EXPERIMENTAL STUDY OF LIVER CIRRHOSIS. WITH SPECIAL REFERENCE TO HISTOLOGICAL FINDINGS OF THE LIVER OF THE DOGS WITH ASCITES FOLLOWING THE INTERRUPTION OF THE HEPATIC ARTERY

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Ⅰ. INTRODUCTION

Since Rienhoff[33)34)] (1951), Berman[3)4)5)6)7)] et al. (1951) reported that they had favorably treated cases of liver cirrhosis with interruption of the hepatic artery, this operative procedure has been followed by many researchers.

Rienhoff stated that the method was effective in cases with ascites. According to Berman, it improved cases with ascites or hemorrhage. Altmeier[1)] (1955) found it rather promising. But Taylor[37)38)]et al. (1953) reported cases which had developed fatal liver necrosis after the interruption. They gave a warning against a careless establishment of indication. Jahnke[21)] et al. (1953) and Desforges[12)] et al. (1953) opposed to this method by reporting cases unsuccessfully treated with it.

Dating back to 1906, HABERER[19] reported that a complete ligation of the hepatic artery in animals resulted in fatality. Since then it has been regarded that the ligation of the hepatic artery distal to the origin of the right gastric was not without danger.

ELLIS[15] (1930) and others explained that the hepatic necrosis due to the ligation of the hepatic artery was attributable to a rapid proliferation of anaerobic micro-organisms which are ever existent in the host's liver.

MARKOWITZ[27][28] et al. (1949) demonstrated that administration of penicillin was effective in preventing the proliferation of anaerobic micro-organisms and in improving survival rate. TANTURI[40] et al. (1950) and CHAU[11] et al. (1951) confirmed this observation.

GRINDLAY[18] (1951) and FRASER[17] et al. (1951) noted the occurrence of hepatic necrosis after the ligation of the hepatic artery despite the intensive antibiotic therapy, and suggested the existence of ischemic necrosis.

HONJO[46][47] and his associates found that the stasis of portal circulation was induced after the occlusion of the hepatic artery presenting the basis upon which hepatic necrosis developed.

No interpretation seems to have been agreed upon as to the cause of the hepatic necrosis which results from the interruption of the hepatic artery. The present author was encouraged to study the developing mechanism of hepatic necrosis and the abnormal intrahepatic circulation in cases of liver cirrhosis. Although the interruption of the hepatic artery appears to be harmful in normal cases there remains much to be clarified in cases of liver cirrhosis especially, accompanied by ascites.

Thereupon, the present author experimentally produced ascitic dogs which hemodynamically have some similarities with human liver cirrhosis. The histological findings of liver of the ascitic dogs after the interruption of the hepatic artery was observed in comparison with those of normal dogs. Moreover, hemodynamics in portal circulation, activity of sphincter mechanism in the hepatic venous system and fluctuation of portal pressure were also studied.

Ⅱ. PRODUCTION OF THE ASCITIC DOGS

1. Materials

Eighty adult mongrel dogs weighing 7 to 16kg of both sexes were employed.

2. Method

McKEE's method was followed. The animals were subjected to thoracotomy on the right 6th. intercostal space on the mammillary line under intravenous isozol (20mg/kg) anesthesia and intratracheal general anesthesia.

After reaching the inferior vena cava, it was separated from the phrenic nerve and the surrounding tissues and its constriction was made with a cellophane tape about 1cm in width.

3. Histological Findings of the Liver of the Dogs with Ascites

Liver tissue specimens were taken at the time of the animal's death or laparotomy for the interruption of the hepatic artery. They were studied by hematoxylin

and eosin staining, van Gieson's staining and silver impregnation. The dogs showed an accumulation of ascites 7 to 10 days after the constriction. At this stage, the liver showed a marked congestion (Fig. 1). It showed some hemorrhagic spots running from the central to intermediate areas; no fibrosis was observed yet. Three to four weeks later with the development of varicosity in the abdominal wall, the congestion became slightly less; atrophy in the hepatic cells was marked; some cases showed a slight fibrosis.

Ascitic dogs which survived for 1 to 2 months showed markedly diminished atrophy of hepatic cells and development of fibrosis (Fig. 2). The fibrosis was marked around the central vein (Figs. 3, 4), and slight in the interstitial space. At the sites of the central and intermediate areas where fibrosis was noticed, there was observed small lumina with endotheliums which seemed to have developed from sinusoids (Figs. 5, 6).

As mentioned above, ascitic dogs which survived for more than 1 month showed the formation of lumina in the liver parenchyma, suggesting the specificity of intrahepatic circulation. At this stage, a slight degree of cirrhotic changes were grossly observed. Therefore, for the purpose of the present experiment, the ascitic dogs should be employed after more than 1 month following the constriction of the inferior vena cava.

During the experiment about 40 per cent of the constricted dogs showed accumulation of ascites and survived for more than a month.

Ⅲ. HISTOLOGICAL FINDINGS OF THE LIVER OF THE DOGS FOLLOWING THE INTERRUPTION OF THE HEPATIC ARTERY.

1. Materials

Twenty normal dogs and thirty-three dogs with ascites were employed.

2. Method for the Interruption

Under subcutaneous morphine hydrochloride anesthesia (0.05g/kg) or intravenous isozol anesthesia (20 mg/kg) laparotomy was performed with an upper median incision.

The common hepatic artery, gastroduodenal artery and right gastric artery which are related to the arterial inflow to the liver were ligated and cut. During the laparotomy no antibiotic was administered.

3. Histological Examinations

Following the interruption, exploratory laparotomy or slaughter was carried out to obtain liver tissue specimens which were examined with hematoxylin-eosin staining immediately after they were obtained.

The specimens were taken from the portions where the most marked macroscopic changes were observed or where necrosis was most likely to occur in normal cases. In taking the specimens, attention was paid so as to give the least artificial damage to liver tissue. Cutting was made without ligature; the tissues separated were fixed in a 10 per cent formalin solution.

4. Results

i. Normal dogs

a) Findings following the lapse of time after the interruption of the hepatic artery.

Nine normal dogs were observed following the lapse of time after the interruption of the hepatic artery.

Fifteen minutes after the interruption: No marked changes were observed in the central veins or sinusoids, although only a slight congestion was visualized in some portal spaces (Fig. 7). Grossly the liver was generally colored reddish brown with a hue of blue.

One hour after the interruption: The congestion in the portal spaces advanced more conspicuously, which was partially accompanied with interstitial hemorrhage (Fig. 8). Congestion was also observed in the sinusoids (Fig. 9).

Three hours after the interruption: Congestion in the lumen of portal veins, sinusoids and central veins became more marked revealing a dilatation of the sinusoids and a tortuous arrangement of hepatic cell cords. Grossly the caudate lobe and middle lobe showed a pigmented islet area whose coloration did not disappear on pressure.

Six hours after the interruption: The tortuousity of hepatic cell cords became more marked (Fig. 10), some hepatic cells showed cloudiness and localized degeneration due to hemorrhage was partially observed in the parenchymal cells (Fig. 11).

Twelve hours after the interruption: The tortuousity of hepatic cell cords was marked. Milder cases showed pycnosis in their central region. Severer cases showed a marked central congestion and hemorrhage revealing an interruption of the hepatic cell cords covering the central to intermediate areas, as an obvious suggestion of necrotic changes (Fig. 12). Although the pathologic involvement reached more peripheral areas, the region adjacent to the interstitial spaces showed no hepatic cell degeneration except for congestion. Grossly markedly pigmented islets were observed.

The gross pigmentation on the surface of the liver due to congestion began to appear 3 to 6 hours after the interruption. Corresponding to the site of pigmentation there always appeared a congestion in the sinusoids and central veins histologically, followed by hepatic cell degeneration.

b) Findings on death

Following the interruption of the hepatic artery 20 normal dogs, employed, all died in 17 to 48 hours with an average of 27 hours.

At immediate autopsy, a slight accumulation of dark brown and foul smelling ascites was observed in the peritoneal cavity. The liver was generally dark brown; it showed localized islet-shaped necrosis especially in the caudate lobe, in the upper region as well as contacting area of the gall-bladder of the middle and quadrate lobe and in the peripheral region of the upper and lower left lobes. Some necrotic areas showed their defect. The region with slight histological changes showed only congestion in the portal and the hepatic vein system. But the region with localized

gross pigmentation demonstrated a marked central hemorrhagic necrosis in the hepatic lobules with an appearance of decomposition in which degenerated hepatic cells were seen floating on bloody lake (Fig. 13). But in the periphery of the lobule some parenchymal cells remained without degeneration (Fig. 14).

A general appearance was a map-like distribution of necrosis involving lobules with central necrosis of various degrees. The stroma partially showed hemorrhage and cell infiltration, but it generally maintained a normal shape on death.

The above results confirm that development of hepatic necrosis is always preceded by stasis of portal veins. It is considered that the stasis (intrahepatic circulation disturbance) due to the interruption of the hepatic artery leads to a local shortage of oxygen resulting in a gradual degeneration of hepatic cells in the central region which allows further stasis and hemorrhage to develop in a vicious cycle, presenting a promoting factor to the growth of anaerobic micro-organisms.

ii. Ascitic dogs which survived for 3 weeks after the constriction

On eight dogs which showed an accumulation of ascites 3 weeks after the constriction of the inferior vena cava, the interruption of the hepatic artery was performed as mentioned above. Histologically they were in a state of congestive liver.

Following the interruption of the hepatic artery 4 of 8 dogs showed an increase in congestion compared with the stage before the interruption (Fig. 15), and eventually developed a central hemorrhagic necrosis which is commonly observed in normal dogs. The other 4 dogs showed no marked increase in congestion following the interruption of the hepatic artery (Fig. 16). Some of them showed a parenchymal degeneration in the central area. Grossly no marked islet-shaped necrosis was observed; localized pigmentated spots were observed in the caudate, the middle and the quadrate lobe.

The above results demonstrate that ascitic dogs which survived for 3 weeks show no specific histological changes yet and maintain, as observed in normal dogs, intrahepatic circulation which threatens to develop into hepatic necrosis which is a sequela of the congestion due to the interruption of the hepatic artery.

iii. Ascitic dogs which survived for 1 to 3 months after the constriction.

This group consisted of 25 dogs. All the dogs showed a marked accumulation of ascites. Histologically the liver cells were atrophic; congestion was slight; fibrosis was found around the central vein; small ductal spaces obviously originating from sinusoids were observed.

a) Findings following the lapse of time after the interruption of the hepatic artery

Fifteen minutes after the interruption: Gross and histological findings were almost the same as compared with the stage before the interruption.

One hour after the interruption: No increase in congestion was observed.

Three hours after the interruption: In some cases, a slight increase in congestion was found in their sinusoids. No congestion was observed around the central veins.

Six hours after the interruption; The congestion or increased tortuousity of

hepatic cell cords as seen in normal dogs was not observed (Fig. 17) ; some cases showed less changes than the stage before the interruption ; grossly localized islet-shaped pigmentation was hardly observed.

Twelve hours after the interruption : The findings were similar to those after 6 hours. No increase in congestion was seen in the middle area or in the peripheral area of the lobule (Fig. 18).

Twenty-four hours after the interruption : Neither congestion nor degeneration of hepatic cells was observed (Fig. 19).

Forty-eight hours after the interruption : Central necrosis as observed in normal dogs was not observed. The general appearance was almost the same as the stage before the interruption.

Four days after the interruption : Gross and histological findings revealed no necrotic signs (Fig. 20).

Seven days after the interruption : Fibrosis in the central area became more marked ; no necrosis was observed (Fig. 21) ; the peripheral area showed no congestion. Obviously the liver maintained its activities only through the portal circulation, without being subjected to necrosis (Fig. 22).

b) Findings on death

Even cases of early death showed no increase in congestion or degeneration of hepatic cells. It is strongly suggested that the cause of these deaths were not attributable to hepatic necrosis but possibly due to general ascitic condition or other causes.

The above results lead to a conclusion that ascitic dogs are not likely to develop necrosis. In other words, intrahepatic circulatory disturbance due to the interruption of the hepatic artery is too slight to produce necrosis.

Half of the cases which survived for 3 weeks after the constriction showed marked congestion followed by hepatic necrosis. All the cases survived over one month showed no necrosis but fibrosis. Thus it is interpreted that the longer the survival of the ascitic dogs, the more they show the trend to develop conditions similar to the hepatic cirrhosis, with the less opportunity of being influenced by the interruption of the hepatic artery.

It is considered that ascitic dogs are not likely to develop circulatory disturbances because of a specific feature of the intrahepatic vascular system.

Ⅳ. PORTAL CIRCULATION FOLLOWING THE INTERRUPTION OF THE HEPATIC ARTERY

1. Materials

Three ascitic dogs and three normal dogs were employed.

2. Method

As the animals began to show a marked hepatic congestion and an irreversible localized pigmented area 3 hours after the interruption of the hepatic artery, 20 cc of india ink was injected spending 10 sec. through the animal's portal vein in the neighborhood of the hilus. Twenty minutes after the injection the dog was slaughtered

and a histological study was performed. The injection consisted of a commercially available india ink diluted to 25 per cent with the physiological saline.

3. Results

Immediately after the injection, the liver was colored with the india ink. Twenty minutes later, the ascitic dogs showed no india ink color in its liver, while the normal dogs still showed a marked map-like coloration.

Histologically the normal dogs showed retention of india ink in the central veins and sinusoids (Fig. 23).

The ascitic dogs showed retention of india ink only in some sinusoids, no india ink was observed around the central vein (Fig. 24).

The ascitic dogs showed only a slight degree of disturbance of portal circulation following the interruption of the hepatic artery and their circulation time of the liver was observed to be short. The absence of india ink around the central vein suggested that a part of the portal blood might directly enter the hepatic vein system from the sinusoid via abnormal intrahepatic anastomosis without passing through the central vein.

V. THE SPHINCTER MECHANISM OF THE HEPATIC VEIN-BRANCHES FOLLOWING THE INTERRUPTION OF THE HEPATIC ARTERY

1. Materials

Nine ascitic dogs and nine normal dogs were employed.

2. Method

Fifteen minutes, an hour and 4 hours after the interruption of the hepatic artery, the dogs were either exploratorily laparotomized or slaughtered under intravenous isozol injection with massive dosage. Histological findings of their liver tissues were examined.

3. Results

Fifteen minutes to 4 hours after the interruption the normal dogs showed a marked contraction of the hepatic vein branches. The contraction was featured with a papillary sphincteric muscle which protruded into the lumina of the blood vessel occasionally occupying its whole inner space. In the surrounding venules and sinusoids there was observed a marked congestion (Fig. 25).

The ascitic dogs showed only a slight contraction of the sphincter even 4 hours after the interruption; no congestion was observed either in the lumen of the vein or in the surrounding sinusoids (Fig. 26).

The above results lead to a presumption that, in ascitic dogs, the weakened contraction of the sphincter of the hepatic vein system may contribute to prevent the portal flow from stagnation. A further study might be added to clarify whether the weakened contraction of the sphincter of the hepatic vein system is due to the damage of peripheral innervation of the sphincter derived from cirrhotic chages or due to a functional factor related to the presence of abnormal anastomosis.

VI. THE CHANGES IN PORTAL PRESSURE FOLLOWING THE INTERRUPTION OF THE HEPATIC ARTERY

1. Materials

Three ascitic dogs and three normal dogs were employed.

2. Method (Determination of Portal Pressure)

The experimental dog was fixed in a spine position. It was subjected to laparotomy under intravenous isozol anesthesia at a dose of 20mg/kg. A small incision was given to the animal's splenic vein ; a vinyl tube, about 1 mm in diameter, was inserted with its tip fixed in the portal vein stem. With the use of physiological saline, portal pressure was measured till 6 hours after the interruption of the hepatic artery.

3. Results

i. The normal dogs showed the portal pressure of 110 mmH O (No. 104), 120 mmH_2O (No. 105) and 125 mmH_2O (No. 106) respectively. Ten to twenty minutes after the interruption they showed an elevation of 40 to 50 mmH_2O followed by a slight decrease 30 to 40 minutes later, and then a re-elevation in 50 to 60 minutes with subsequent slight changes. In 3 hours they began to show a constant portal pressure which revealed higher than the stage before the interruption even 6 hours after the interruption.

Namely it is disclosed that the interruption of the hepatic artery in the normal dogs results in an increase of portal pressure (Fig. 27, Tab. 1).

ii. The ascitic dogs showed the portal pressure of 275 mmH_2O (No. 101), 250 mmH_2O (No. 102) and 280 mmH_2O (No. 103) respectively. They showed a decrease of 35 to 60 mmH_2O immediately after the interruption. Although a slight increase was observed one hour later in No. 101, two hours later in No. 103 and an increase to the level before the interruprion was observed in No. 102, 20 minutes after the interruption. These cases were shortly followed by a gradual decrease, showing decrease of 45 to 50 mmH_2O less than the level before the interruption, 6 hours after the interruption. Thus it is revealed that the interruption of the hepatic artery in the ascitic dogs results in a decrease in portal pressure (Fig. 27, Tab. 1).

The above results lead to an assumption that an increase in portal pressure due to the interruption in the normal dogs

Fig. 27

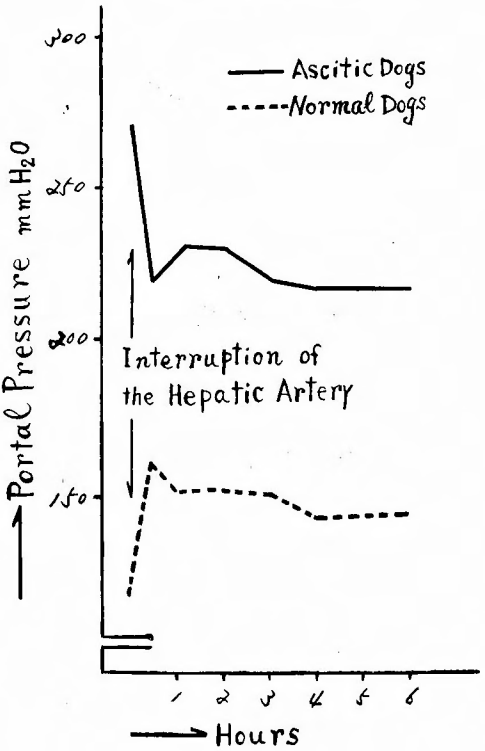

Table 1

Portal Press. \ Dog No.		Ascitic Dogs			Normal Dogs		
		101	102	103	104	105	106
Before Interrupt.		275 mmH_2O	250	280	110	120	125
after Interruption	5 min	215	215	220	125	130	130
	10	225	210	220	160	170	155
	20	225	250	235	130	160	165
	30	225	225	240	130	165	150
	40	225	235	235	140	155	160
	50	220	240	235	145	150	160
	1. hour	230	240	240	145	155	160
	1.5	220	235	240	145	160	150
	2.0	220	230	235	140	135	145
	2.5	220	215	240	145	140	140
	3.0	220	205	235	150	145	135
	3.5	220	205	230	145	140	135
	4.0	225	205	230	140	140	135
	4.5	225	200	225	140	135	130
	5.0	220	200	225	140	140	130
	5.5	220	205	225	140	135	130
	6.0	220	205	225	140	135	130

obviously indicates an increase in resistance of blood flow attributable to intrahepatic circulatory disturbance and that the interruption in the ascitic dogs alleviates the resistance against portal circulation resulting in lessening of portal hypertension.

VII. DISCUSSION

WOLBACH[42] et al. (1909) reported that anaerobic bacilli are constantly existent in the liver of normal dog. This report led to the assertion of ELLIS[15] (1930) and others that etiologically a hepatic necrosis following the interruption of the hepatic artery is caused by a growth of anaerobic organisms due to the lack of oxygen after the interruption.

MARKOWITZ[27][28] et al. (1949) reported that administration of penicillin directly after the interruption of the hepatic artery resulted in a higher survival rate of the dogs. They assumed that penicillin would inhibit a growth of anaerobic organisms. TANTURI[40] et al. (1950) stated that α-toxin (Lecithinase) produced by anaerobic organisms would cause the fatality. Their assertion was advocated by CHAU[11] (1951) and others. But POPPER[30] et al. (1952), and GRINDLAY[13] et al. (1951) stated that after the interruption of the hepatic artery the arterial circulation could be compensated mainly by collateral circulation originating from the phrenic artery and that a concurrent interruption of such collaterals would result in animals' death in spite of administration of any antibiotics.

EZE[16] (1952) explained that penicillin was effective in preventing infection prior to the establishment of collateral circulation.

However, URABE[50] (1959) confirmed that the same survival rate as MARKOWITZ's was obtained with a single administration of 100,000 units of penicillin; FRASER[17] and others asserted the presence of ischemic necrosis observing the development of hepatic necrosis even with the administration of antibiotic.

HONJO[46][47] and his associates pointed out that the disturbance of portal circulation came to occur directly after the interruption of the hepatic artery, and that this disturbance —stasis— would bring about the more hypoxic state to the liver on which the proliferation of the anaerobic bacteria bursts out.

In the present experiment, the normal dogs showed hepatic necrosis developing as a sequela to a marked congestion following the interruption of the hepatic artery but the ascitic dogs having no hepatic necrosis showed no congestion even after the interruption. These findings lead to an assumption that a lack of oxygen in the congested area gives rise to hepatic necrosis. Namely it is ascertained that the reason why hepatic necrosis seldom occurs in ascitic dogs must be explained by a fact that no portal congestion is observed in those livers.

HERRICK[20] (1907) performed perfusion experiments with a normal and a cirrhotic liver and noticed the existence of anastomosis between hepatic arterial branches and portal vein branches. POPPER[29][31] et al. (1952) studied on cirrhotic liver using india ink and observed the existence of reticulated anastomsis between hepatic arterial branches and portal vein branches. MADDEN[24] et al. (1954) demonstrated the existence of anastomosis by the use of plastic resin specimens.

WAKIM[44][45] (1949) and others observed changes in the vascular system in cirrhotic livers experimentally induced.

UNGER[41] (1951) first reported a formation of porto-hepar-shunt in experimentally poisoned livers with CCl_4.

DANIEL[13] et al. (1952) presumed the existence of porto-hepar-shunt on angiography by a finding that, in cases of CCl_4 poisoned liver, a contrastmedium injected via the portal vein reached the hepatic vein earlier than in normal cases. MIYAWAKI[48] confirmed by x-ray photographs that any disturbance in portal circulation could not be observed in the ascitic dogs after the interruption of the hepatic artery. POPPER et al. explained that the development of such a short passage as suggested above might be attributable to portal hypertension which resulted in enlargement of sinusoids leading to venularization.

In the present experiments on ascitic dogs using india ink, the india ink injected was scarcely observed showing no retention at all around the central veins. This finding suggests that the tubular space developing from the sinusoids of an ascitic dog may serve as a short vascular passage.

It remains yet to be solved how this short vascular passage is related with DEYSACH's[14] (1941) small endothelial tube (sluice channel) which is directly connected with the sublobular vein without passing the central vein in normal dogs.

AREY[2] (1920) and others observed the existence of the sphincters in the peri-

pheral branches of the hepatic vein, which were responsive to pharmacological or neurogenic stimulus in normal cases. BAUER[8] et al (1932) observed an increase or a decrease in hepatic circulation, which was subjected to the influence of adrenalin or histamin.

ROSENBLEUTH[32] (1937) and SNYDER[36] (1940) stated that the sphincter was a smooth muscle which spirally surrounded the blood vessel and was controlled by the autonomic nerves cooperating with DEYSACH's channel. Based on the experiment with a polyethylene injection THOMAS[39] et al (1949) reported that the finer the venous branch was, the more marked was its contraction and that the maximum contraction occurred 2 hours after the interruption of the hepatic artery.

With plastic resin specimens, YOSHITOMI, in our clinic, observed the contraction covering several hours immediately after the interruption, stating that the contraction constituted a main factor of developing a congestion after the interruption. His findings were similar to those obtained histologically in the present experiment. It is considered that an weakened contraction of the sphincter in the ascitic dog as well as a formation of shunt may effectively alleviates a portal stagnation.

HERRICK[20] explained that high portal pressure was due, to some extent, to the arterial blood which directly elevates the pressure through arterio-portal vein anastomosis. On the other hand, MCINDOE[26] (1920) noted a decrease in a whole vascular bed.

POPPER[29][31] et al. and MADDEN[24] et al. considered that a decrease in the venovascular bed resulted in an increase in portal pressure and ascites.

BERMAN, and WITTER[43] et al. (1953) advocate that the interruption of the hepatic artery in cases of liver cirrhosis with ascites favorably decrease their increased portal pressure.

ALTMEIER[1] reported some clinical cases that showed a decrease of 10 to 40 mmH_2O in portal pressure. TSUCHIYA[49] (1959) observed a decrease of 35.4 mmH_2O in a dog whose hepatic vein had been ligated. In the present experiment on dogs with ascites produced by the constriction of the inferior vena cava, a decrease of about 50 mmH_2O was observed 6 hours after the interruption of the hepatic artery. The present author is strongly supported to assume that the interruption of the hepatic artery in the ascitic dogs favorably decreases the animals' elevated portal pressure.

VIII. CONCLUSION

Histological changes of the liver of dogs with experimentally produced ascites following the interruption of the hepatic artery were studied in comparison with those of normal dogs and the following results were obtained.

1) More than a month after the constriction of the inferior vena cava there developed fibrosis in the liver; small ductal spaces with endothelium possibly made of collected sinusoids were observed. At least, one month was required after the constriction of the inferior vena cava to produce the state similar to liver cirrhosis in dogs.

2) All the normal dogs died of a marked central hemorrhagic necrosis within

48 hours after the interruption of the hepatic artery.

3) Necrosis always developed as a sequela of congestion in the portal system. A lack of oxygen in the congested region was assumed to be a cause of hepatic necrosis.

4) Ascitic dogs which survived over one month rarely developed congestion or hepatic necrosis after the interruption of the hepatic artery.

5) An intrahepatic passage of the portal blood after the interruption of the hepatic artery in ascitic dogs required less time than in normal dogs.

6) Normal dogs showed a marked contraction of the sphincter of the hepatic vein branches following the interruption of the hepatic artery, while ascitic dogs showed only a slight contraction.

7) An increased portal pressure in ascitic dogs was favorably decreased by the interruption of the hepatic artery.

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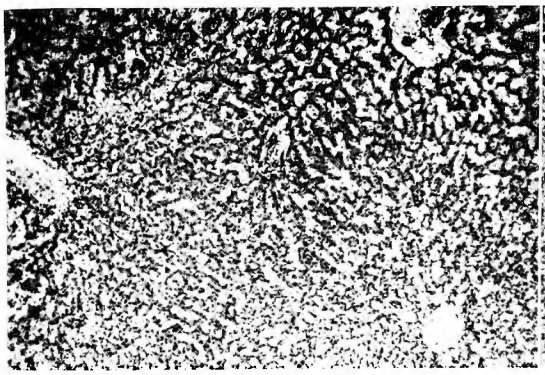

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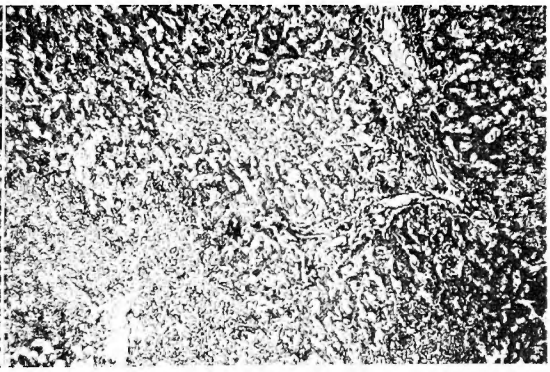

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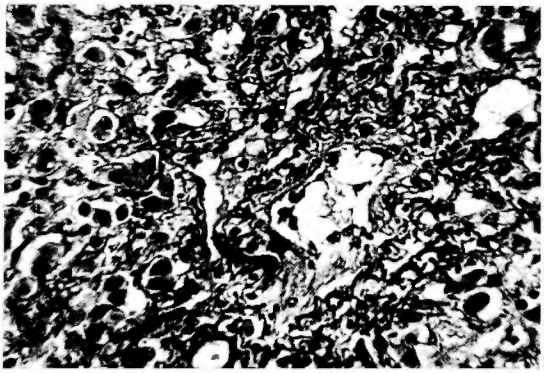


Fig. 3 V-G Stain ×400

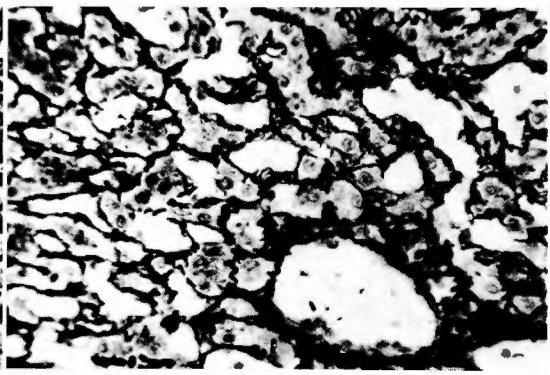
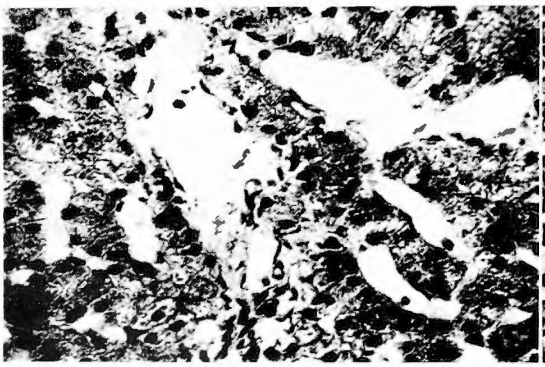


Fig. 4 Silver Stain ×400



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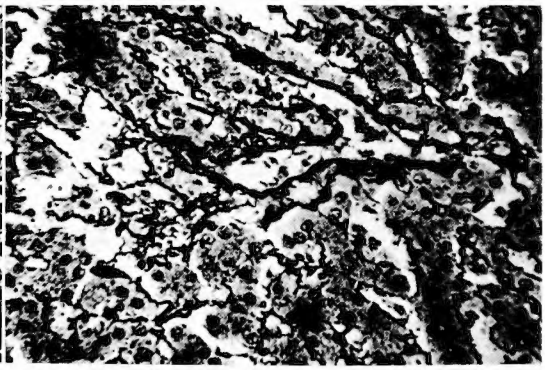

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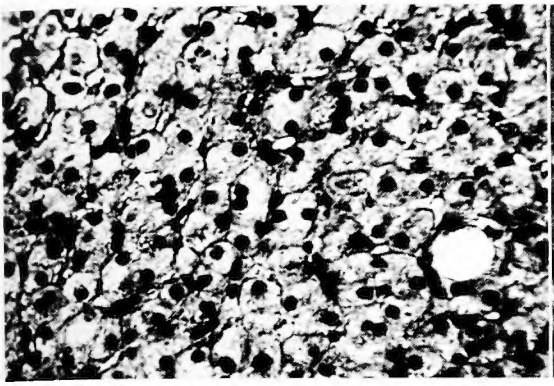

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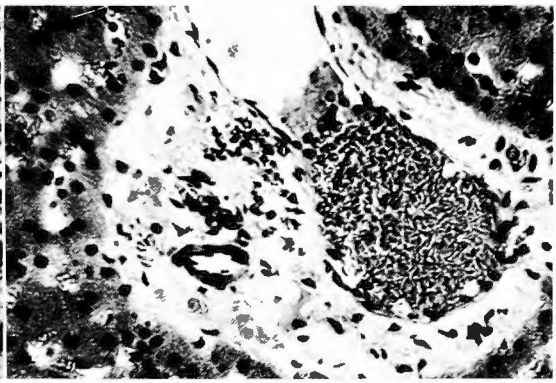

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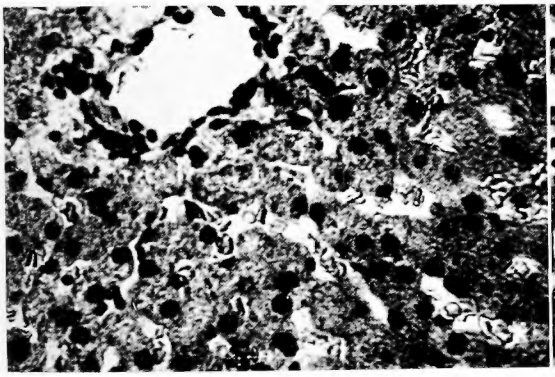

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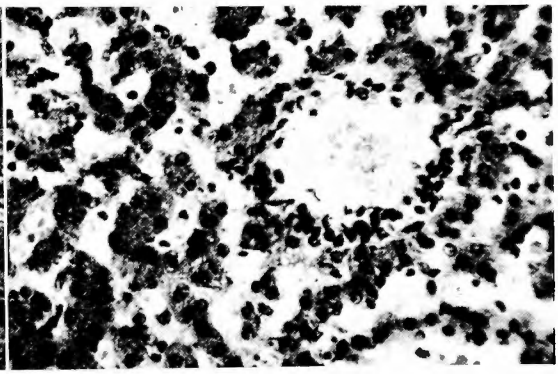

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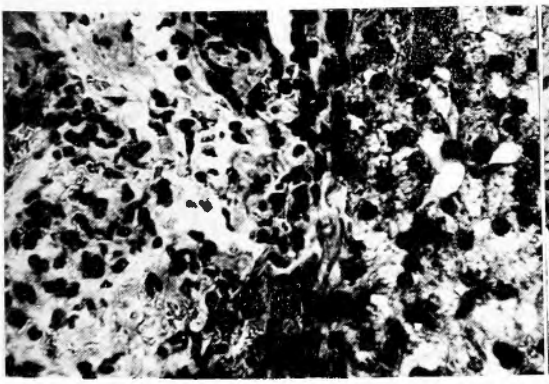

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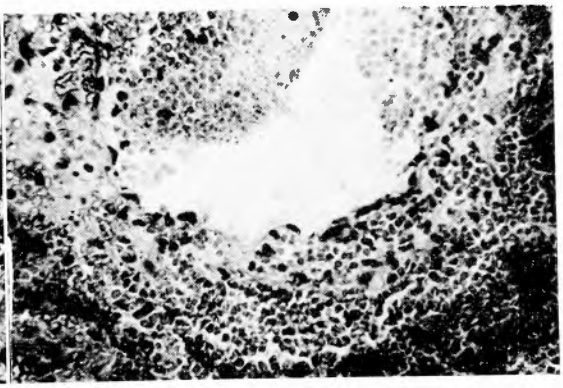

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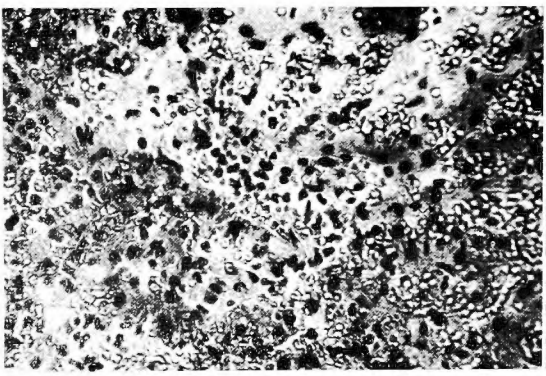

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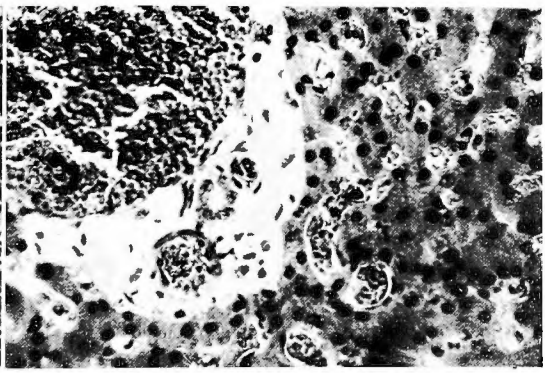

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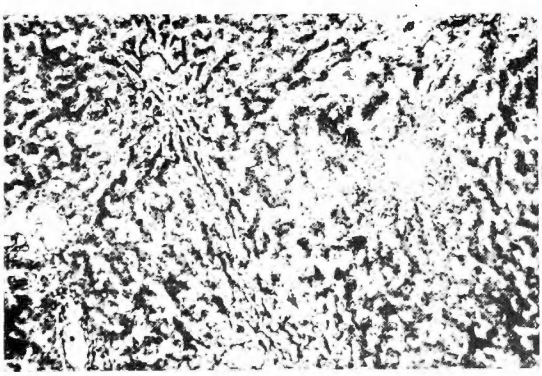

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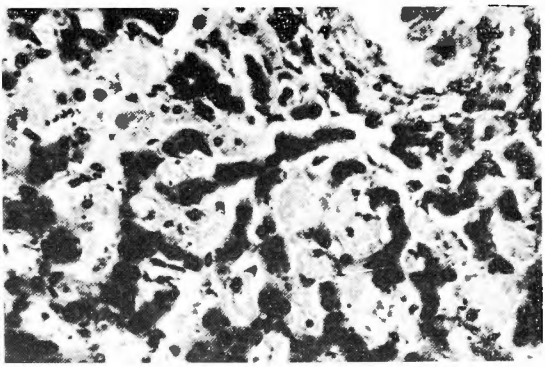

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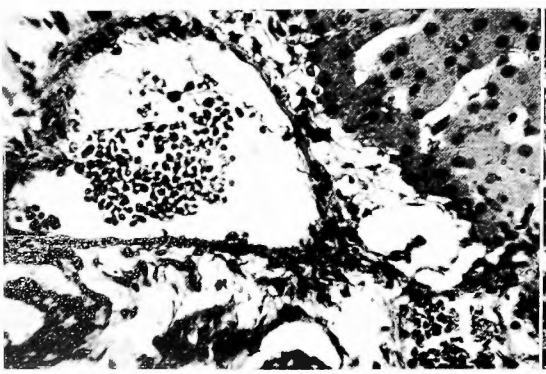

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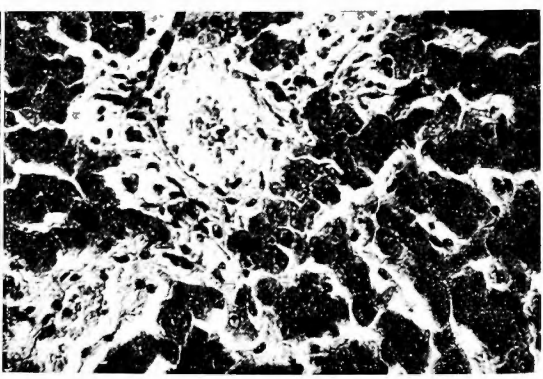

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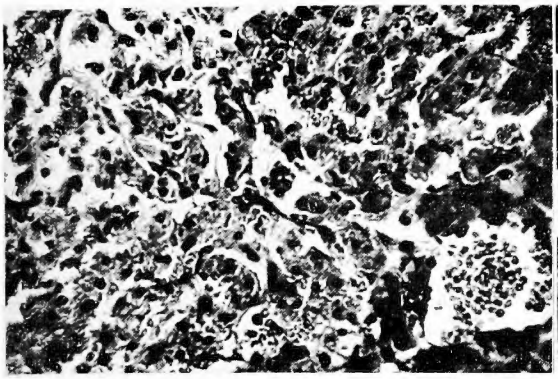

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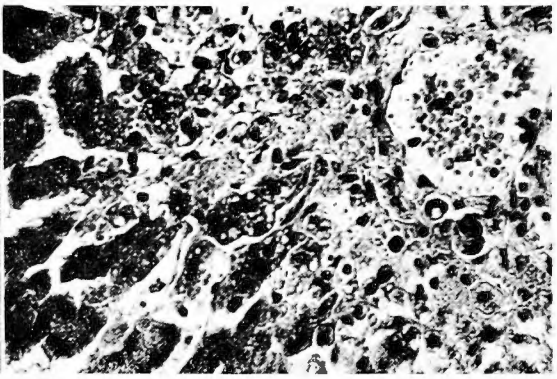

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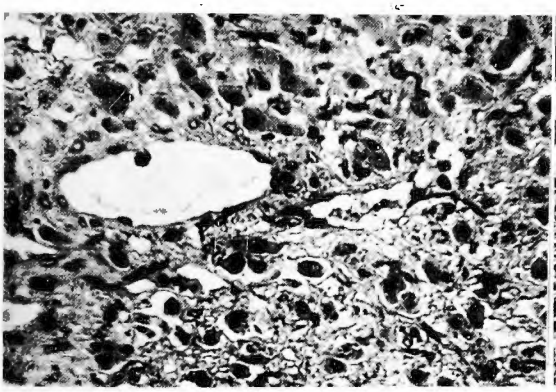

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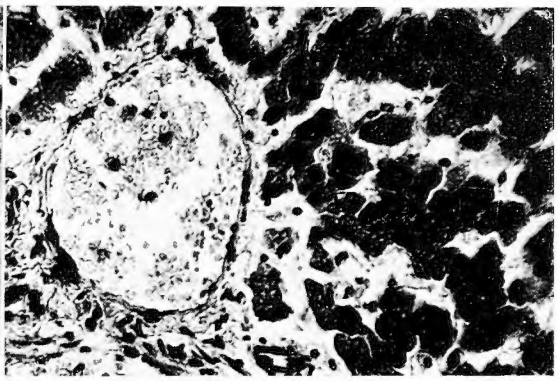

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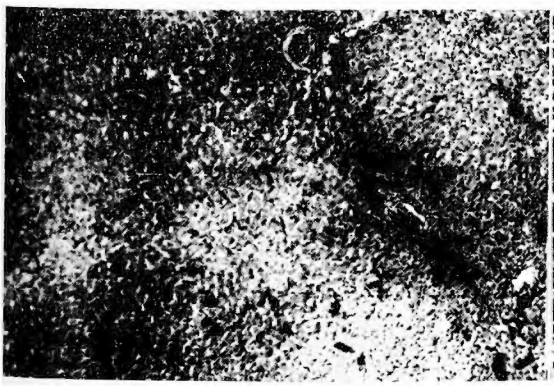

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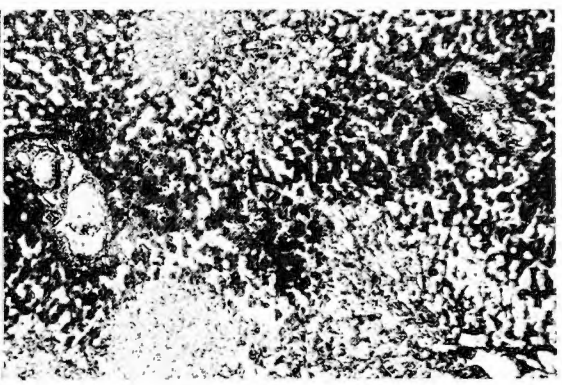

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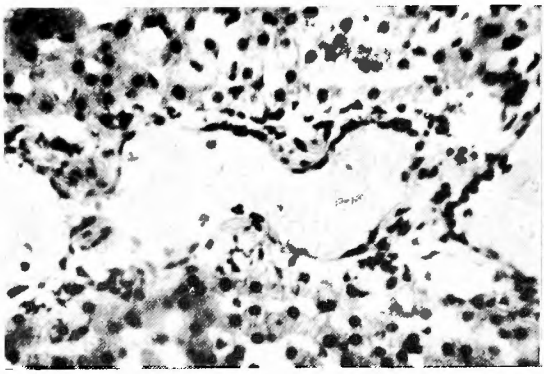

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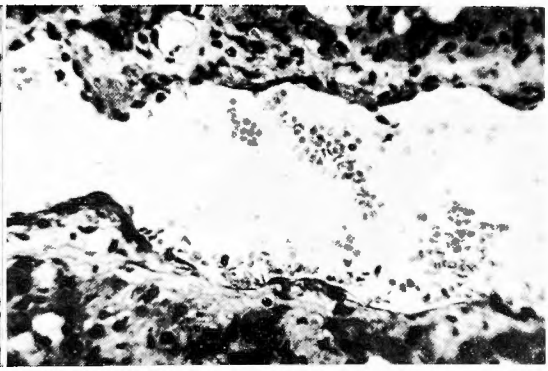

Fig. 26 ×400

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和文抄録

肝硬変症の実験的研究
特に腹水犬に於ける肝動脈遮断後の肝の組織学的所見について

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森田宗博

肝硬変症では肝動脈が遮断されても，其の硬変肝に壊死の発生し難い事実に対しては，未だ明確な説明がなされていない．著者は実験的に下大静脈を狭窄して作成した腹水犬に対し肝動脈遮断術即ち総肝動脈，胃十二指腸動脈及び右胃動脈の結紮切断を行い，遮断後の肝の経時的推移を組織学的に検索し，正常犬に対する場合と照合した．其の結果，

1) 下大静脈を狭窄して1ヵ月以上経過すると肝にFibrosisが多少とも発生し，しかも静脈洞の集合より成ると思われるEndothelを持つた小管腔の発生を認めた．それ故，肝硬変症類似の腹水犬の作成には少くとも1ヵ月を要した．

2) 正常犬に於ては肝動脈遮断後，次第に中心静脈，静脈洞にうつ血を来し，3時間後頃よりうつ血のために静脈洞の拡張，肝細胞索の蛇行が著明となり，其の後時間の経過と共に肝細胞の蛇行，断裂，肝細胞の変性，実質内出血等の所見が増強し，遂には著明な中心性出血性壊死を来して全例48時間以内に死亡した．

3) 下大静脈狭窄前3週間までの腹水犬に肝動脈を遮断すると，其の半数に肝壊死発生を来した．此の事は，3週までの腹水犬では腹水貯溜は認めるが未だ正常犬に類似せる肝内血行状態を維持しており，肝壊死を発生し得る危険性が存するものと思われる．

4) 下大静脈狭窄後，1ヵ月以上を経た腹水犬に於ては肝動脈遮断3時間後に，一時軽度のうつ血を認めた例もあつたが，24時間，4日，7日と観察しても，うつ血を来し難く，従つて肝壊死発生を認めなかつた．

5) 肝動脈遮断3時間後に門脈より墨汁を注入するに腹水犬では墨汁の肝内通過時間は正常犬に比して短時間であつた．組織学的にも此の事実を確認し得た．

6) 肝動脈遮断後正常犬では著明な肝静脈細枝括約筋の収縮を認めた．此の括約筋の収縮は門脈血行障害の一因と目されるのであるが，腹水犬では著明な収縮を認めなかつた．

7) 正常犬では肝動脈遮断直後より著しい門脈圧の上昇を来し漸次下降はするが6時間後に至るも決して遮断前値にまで復さないのに反し，腹水犬では遮断直後より急激に下降し，一時軽度の上昇を来した例もあつたが次第に遮断前値より低い門脈圧を維持した．

即ち腹水犬では正常犬と異り特異な肝内血行状態を呈しており，肝静脈系括約筋の動態とも関連して肝動脈遮断後に門脈血行障害を来し難く，従つて肝壊死発生を来し難い事実を或る程度説明し得たと共に，肝動脈遮断は亢進せる門脈圧に低下の方向に作用する事実を指摘し得た．

（尚本論文の要旨は昭和36年5月の第89回近畿外科学会に於て発表した）