE HEPATIC ARTERY

Markowitz, Rappaport & Scott have stated that about 35% of the dogs subjected to ligation of the hepatic artery die but half of these fatalities are due to bile peritonitis from rupture of the gall bladder.

Jefferson & Popper[18,19] concluded that survival of animals with or without antibiotics could be explained by the presence of collateral arterial circulation to the liver. They mentioned a concurrent cholecystectomy at the time of ligation of the hepatic artery adds considerably to the mortality, largely by abolishing the filamentous arterial supply along the common bile duct.

As massive liver necrosis was found in the dog regardless of the presence or not of bile peritonitis due to perforation of the gall bladder, it can not determine easily that the immediate cause of death following ligation of the hepatic artery be due to liver necrosis or bile peritonitis.

METHOD

Seven dogs were divided into 2 groups.

Of all the dogs in each group, the hepatic artery was ligated without using antibiotics.

Group I: Cholecystectomy was accomplished at the same time in the 4 dogs.

Group II: The gall bladder was not removed from the other 3 dogs.

RESULT

Any essential difference between the two groups was not found. The gall bladder, however, contains a lot of bacterium. It is assumed that it damages the liver of the dog after ligation of the hepatic artery. I think it preferable that in addition to ligation of the hepatic artery, cholecystectomy should be performed simultaneously (Table 2).

EXPERIMENT VI
EFFECTS ON THE INTRA-INTESTINAL SUPPLY OF OXYGEN FOLLOWING LIGATION OF THE HEPATIC ARTERY

The parenchym of the liver are very sensitive to lack of oxygen. Jefferson & Popper[18,19] conclude as follows; namely, the dog will survive without the hepatic

Table 2. Ligation of the Hepatic Artery with or without Cholecystectomy

Dog No.	Cholecystectomy	Findings of Liver	Length of Survival
95	yes	Liver Necrosis	38 hours
96	yes	Liver Necrosis	20
97	yes	Liver Necrosis	40
98	yes	Liver Necrosis	36
99	no	Liver Necrosis	20
100	no	Liver Necrosis	60
102	no	Liver Necrosis	24

artery and its collateral if, in addition to the intact hepatic branches of the phrenic arteries, a normal portal blood flow is present because the liver always gets some oxygen from these both, but the portal blood alone or the phrenic arteries alone seemed to be insufficient to prevent fatal liver necrosis. The liver necrosis may be protected if oxygen was given as rapidly as possible by some means after ligation of the hepatic artery. To ascertain this possibility, next experiment was undertaken.

METHOD

The abdomen was opened. The vinyl tube was inserted into the small bowel at 20 cm anal from the TREIZ's band. The intra-intestinal supply of oxygen was given through the vinyl tube immediately after ligation of the hepatic artery.

Oxygen was given from 50 to 60 cc per minute. No antibiotics was used, but chlorpromazine was used intramuscularly in order to keep up sleeping during the experiment.

RESULT

All the 14 dogs died. The average time of survival was 40 hours. A massive liver necrosis was observed in all animals. Oxygen supply was continued for 18 hours after the operation without showing any distension of the abdomen. Considering from the fact that when the dog died, its abdomen extended extremely, it may be assumed that the oxygen supplied was well absorbed in the intestines. It became clear that even if the amount of oxygen in portal blood was increased by intra-intestinal infusion of oxygen it could not protect necrosis of the liver due to ligation of the hepatic artery. Therefore, the mechanism by which ligation of the hepatic artery causes death could not be explained by the lack of oxygen in the liver.

EXPERIMENT VII
STUDIES ON THE TERM (HOURS) OF EFFICIENCY OF PENICILLIN RETAINED IN THE LIVER

HOFFMAN and UNGAR showed that 100,000 units of penicillin disappeared from the plasma in 3 hours. As stated above, I disclosed the fact that the same units of penicillin given immediately after ligation of the hepatic artery could prevent the experimental dogs from the development of liver necrosis.

I tried to make it sure how long 100,000 units of penicillin could display its effectiveness in the liver when given intra-abdominally or intramuscularly.

METHOD

The bacillus subtilis and ordinary agar medium were used in this experiment. Ligation of the hepatic artery was performed in 6 dogs, and a segment of the liver (2.0g) was removed at intervals of 3,5 and 8 hours respectively after the operation, and its segment was placed in the centre in ordinary agar medium mixed with bacillus subtilis. Six dogs were divided into 2 groups.

Group I: Three dogs were administered 100,000 units of penicillin into the abdominal cavity.

Group II: Another 3 dogs were given same units of penicillin intramuscularly.

Inhibition of growth of bacillus subtilis by penicillin was observed.

RESULT

The width of so-called inhibiting ring was examined. As shown in Table 3,

Table 3. Inhibiting Action of Growth of Bacillus Subtilis by Penicillin (100,000units)

	Width of Inhibition Ring (mm)		
	Administration into the Abdominal Cavity	Administration intramuscularly	no Penicillin
3 hours	8 mm	3 mm	0 mm
5	7	8	0
8	1	3	0

the inhibiting action of growth of bacillus subtilis by penicillin was observed during about 8 hours after its administration showing its maximum effect at the 5th hours.

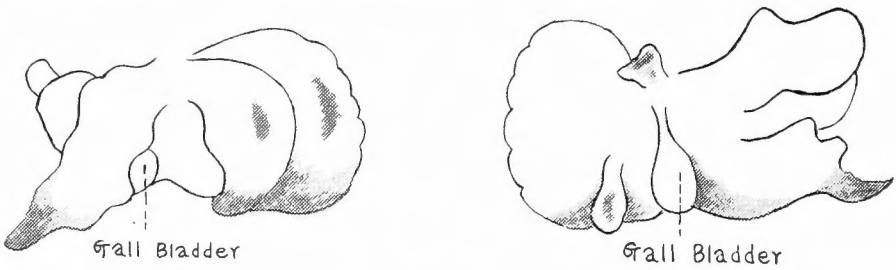
Therefore, it may be assumed that 100,000 units of penicillin given immediately after ligation of the hepatic artery was retained in the liver during 8 hours and displayed its antibiotic effects.

EXPERIMENT VIII

THE GROSS FINDINGS OF THE LIVER AFTER LIGATION OF THE HEPATIC ARTERY

The congestion-like state of the liver following ligation of the hepatic artery attracted my attention. When the liver was observed grossly in the order of hours, it turned dark red in general and very small, densely located congestion speckles began to appear from 10 to 30 minutes after ligation of the hepatic artery. After the lapse of time these congestion speckles gradually melted with each other and appeared in the left, middle and quadrate lobes of the liver as localized congestion areas 4 hours after this operation. After that the out-line of the congestive areas became more clearly and this state continued for about 18 or 20 hours.

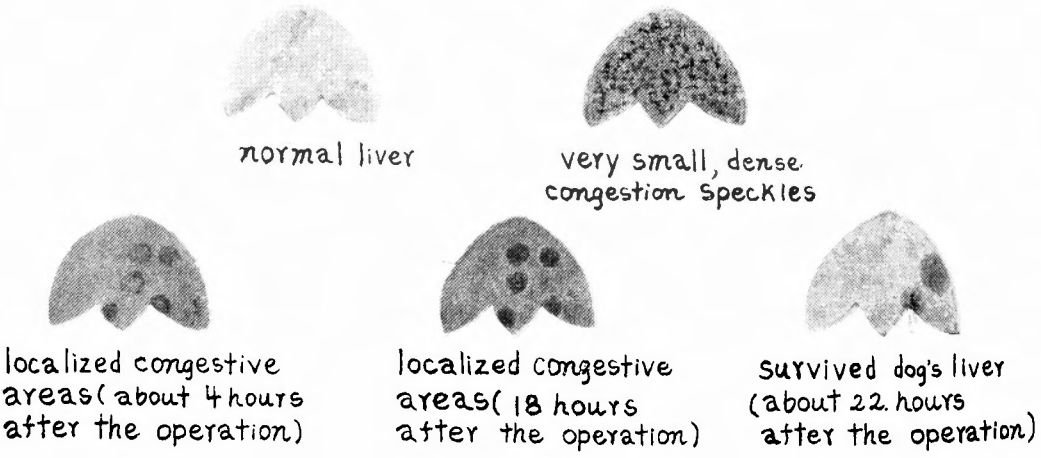
Fig. 6 The Favorite Sites of the Necrosis and the Congestion of the Liver after Ligation of the Hepatic Artery



Anterior Surface of the Liver　　Posterior Surface of the Liver

The congestive area recognized almost at the same position where necrosis of the liver was usually developed, perhaps, the latter might have occurred on the basis of the former (Fig. 6). In the case of the survival (antibiotics was given), these congestive process of the liver showed almost the similar progress as described above during 18 hours after surgery, but this congestion disappeared almost entirely 22 hours after the ligation. It was assumed that the congestion is the result of disturbance of intrahepatic portal circulation due to ligation of the hepatic artery and if penicillin is given, this disturbance may turn out to be a reversible phenomenon. These gross observations are sketched in Fig. 7.

Fig. 7 Macroscopic Observations of the Liver after Ligation of the Hepatic Artery



EXPERIMENT IX
INTERMITTENT INTERRUPTION OF ARTERIAL FLOW TO THE LIVER

Regardless of the presence or absence of antibiotic therapy, the congestion of the liver was observed in the dog that subjected to ligation of the hepatic artery. If such temporary congestion could be removed by some means at all, necrosis of the liver would not occur. Under these consideration, next experiment was undertaken.

METHOD

Interruption of arterial flow to the liver was performed intermittently.

In a series of 17 dogs, the common hepatic artery was interrupted intermittently immediately after the gastroudodenal and the right gastric arteries were ligated permanently.

Table 4. Intermittent Interruption of the Hepatic Artery

First Group		Second Group	
Interruption	Release	Interruption	Release
30 minutes	30 seconds	15 minutes	30 seconds
30 min.	30 sec.	15 min.	30 sec.
60 min.	30 sec.	This procedure was repeated 8 times within 2 hours and then ligated permanently.	
Permanent Ligation			

In the first group as shown in Table 4, the interruption was performed intermittently allowing a thirty second release three times during 2 hours and then the common hepatic artery was ligated permanently. In the second group, the 15 minutes' interruption followed by 30 seconds' release was repeated 8 times within 2 hours and then the common hepatic artery was ligated permanently.

RESULT

The result in this experiment are summarized in Table 5. There was a 50% survival rate in the first group of dogs which were operated upon without antibiotic administration. Although a larger amount of arterial blood was supplied in the second group in comparison with the first one all of the experimental dogs died. This difference between these two groups may indicate that the grade of congestion in the latter is much higher than that in the former.

Table 5. Results of Intermittent Interruption of the Hepatic Artery

	Cases	Survivals	Mortality Rate(%)
First Group	12	6	50
Second Group	5	0	100

DISCUSSION

In order to evaluate the effects of the interruption of arterial flow to the liver, I have done macroscopic or roentogenologic examination of the course of extrahepatic artery on numerous healthy dogs. As a result, it was made clear that the extrahepatic artery system showed almost uniform course.

When the common hepatic, the gastroduodenal and the right gastric arteries were ligated simultaneously at the position as described previously as shown in Fig. 3, the arterial flow to the liver was almost interrupted completely and all dogs died

of massive necrosis of the liver within from 1 to 3 days postoperatively. However, a number of dogs survived by penicillin administration as reported by MARKOWITZ, RAPPAPORT & SCOTT. They attributed the survival of dogs to the suppression of bacterial growth present constantly in the liver by the antibiotic action of penicillin. In studying these experimental results further, MARKOWITZ showed that treatment of penicillin need not be continued longer than a week and thereafter, penicillin was not needed for survival. However, MANN, BOLLMAN & GRINDLAY have asked a question; "Why do dogs survive after penicillin has been discontinued?" This question remains unexplained. Several investigators maintain vaguely that this is the result of development of arterial collateral flow to the liver within that period. But it must be emphasized that no difference of the death ratio after ligation of the hepatic artery could be found between the case in which 100,000 units of penicillin was given only one time immediately after the ligation and that in which a larger amounts of penicillin was given continuously several days before and after the procedure. Furthermore, I have not been able to demonstrate the arterial collateral flow to the liver within 2 weeks in the dog that died or survived after this procedure. Moreover, I have confirmed the fact that the inhibiting action of 100,000 units of penicillin disappears about 8 hours after injection.

Therefore, I presumed that ischemia and lack of oxygen inducing necrosis of the liver after ligation of the hepatic artery. In order to ascertain this problem, oxygen was supplied into the intestine in order to increase the oxygen volume of the portal blood. Although sufficient portal-arterialization was attained by this procedure, the mortality rate did not improve and necrosis of the liver developed as usual.

On the other hand, I noticed the occurrence of congestive state of the liver after ligation of the hepatic artery. If this congestion occur, the lack of oxygen will increase in the liver and the liver will be placed in a environment of oxygen deficiency, and then anaerobes present in the liver will propagate themselves rapidly on the basis of these congestion about 15 hours after ligation of the hepatic artery. Moreover, it was found that this congestion was not demonstrated in the dogs survived by penicillin therapy. Accordingly, it is assumed that this congestion is a reversible phenomenon, and it is suggestive that penicillin depresses the bacterial reproduction at the period of portal congestion and penicillin is no required more when the protal circulation is restored to its normal condition.

These findings have directly stressed the importance of the congestion due to ligation of the hepatic artery. If this congestion could be removed by some means, the dog would survive after the operation. Thereupon, intermittent interruption of the hepatic artery was performed. As a result, half the dogs could survive. These findings showed a new fact that development of necrosis of the liver could be avoided by recovery of the temporary disturbances of the portal circulation due to the intermittent supply of a small amount of arterial blood within a short period of time.

By some unknown mechanism, the liver was able to adjust itself to a disturbed portal circulation due to the interruption of the hepatic arterial flow. This

mechanism, perhaps, may be explained by some sort if anastomosis between the intrahepatic arteries and portal veins and changes of nature and quantity of the hepatic circulation which occurred in the liver due to interruption of the hepatic arterial flow may be compensated by this complicated vascular connection.

Up to this time, it was explained that necrosis of the liver occurred due to infection of anaerobes as a result of lack of oxygen in the liver following ligation of the hepatic artery. However, from present experimental result, another important factor must be induced for the cause of death besides lack of oxygen in arterial blood per se. The factor which appeared to play the most important role in the immediate cause of death was temporary disturbances of portal circulation due to the result of ligation of the hepatic artery.

SUMMARY AND CONCLUSION

Physiological studies of interruption of arterial flow to the liver were carried out in numerous adult dogs. The results obtained in this experiment are as follows.

1) When the common hepatic, right gastric and gastroduodenal arteries were ligated simultaneously the interruption of the arterial flow to the liver may be said to be almost complete. Within 1 to 3 days all dogs died of a massive liver necrosis after this sort of ligation.

2) Although penicillin treatment greatly reduced the mortality rate from 100 % to 30 % in the dogs which received a large doses of penicillin both before and after ligation of the hepatic artery, the mortality rate was not remarkably different from that of the dogs receiving only 100,000 units of penicillin.

3) Inhibiting action of anaerobes existing in the liver by 100,000 units of penicillin continued about 8 hours after given intraperitonealy or intramuscularly.

4) While a disturbance of the portal circulation (congestion) is always found in the liver after interruption of the hepatic artery, this findings is never recognized in survived dogs treated with penicillin suggesting that the disturbance of the portal circulation is reversible if penicillin administered. Necrosis of the liver, perhaps, will occur on the basis of this congestion.

5) Of the penicillin treated dogs only 8 out of 27 died and in these no arterial collateral circulation was found to account for survival.

6) In order to make up the lack of oxygen in the liver due to interruption of the hepatic artery, continuous supply by way of the intestinal canal was attempted. However, it is not enough to affect the result obtained by ligation of the hepatic artery.

7) The reason why do dogs survive after penicillin has been discontinued may be explained by assuming that penicillin depresses the bacterial proliferation at the period of portal congestion and penicillin is required no more when the portal circulation is restored to its normal condition.

8) Half of the dogs could survive by intermittent interruption of the hepatic artery.

9) I believe that the important factor of the occurrence of liver necrosis

following after ligation of the hepatic artery, is not due to the lack of oxygen supply by means of the arterial ciruclation, but due to a temporary disturbance of the portal circulation induced by the ligation of the hepatic artery.

I wish to thank Prof. Dr. CHISATO ARAKI and Assist. Prof. Dr. ICHIO HONJO for their guidance during the period of my research work.

REFERENCES

1) Altemeier W. A., McElhinney W. T.: Treatment of Portal Hypertension with Hepatic Artery Ligation. Arch. of Surg., **571**, 71, 1955.
2) Berman K.: Experimental Ascites. Surg., **67**, 32, 1952.
3) Berman K.: Circulation in the Normal and Cirrhotic Liver. Ann. Surg., **424**, 137, 1953.
4) Bradley E. Stanley: Variation in Hepatic Blood Flow in Man during Health and Disease. New Ingl. J. of Medec., **456**, 240, 1949.
5) Bulton Giges: Experimental Hepatic Coma. Surg. Gynec. & Obst., **763**, 97, 1953.
6) Child: The Hepatic Circulation and Portal Hypertension. W. B. Saunders, 1954.
7) Chenoweth I. Arthur: Early Results following Therapeutic Ligation of the Hepatic Artery. Ann. Surg., **756**, 135, 1952.
8) Constante Bandiera: Experimental Study on the Collateral Circulation after Ligation of the Hepatic Artery. Surg. Gynec. & Obst., **62**, 101, 1955.
9) David Rosenbaum: Liver Necrosis and Death following Hepatic Artery Ligation. J. Am. Med. Asso., **1210**, 149, 1952.
10) Eze W. C.. Cause of Survival of Dogs without a Hepatic Artery. Arch. Surg., **684**, 65, 1952.
11) Eugenio Marcos: The Importance of the Superior Mesenteric Artery in the Blood Supply of the Liver. Surg. Gynec. & Obst., **94**, 550, 1952.
12) Emil Berecherl and Walter Dueben: Experiments on Oxygen Saturation and Pressure in the Portal Vein and after Ligation of the Hepatic Artery. Surg. Gynec. & Obst., **100**, 375, 1955.
13) Fitts T. William: The Antibiotics and Liver Injury. Surg., **31**, 612, 1952.
14) Fraser D., Rappaport A. M.: Effects of the Ligation of the Hepatic Artery in Dogs. Surg., **30**, 624, 1951.
15) Grindlay John and Frank C.: Removal of the Liver of the Dog an Experimental Surgical Technique. Surg., **31**, 900, 1952.
16) Haberer H.: Experimental Ligation of the Hepatic Artery. Arch. of Klin. Chir., **78**, 557, 1906.
17) Hines R. James and Mario Roncoroni: Acute Hepatic Ischemia in Dogs. Surg. Gynec. & Obst., **102**, 689, 1956.
18) Jefferson N. C., Hassan M. I. & Popper H. L.: Formation of Effective Collateral Circulation Following Excision of Hepatic Artery. Am. J. of Physio., **184**, 589, 1956.
19) Jefferson N. C.: Collateral Arterial Circulation to the Liver of Dog. Surg., **31**, 724, 1952.
20) Tokuo Kagitani: Study on Hepatic Circulation in Surgery of Portal System. J. J. S. S. ("Nihongekagakkai Zasshi" in Jap.), **55**, 155, 1954.
21) Laufman Harold: Graded Hepatic Arterial Ligations in Experimental Ascites. Surg. Gynec. & Obst., **96**, 409, 1953.
22) Lucian Leger, Guy Albot & Jean Zerolo: Ligation of the Common Hepatic Artery in the Treatment of Cirrhosis. Surg. Gynec. & Obst., **695**, 258, 1952.
23) Markowitz, Rappaport & Scott.: Prevention of Liver Necrosis Following Ligation of Hepatic Artery. Proc. Soc. Exper. Biolo. & Med., **70**, 305, 1949.
24) Markowitz J.: The Hepatic Artery. Surg. Gynec. & Obst., **95**, 644, 1952.
25) Markowitz J.: The Function of the Hepatic Artery in the Dog. Am. J. of Digestive Diseases, **16**, 344, 1949.
26) Madden L. John: Ligation of the Hepatic and Splenic Arteries in the Treatment of Cirrhosis of the Liver. Surg. Gynec. & Obst., **96**, 594, 1953.
27) Milnes F. Roger: An Evaluation of Hepatic and Splenic Artery Ligation in Dogs with Experimental Ascites. Surg., **32**, 704, 1952

28) Popper H. L. and Jefferson N. C. Survival of the Liver after Gradual Devascularization. Am. J. of Physiol., **177**, 444, 1954.
29) Popper H. L. and Jefferson N. C.: Liver Necrosis Following Complete Interruption of Hepatic Artery and Partial Ligation of Portal Vein. Am. J. of Surg., **85**, 309, 1953.
30) Popper H. L. and Jefferson N. C.: Interruption of all Arterial Blood Supply to the Liver not Compatible with Life. Am. J. of Surg., **84**, 429, 1952.
31) Popper H. L.: Ligation of Accidentally Torn Hepatic Artery. Am. J. of Surg., **85**, 113, 1953
32) Popper H. L. and Jefferson N. C.: Survival of Dogs after Partial or Total Devascularization of the Liver. Am. J. of Surg., **140**, 93, 1954.
33) Rienhoff Jr.: Ligation of Hepatic and Splenic Arteries in Treatment of Cirrhosis with Ascites. J. Am. Med. Asso., **152**, 687, 1953.
34) Raycohn and Rather J.: Some Effects upon the Liver of Complete Arterialization of its Blood Supply. Surg., **34**, 207, 1953.
35) Rappaport A. M.: Hepatic Coma Following Ischemia of the Liver. Surg. Gynec. & Obst., **97**, 748, 1953.
36) Schilling. J. A., McKee F. W. & Wilt. W.: Experimental Hepatic-Portal Arteriovenous Anastomosis. Surg. Gynec. & Obst., **90**, 473, 1950.
37) Tadahisa Yajime: Experimental Studies on Therapeutic Effects of the Intraperitoneal Use of Penicillin in Peritoneal Infections. Arch. of Antibiotics, **195**, 4, 1951.
39) Theodore Drapans and Donald R.: Some Effects of Interrupting Hepatic Blood Flow. Ann. Surg., **142**, 831, 1955.
40) Witter A. Joseph and Max First: Ligation of the Hepatic and Splenic Arteries for Advanced Periportal Cirrhosis. Surg., **33**, 663, 1953.

和文抄録

肝動脈血流遮断の実験的研究

京都大学医学部外科学教室第一講座 （指導：荒木千里教授）
占部英彦

正常犬に於ける肝動脈血流遮断の影響を知るために，先づ肝外肝動脈の解剖学的並にX線的検査を行つた．その結果，総肝動脈，胃十二指腸動脈並に右胃動脈を同時に結紮切断すれば，肝臓に流入する動脈血は大略完全に遮断され，犬は術後1乃至3日で殆ど死亡し，広汎な肝壊死の発生する事実を知つた．処が肝動脈結紮直後，ペニシリン(以下 P. c. と略す)10万単位只1回投与により死亡率を約30%に減少せしめ得た．また肝動脈結紮術前後に亘りその大量を投与したからといつて更に死亡率を改善せしめ得なかつた．そこで肝動脈遮断直後に投与された P. c. の，肝臓内に保有され得る時間を知るため，時間的経過を追つて肝切片を採取し，肝切片による枯草菌寒天培地の細菌繁殖抑制作用の有無を検した処，肝動脈遮断直後に投与された P. c. 10万単位は，投与後約8時間前後迄しかその効果を示さぬことが判明した．細菌繁殖抑制作用がかゝる短時間で消失するにも不拘，その後は抗生物質を投与せずとも肝壊死の発生が避け得られる事実を，単に肝動脈以外の肝臓に流入する動脈細枝の代償作用が急速に発揮されるに至つたからと説明する事は困難である．

肝動脈を遮断された肝臓の肉眼上最も注目すべき所見は，遮断直後より肝全体に亘り鬱血状態を呈する事である．この現象に着目して更に経過を追い観察すると，この全般的鬱血は間もなく消褪するが，その際肝臓の処々に局在性の鬱血斑の残置する事が判明し，更に P. c. 投与で生存し得た肝動脈遮断犬の約22時間後の肝所見では，全くこれらの鬱血斑も消失している事実を知つた．肝動脈遮断により門脈性鬱血が惹起されるならば，肝組織は高度の低酸素環境に置かれる事は

容易に推定され，この部位を培地として嫌気性菌の繁殖を来すであろう事は想像に難くない．しかもP. c. 投与により生存し得た犬の肝臓にかゝる鬱血斑の存在を発見し得ぬ事実は，この門派性鬱血は可逆的の現象と解釈せざるを得ない．P. c. 投与はこの門脈性鬱血の時期に発生せんとする細菌繁殖を抑制するものであり，門脈血行が暫時にして正常化すると共にその必要も認められなくなるものと解釈される．

胃十二指腸動脈並に右胃動脈を結紮切断した後，総肝動脈の血流を2時間内に3回に亘り遮断と解放を反覆し，最後に永久的にこれを結紮切断した処，何等の抗生物質を投与せずとも実験犬の約半数を救命し得た．この事実も，かゝる操作により肝動脈は遮断されても，随伴する一時的門脈血行障害が防止され得たためと理解される．一方，肝動脈遮断犬に対して酸素注腸法により門脈の動脈化は一応その目的を達し得たが肝動脈遮断後の死亡率には何等の影響を与える事は出来なかつた．即ち，肝動脈遮断後の肝壊死発生の重大因子は，肝動脈遮断による動脈中の酸素補給不能自体によるのではなく，実に上述の肝動脈遮断により惹起される一時的門脈循環障害に基因するものと信ずる．