REGENERATIVE ABILITY OF LIVER IN PORTAL DOGS AFTER PARTIAL HEPATECTOMY

by

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Received for publication Dec. 24, 1959

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I. INTRODUCTION

A portal dog is one whose hepatic artery has been interrupted. That the function of hepatic artery is not only to carry oxygen but also to adjust the portal flow mechanically was pointed out by GAD in 1873.

Next HERRICK suggested in 1907 a theoretical basis for ligation of the hepatic artery as surgical treatment of portal hypertension due to cirrhosis of the liver. In spite of the fact that most of the blood flow goes through the portal vein, the liver can survive even when it is deprived of all the blood from the portal vein by an ECK fistula. However, a wide-spread necrosis occurs in the liver when the hepatic artery is interrupted. NARATH in 1916, trying to prevent liver necrosis by means of arterialization of the portal vein after interruption of the hepatic artery, succeeded in having three survivals out of seven. MARCOWITZ, while repeating NARATH's experiment, discovered in 1949 that penicillin could prevent liver necrosis in dogs after ligation of the hepatic artery. He ascribed the cause of liver necrosis brought about by interrupting the hepatic artery to the proliferation of anaerobes. However, JOHN LEWIS reported in 1950 that no anaerobes were found in the liver of human beings, and FRASER, RAPPAPORT and many other investigators paid attention in 1951 to the fact that anoxic necrosis occurs in the liver after the hepatic artery is interrupted whether antibiotics are used or not. Further in 1952, EZE

questioned the mechanism of penicillin activity following his discovery that liver necrosis could be prevented by a single subcutaneous injection of 100,000 units penicillin alone.

HONJO et al. in our laboratory claim that the liver can survive with portal blood alone, and URABE discovered that a disorder of portal circulation follows the ligation of the hepatic artery, causing the liver necrosis. Later the mechanism of penicillin's prevention of the disorders in portal circulation was elucidated by NAKASE. Yet the function of the liver that survives with portal blood alone has not yet been made clear. The author, therefore, investigated whether the liver, after removal of a large part, could regenerate or not in order to obtain some information on the pathophysiology of the liver in a portal dog whose hepatic artery had been interrupted and which depended on portal blood alone.

It has long been known that regeneration of the liver is vigorous as seen in the myth of Prometheus, and clearly demonstrated by BOLLMAN in 1936. Such vigorous regeneration of the liver is, however, almost entirely lost when the blood flow through the portal vein is by-passed by setting up an ECK fistula, and it has been shown that the liver atrophies and growth ceases in growing animals. MANN stated in 1936 that the mechanical extension of the sinusoids induces cell division, and in 1951 BUCHER proved the existence in the blood of a factor that induces cell division. Moreover, GRINDLAY reported in 1952 that regeneration of the liver requires the filling of the portal flow area by portal blood but it may be replaced by congestion with venous blood. However, it was shown by CHILD in 1954 that the rate of hepatic regeneration was two thirds of that in normal dogs when the blood from the inferior vena cava alone flowed into the portal flow area, suggesting the unique quality of portal blood. The next question is : can the liver regenerate with portal blood alone when the hepatic artery is missing ? No report of such a study has been found in the literature.

II. EXPERIMENTAL METHODS

Mongrel dogs, as mature as possible, were used as test animals. Food is an important factor, and all the test dogs were fed with rice almost constantly.

1) Preparation of portal dogs

Some investigators doubt whether the artery that flows into the liver can be interrupted so thoroughly as to remove the functional influence of arterial blood on the liver even if the blood flow of the hepatic artery is shut off. They attach importance to the existence of collateral arterial circulation to the liver. GRINDLAY, after interrupting the hepatic artery, reported in 1951 the possibility of minute arteries going into the liver through adhesions of the liver to the diaphragm, abdominal wall, or other viscera. In 1952 JEFFERSON pointed out, as shown in Fig. 1, the existence of inferior phrenic arteries on both sides and a right superior phrenic artery in addition to the hepatic artery. Further, LAUFMAN mentioned in 1953 the existence of additional fine vessels that go through the gastrohepatic and hepatorenal ligaments and of a fibrillary network over the surfaces of the common bile duct

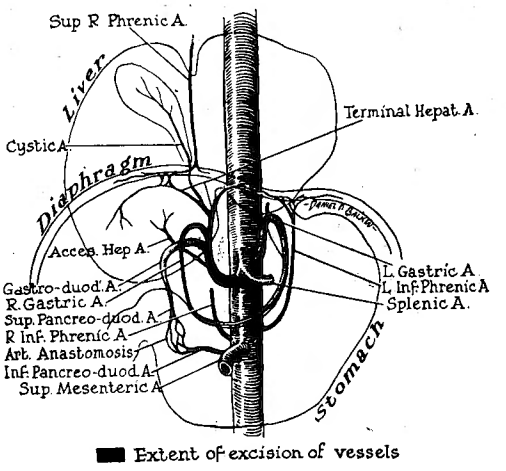


Fig. 1—Diagram of arterial supply to dog's liver, indicating observed collaterals. (After JEFFERSON)

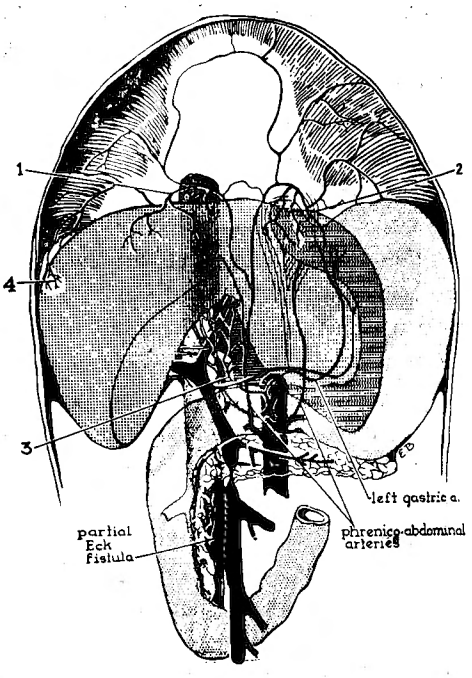


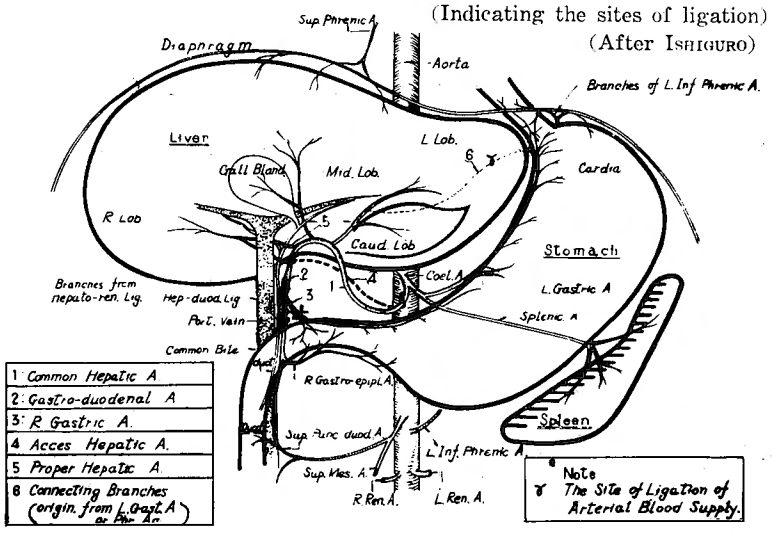
Fig. 2 Collateral circulation of the dog's liver with partial ECK fistula and complete ligation of the hepatic artery.
(1) A crown of collateral vessels around the vena cava coming up from the phrenico-abdominal arteries and sending fair sized twigs to the right and central liver lobes.
(2) Collateral arterial twigs to the left liver lobe arising from the left gastric artery and its anastomosis with branches of the phrenico-abdominal arteries.
(3) A plexus of collateral vessels spun around the bile duct and situated in the subserosa of the hepato-duodenal ligament sends twigs into the liver. This plexus is formed by the anastomosis of branches from the left gastric with ones from the phrenico-abdominal arteries.
(4) Collateral arterial twigs coming up from the right phrenico-abdominal artery and coursing through the right coronary ligament into the liver.
(After RAPPAPORT)

and inferior vena cava.

ISHIGURO of our laboratory elucidated that the arteries of the hilus hepatis alone systematically reach the entire liver, and further pointed out as shown in Fig. 2 that the left inferior phrenic artery reaches the hiatus oesophageus through the lower surface of the diaphragm, and there growing into a network together with a branch of the left gastric artery sends collateral arterial twigs into the hilus hepatis. He stated that these arterial twigs are normally very fine.

Considering the possibility of the presence of an accessory hepatic artery, the author as shown in Fig. 3 made ligation and division in the common hepatic artery as close to its origin from the celiac axis as possible, and also divided the gastroduodenal artery and right gastric artery and further cut off the gastrohepatic ligament, leaving only the portal vein and the common bile duct intact. The operation was terminated after removing the gall bladder. In a few cases, the fine vessels that reach the hilus hepatis from the network of the hiatus oesophageus in the diaphragm through the omentum minus were ligated and

Fig. 3 Diagram of extra-hepatic arterial circulation of the dog (Indicating the sites of ligation) (After ISHIGURO)



divided after hepatectomy. In order to investigate how long the interruption of the hepatic arterial circulation persists following the above procedure, India ink was injected into the thoracic aorta to see whether the liver was colored or not after the termination of the experiment before sacrificing the animal. Commercial India ink was filtered through three layers of gauze and diluted two times with water to obtain 50 cc for each injection. At the time of injection, the inferior vena cava was not touched although the portal vein was ligated.

2) Preparation of dogs with ECK fistula

In a dog, the branching of the portal vein at the hilus hepatis is close to the inflowing portion of the lienal vein and is not easy to handle. Thus a side to side anastomosis between the portal vein and the inferior vena cava was prepared 2~3 cm below the junction of the portal vein with the lienal vein prior to the ligation and division of the portal vein on the liver side of the inflowing portion of the lienal vein. Although suture of blood vessels can be done by the usual continuous suture, in this case the U-form node suture was used at the upper and lower edges and the mattress suture on the front and rear surfaces.

3) Determination of regenerating ability of the liver

i) Percentage of regeneration

Both GRINDLAY in 1952 and CHILD in 1954 removed the middle, quadrate, left upper and lower lobes of the liver, deduced the amount of the remnant from the weight of these lobes which was presumed to be 70 % of the entire liver, and used this amount as the basis for calculating the percentage of hepatic regeneration from the weight of regenerated liver at the time of sacrifice 6~8 weeks later. GRINDLAY expressed the percentage by the proportion of the amount of regenerated liver to the presumed amount of remnant at the time of removal, while CHILD by the proportion of the regenerated amount of liver to the amount removed. The author examined the proportion of the amount removed to the entire amount in 18 cases

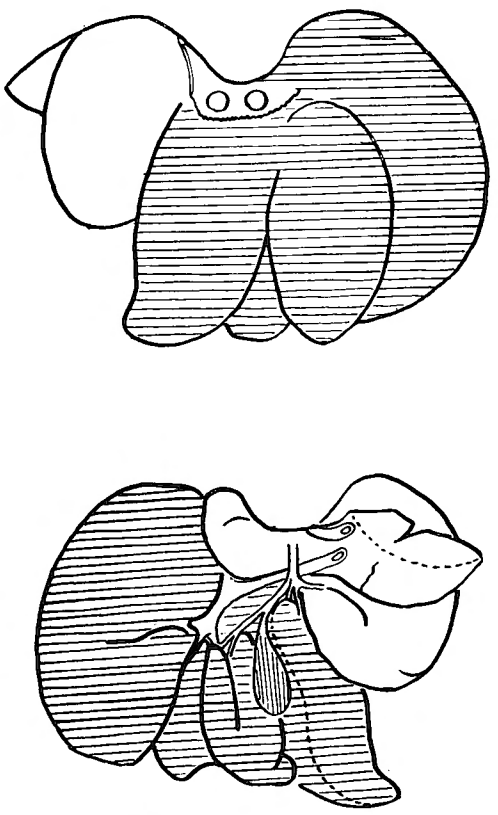


Fig. 4 Diagram of extent of hepatic resection (Middle, quadrate, and left upper and lower lobes)

Table 1. Ratio of the Weight of the Removed Liver to the Weight of the Whole Liver and to the Body Weight

Weight of Liver Removed (gm)	Weight of Whole Liver (gm)	Ratio (%)	Weight of Dog (kg)	Ratio (gm/kg)
180	320	56.3	7.0	25.7
280	490	57.1	12.0	23.0
180	300	60.0	6.5	27.7
410	670	61.2	13.0	**31.5**
260	410	63.4	8.3	31.3
180	280	64.3	7.0	25.7
260	400	65.0		
300	460	65.2	12.0	25.0
170	260	65.4	10.0	**17.0**
120	180	66.7	7.0	17.1
260	390	66.7	13.0	20.0
180	270	66.7		
310	460	67.4	12.0	25.8
220	320	68.7	11.0	20.0
270	390	69.2	9.5	28.4
380	540	70.4	16.0	23.8
240	340	70.6	8.5	28.2
270	380	71.1		
Average :		65.85		24.68

Maximum 71.1%
Minimum 56.3%
Mean 65.85%
Median ..... 65.4～66.7%
Mode 67.7%
S. D. 4.39%

as shown in Table 1. The minimum, maximum and mean were 56.3 %, 71.1 % and 65.85 % respectively, while the standard deviation, median and mode were 4.39 %, 65.4～66.7 % and 67.7 % respectively. According to MORITA in 1957, the mean with 20 cases was 64.15 %. These data suggest that the rate of removal in mongrel dogs in Japan is smaller than that in America. As a matter of convenience, the author used the percentage 65 as the rate of removal to obtain the percentage of regeneration according to CHILD's method. That is, the percentage of regeneration R is given by the following equation.

$$R = \frac{L - \frac{100-65}{65} l}{l} \times 100\,(\%)$$

in which l stands for the amount of liver removed and L the weight of liver at the time of sacrifice. If the rate of removal is 71%, the percentage of regeneration is R +13.0, and if 56%, it is R −24.7. Judging from the distribution of the rate

of removal in the 18 cases the author dealt with, the percentage of regeneration calculated with the rate of removal as 65% is liable to have an error from +13% to −24.7%.

ii) Removal of a large part of the liver

The liver was removed by the following procedure. Laparotomy was made by an incision along the costal margin together with an upper midline incision. First the twigs of the portal vein leading to the middle and quadrate lobes were ligated and divided, then the hepatic veins belonging to these lobes were ligated and divided. Further, hepatic parenchyma was removed by stripping so that it would not remain on the wall of inferior vena cava. In the two cases that died because of surgical error, the amount of liver remaining on the wall of the inferior vena cava was less than 2% of the entire liver.

iii) Time required for regeneration

According to SOEJIMA (1958), the blood flow in the portal vein decreases by 20 % when 50% of the liver is removed, and the reduction rate is only 25% even when 70% is removed. Also, according to MIKAMI (1957), the remaining liver shows an appearance of regressive change about six hours after removal. Although tissue respiration is also markedly decreased, it rapidly recovers in 24 hours, and binuclear cells multiply greatly. The weight of liver doubles in 48 hours. The increase in weight at this stage is ascribed to the liquid constituents. Vigorous nuclear division persists even after three weeks. It gradually decreases thereafter, but is still noticeable after eight weeks. MIKAMI also stated that the liver weight exceeds that prior to the removal in four weeks showing a temporary hypertrophy, and it is only after 6～8 weeks that it returns to the pre-operative weight. The amount of blood flow through the liver decreases at first, then returns to the pre-operative level at this stage. But the increase in portal pressure persists over a long period of time, and is believed to take more than 15 weeks for complete recovery.

As for the recovery of hepatic function, it is said that the tests of blood sugar, pyroracemic acid, amino acids, ammonia, urea and galactose require 1～2 weeks for recovery, the serum Na and Cl, the extracellular fluid, urobilinogen, and the bromsulphalein and hippuric acid tests take about two weeks, and the plasma protein, serum bilirubin, serum alkaliphosphatase, cholinesterase and TAKADA's reaction four weeks.

Therefore, the author decided to examine regenerated livers eight weeks after the removal. First the bromsulphalein test was done. Bromsulphalein is excreted far more rapidly in dogs than in human beings. Therefore, in accordance with the theory of GORNALL (1952), blood was collected from the opposite vein after intravenous injection of 10 mg per kg of bromsulphalein. Into the serum of the blood collected 10% solution of sodium hydroxide was added to make it colored. Using a series of standard solutions, the amount of bromsulphalein remaining in the blood was determined colorimetrically. The standard solution is considered to be 100% when 1 mg bromsulphalein is contained in 10 ml. In normal dogs it is under 6%

according to GORNALL.

4) Preparation of tissue specimens of regenerated liver

The portions of regenerated liver from which pieces of tissue were collected for histological examination were between the most strongly and the least colored sections in the cases where India ink, injected into thoracic aorta before sacrificing, had stained the liver. In the cases with no coloring of the liver sections were selected arbitrarily. However, it is believed that when the liver regenerates, the regeneration is not restricted to certain limited areas. The pieces of tissue collected were stained with hematoxylin-eosin. The following are their microscopic photographs enlarged 200 times.

III. EXPERIMENTAL RESULTS

1) Control dogs (normal dogs)

As Table 2 shows, there was no case that was perfectly healthy all through the eight weeks, and the control dogs cannot be said to have been normal either. Especially in Dog No. 5, the percentage of regeneration was only 38.6, suggesting the presence of some factor deterring cell division although it appeared normal except for having a great many intestinal parasites. The tissue of this case is shown in Photo. 1. Also, Dog No. 6 died of distemper at the end of the fourth week. Yet the percentage of regeneration was as great as 141.6, and it must have been more than 116.9 even when the error due to the rate of removal is taken into consideration. This dog was probably at the stage of temporary hypertrophy. Dog No. 2 died almost the same time. This dog slipped its chain more than four weeks after operation and was very fierce and difficult to catch. Therefore it had to be fed meat containing isomythal to sedate it. This attempt failed, so the dose was repeated till the total amount reached 6.0 g which finally caused death. Although

Table 2. Regeneration after Partial Hepatectomy (Normal Hepatic Circulation)

Dog Number	Weight of Dog at Partial Hepatectomy (kg)	Weight of Liver Removed (gm)	Weight of Dog at Autopsy (kg)	Weight of Liver at Autopsy (gm)	Interval between Operation and Autopsy (days)	B. S. P. Test at Autopsy (%)	India Ink Test at Autopsy	Liver Regeneration (%)
1	7.5	170	7.5	280	56	12.5	(卅)	110.9
2	6.5	220		350	33			105.2
3	12.5	240	14.0	420	56	2.5		121.2
4	8.5	180	8.0	220	56	5.0	(卅)	68.4
5	16.3	500	17.0	460	56	7.5		38.6
6	10.3	220		430	28			141.6

Average Rate of Regeneration : 96.0

Dog No. (Normal Dogs)	Complication
1	Distemper-like symptoms
2	Poisoned to death by isomythal
3	Distemper-like symptoms, Bloody excrement
4	Frequent diarrhea
5	Intestinal parasites
6	Distemper

the percentage of hepatic regeneration was 105.2% in this dog, in the tissue, the sinusoids were markedly distended and filled with blood corpuscles as shown in Photo. 2. It is not worth comparing the weight under these conditions. Among the above three cases, Dogs No. 2 and No. 6 should naturally be excluded for both of them died at about four weeks in the stage of temporary hypertrophy, although it is doubtful whether Dog No. 5 should be excluded for the factor that hindered regeneration is not clear.

Among the remaining normal dogs, Dog No. 1 showed 110.9 % regeneration in the eight weeks of the regeneration period, and although it showed distemper-like symptoms for a time it had recovered completely when killed. The body weight neither decreased nor increased over that at the time of removal. The bromsulphalein test showed 12.5%. Photo. 3 shows the tissue. In this case, India ink was injected before sacrificing for the purpose of comparing it with a portal dog, and the blood vessels and sinusoids were filled with India ink. Hepatic cells were light-colored suggesting an increase of glycogen. Cellular membranes were thickened, nuclei were uniform, no pyknosis was found, and nucleoli were large suggesting accelerated function. The duration of hepatic regeneration was eight weeks for the rest of the dogs. In Dog No. 3, the percentage of regeneration was 121.2. Although this dog also showed symptoms of distemper and a continuing bloody excrement, it had almost recovered when sacrificed. The body weight which was 12 kg at the time of removal increased to 14 kg. Although the tissue, as in Photo. 4, showed a cellular infiltration in the sinusoids, it was not severe and the author considers it unnecessary to exclude this case. The hepatic cells were light-colored, their membranes thickened, their nuclei large with large nucleoli. The bromsulphalein test was slightly less than 2.5%. In Dog No. 4 the percentage of regeneration was 68.4. This dog also suffered from frequent diarrhea, but the body weight reduced only by 0.5 kg from 9.5 kg measured at the time of removal, and the bromsulphalein test was slightly less than 5%. Photo. 5 shows the hepatic tissue of this case. The India ink injected for comparison is abundant. In some parts the tissue cells are colored very weakly, while in the rest of the section the coloring is not so weak. Cellular membranes are found to be thick. No nuclear pyknosis is seen.

2) Portal dogs

As shown in Table 3, the percentage of hepatic regeneration in Dog No. 1 was 123.1. Although this dog was also having diarrhea, the weight that was 7.5 kg when the liver was removed increased to 8.0 kg. The bromsulphalein test was slightly under 2.5%. When India ink was injected into the thoracic aorta, first the stomach and intestines, then the diaphragm immediately turned black. But the liver was colored very slowly and weakly all over. Photo. 6 shows its tissue in which no India ink can be found in the artery but only slightly in the sinusoids. Hepatic cells are somewhat larger than the regenerated hepatic cells in normal dogs. The color of the cells is not so bright and the membranes are not so thick as in the controls, while both nuclei and nucleoli are large. The percentage of hepatic regeneration in Dog No. 2 is 123.9. Although this dog showed strong distemper-

Table 3. Regeneration after Partial Hepatectomy (Hepatic Arterial Ligation and Division : Portal Dog)

Dog Number	Weight of Dog at Partial Hepatectomy (kg)	Weight of Liver Removed (gm)	Weight of Dog at Autopsy (kg)	Weight of Liver at Autopsy (gm)	Interval between Operation and Autopsy (days)	B. S. P. Test at Autopsy (%)	India Ink Test at Autopsy	Liver Regeneration (%)
1	7.5	130	8.0	230	56	2.5	(+)	123.1
2	8.5	180	10.5	320	56	5.0	(+)	123.9
3	9.0	300	11.7	430	56	5.0	(−)	89.5
4	6.5	160	7.0	200	56	7.5	(+)	71.1
5	7.7	200	7.2	220	56	15.0	(−)	56.2
							Average Rate of Regeneration :	92.8
(Dog with Eck Fistula)								
1		200		150	17			21.2

(Portal Dogs)

1 Diarrhea
2 Strong distemper-like symptoms
3 Abdominal hernia
4 Erosion on the nape
5 Fistula stercoralis in the operative wound

(Dog with Eck fistula)

1 Keratomalacia

like symptoms after the hepatic artery was interrupted, it gradually recovered vitality after eight weeks. The weight of the body increased from 8.5 kg at the time of hepatic removal to 10.5 kg when sacrificed. The bromsulphalein test was a little under 5%. The flow of India ink into the liver was slow and limited to a small section. India ink is, as shown in Photo. 7, found histologically in the arteries and in the bile duct. Most of the hepatic cells are weakly colored, the cellular membranes thickened, nuclei and nucleoli large giving an appearance of regeneration. The percentage of hepatic regeneration in Dog No. 3 was 89.5. In this dog, the arterial twigs that reach the artery of the hilus hepatis from the arterial network near the hiatus oesophageus in the diaphragm as pointed out by Ishiguro were also interrupted through the caudate lobe. After the removal of a large part of the liver, the operative wound opened and left a large abdominal hernia, but it was mostly healthy during the eight weeks. The weight had increased from 9 kg to 11.7 kg when sacrificed. This is probably because it was a young dog. The bromsulphalein test was a little less than 5%. The injection of India ink did not cause visible coloring. In histological observation, no India ink could be detected as shown in Photo. 8. Hepatic cells were very weakly colored, and cellular membranes were thickened. Nuclei were large with no pyknosis, and nucleoli were also large. The percentage of hepatic regeneration in Dog No. 4 was 71.1. An erosion as if due to strong acid appeared on the nape of this dog for an unknown reason, which disappeared in about six weeks. The weight increased from 6.5 kg at removal to 7.0 kg when sacrificed. The bromsulphalein test was a little under 7.5 %. Coloring of the liver by the injection of India ink was slow, faint and restricted to a small

portion. But the tissue showed the inflow of India ink as in Photo. 9. Hepatic cells are light-colored and are somewhat large, cellular membranes are thickened and nuclei and nucleoli are large. The percentage of hepatic regeneration was only 56.2 in Dog No. 5. Even if the error for the regeneration percentage is taken into account, it is below 69.2%. In this case, the arterial twigs pointed out by ISHIGURO were intercepted as in Dog No. 3. Although it developed fistula stercoralis in the operative wound after the removal of the liver, lost appetite and was very weak, it recovered in the seventh week and the fistula was completely closed at the time of sacrifice. At necropsy it was found that the duodenum was perforated and adhered to the liver. The body weight was 7.7 kg at the time of removal, which fell to 7.2 kg. The bromsulphalein test was a little under 15%. Coloring due to the injection of India ink could not be found either macroscopically or microscopically. In the tissue shown in Photo. 10 cellular infiltration in sinusoids was marked and KUPFFER cells tended to become large which clearly shows that a strong sinusoid catarrh took place. Since it is obvious in this case that a factor other than incision of the hepatic artery lowered the percentage of regeneration, this case should be omitted. In any of the cases, neither thickening of interlobular connective tissue nor increase of bile duct was observed.

Both in groups (1) and (2), the weight of the body increased in some cases after removal of the liver. The percentage of hepatic regeneration sometimes exceeded 100 to a considerable extent in these cases. It is hard to decide whether this can be ascribed to error due to the amount removed.

3) Dogs with ECK fistula

The liver was removed in three dogs with ECK fistula. None of these dogs developed well. One case that barely survived developed keratomalacia and died in 17 days. A subphrenic abscess was found at necropsy. The percentage of hepatic regeneration in 17 days was 21.2. If the error due to amount removed is taken into account, this can mean any value between -3.5% to $+34.2\%$, namely it does not necessarily mean that regeneration actually took place. However, as shown in Photo. 11, binuclear cells were found in the tissue which gives a basis for judgment that regeneration was progressing.

Photo. 12 shows the regenerated hepatic tissue of a portal dog that died of distemper on the eighth day after the removal. The percentage of regeneration was 50.2. As this value should also be interpreted to mean a value in the range of 25.5% to 63.2%, it is likely that this percentage is greater than that of dogs with ECK fistulas.

IV. SUMMARY AND DISCUSSION

Among normal dogs, it was Dogs No. 1 and 4 that were injected with India ink. Their hepatic tissues were filled with India ink as shown in Photos. 3 and 5. Among the portal dogs, slight coloring was detected in those whose arterial twigs near the caudate lobe, pointed out by ISHIGURO, were not interrupted. But coloring was very slow and weak as compared with that in the normal dogs. The histolo-

gical examination also indicates that the inflow of India ink was markedly limited as shown in Photos. 6, 7 and 9. Moreover, when the arterial twigs that join the arteries at the hilus hepatis passing over the caudate lobe were interrupted, no inflow of India ink could be detected even microscopically.

The average percentage of hepatic regeneration in the six normal dogs and the five portal dogs, were 96.0% and 92.8% respectively. In the t-test, t is 0.15 and the probability is over 0.8. The difference in the above two averages is not significant. But it is clear that among the normal dogs Dogs No. 2 and 6 were still at the stage of hypertrophy, and it is therefore not appropriate to take their weights into account. Also Dog No. 5 among the portal dogs had a severe inflammation and was obviously a special case, and therefore it should be excluded. If these three cases are excluded, the average percentage of hepatic regeneration is 84.8% for the normal dogs and 101.9% for the portal dogs. The t is 0.74 and the probability falls between 0.4 and 0.5. This implies that if the regenerating ability of a normal dog is assumed to be equal to that of a portal dog, the probability for such an experimental result as the author obtained is between 40% and 50%.

The percentage of hepatic regeneration of Dog No. 5 among the normal dogs was very slow, which may be attributed to the marked propagation of intestinal parasites. If this case is omitted, the average will be 100.2% for the normal dogs and 101.9% for the portal dogs, the t and the probability being 0.07 and over 0.9 respectively.

The above experiments and statistical considerations led the author to the conclusion that the ability of the liver to regenerate after partial remove in portal dogs is by no means different from that of normal dogs. Yet the fact that the regenerated hepatic cells in portal dogs are slightly less colored that those of normal dogs seems to suggest some peculiarity. The results of the bromsulphalein test in the two groups did not differ from each other, and cases in which the weight increased during the regenerating period were found in both groups. On the contrary, in the dog with an Eck fistula, though only a single case, the regenerating ability of the liver was found to be lower. It has been well known that the regenerating ability of the liver after a large part has been removed is extremely vigorous, but it has been stressed by Mann, Bollman and others that regeneration becomes very limited in dogs with Eck fistulas. There was only one case in the author's experiment, and observations were made for only 17 days after removal of part of the liver. Child reported in 1954 on only one case of Eck fistula that the percentage of regeneration was zero on the 29th day. In 1952 Grindlay determined the percentage of hepatic regeneration in six dogs with Eck fistula 30～105 days after the partial removal of the livers. The calculation according to Child's method was $20.1 \pm 5\%$, which is similar to that obtained by the author. Thus it is evident that the ability of hepatic regeneration is poor in dogs with Eck fistulas as compared with portal or normal dogs.

Recently attention has been paid to the incision of the hepatic artery as a means of surgical treatment for cirrhosis of the liver with severe ascites. As indi-

cated by HONJO et al., the liver in cirrhosis has a strong resistance against interruption of the hepatic artery. Moreover, it has been made clear that the circulatory disorder to portal flow that occurs after interruption of the hepatic artery in normal dogs can be overcome by injections of penicillin with the result of preventing liver necrosis. This removed the fear of ligating the hepatic artery.

Even those who claim that an ECK fistula is required for the medical treatment of portal hypertension admit that the cases in liver cirrhosis with markedly lowered hepatic function cannot stand the operation and that many of the cases with obvious ascites show unfavorable results. Although some insist that the drop in hepatic function due to the preparation of the ECK fistula is temporary, it is a generally accepted fact that it causes liver atrophy and greatly decreases the regenerating ability. By determining the ability of the liver to regenerate after partial removal, the author believes that at least as far as hepatic regeneration is concerned, interruption of the hepatic artery has been proved to be superior to the formation of an ECK fistula.

V. CONCLUSION

1) The percentage of hepatic regeneration in six cases of normal dogs 4～8 weeks after partical resection of the liver was 96.0 on the average.

2) The percentage of hepatic regeneration in five cases of portal dogs eight weeks after partial removal of the liver was 92.8 on the average. The t-test according to the STUDENT-FISHER method proved that the difference between these and normal dogs was not significant.

3) In one dog with an ECK fistula, the percentage of hepatic regeneration 17 days after partial removal of the liver was 21.2.

4) The bromsulphalein test showed no difference between the function of the regenerated liver in the normal dogs and that in portal dogs.

In completing his report, the author would like to express his deepest gratitude to Professor Dr. CHISATO ARAKI for his kind encouragement and supervision and to Assistant Prof. Dr. ICHIO HONJO for his zestful encouragement and supervision throughout his work. Also regarding histological findings he is greatly indebted to Instructor Dr. FUMIHIRO ICHIDA of the First Department of Internal Medicine of Kyôto University Medical School.

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和文抄録

門脈犬に於ける肝切除後の肝再生能

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最近，高度の腹水を伴う肝硬変症に対する外科的治療法として，肝動脈の遮断が考慮されるようになつた．私は，肝動脈を遮断された後の肝の病態生理の一面を窺う為に，肝切除後の肝再生能に就て検討を加えた．

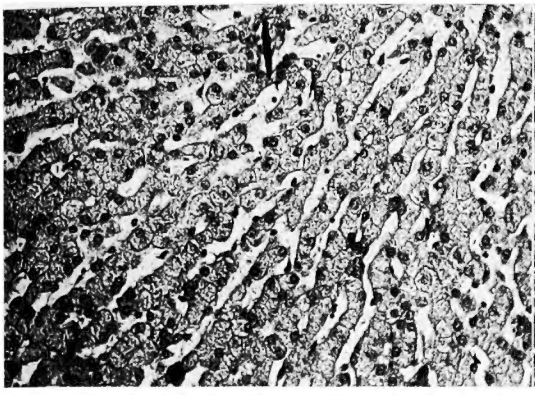
実験動物は，成熟した雑種犬を用いた．肝動脈遮断は，総肝動脈と胃十二指腸動脈，右胃動脈とを夫々結紮切断し，なお数例に於ては更に，左胃動脈から横隔膜下面を経て肝動脈に連絡する細い動脈枝をも結紮切断した．以上の如く，肝に注ぐ動脈流を遮断した犬を門脈犬と呼称する．

肝再生能測定には，先づ肝の中葉，方形葉，左上下葉を切除計量し，これを肝全量の65%として残された肝重量を推定する．8週後，屠殺して肝重量を計測し，この値から切除時推定肝残量を差引いた量が最初の肝切除量に対する比率によつて肝再生率を表わした．

屠殺に先立つて，B. S. P. 検査を行ない再生肝の機能を検討し，開腹後，門脈を結紮して胸部大動脈から墨汁を注入し，肝の黒変するか否かによつて，肝の動脈流遮断の状態を検討した．最後に再生肝の一部を採取し，Hematoxylin-eosin染色によつて組織標本を作製した．

実験成績：正常犬6例の肝再生率平均は96%，B.S.

1



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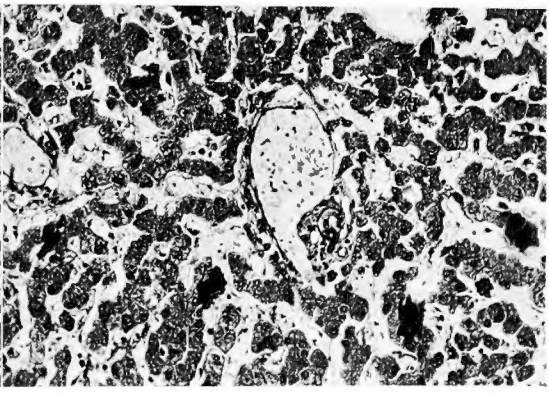

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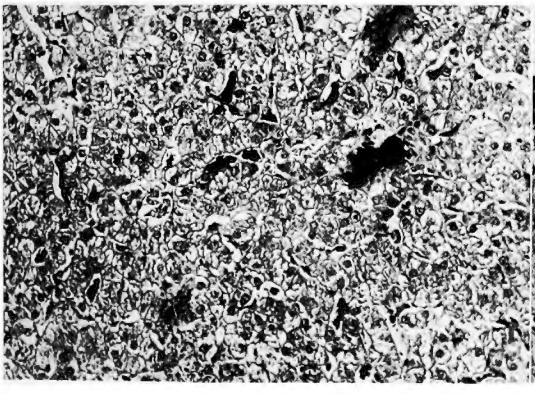

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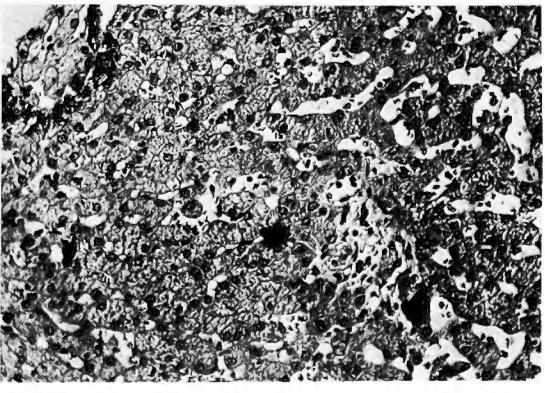

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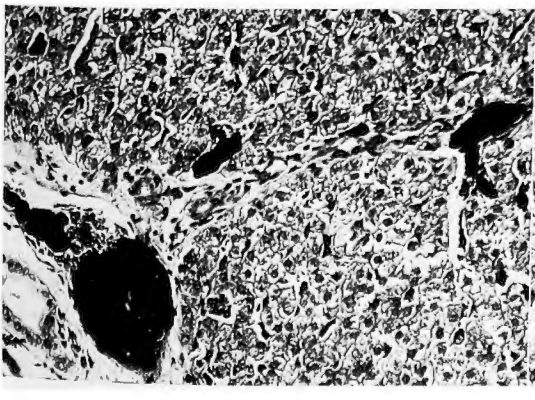

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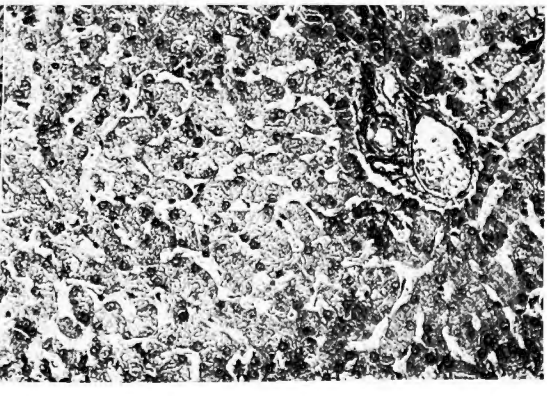

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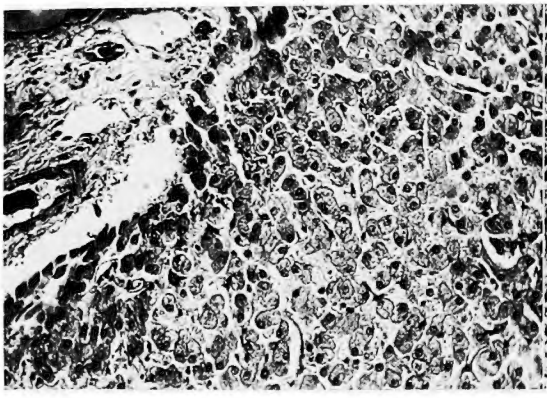

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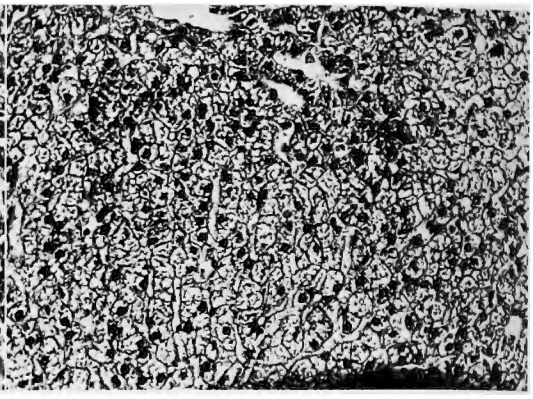

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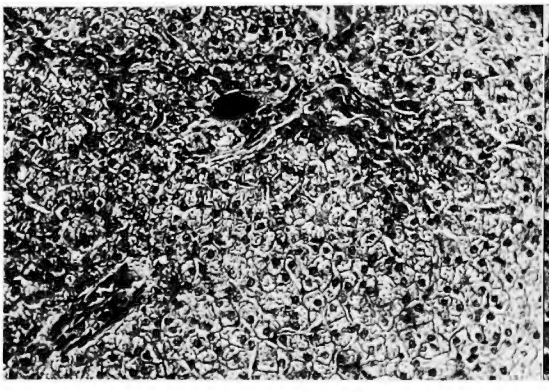

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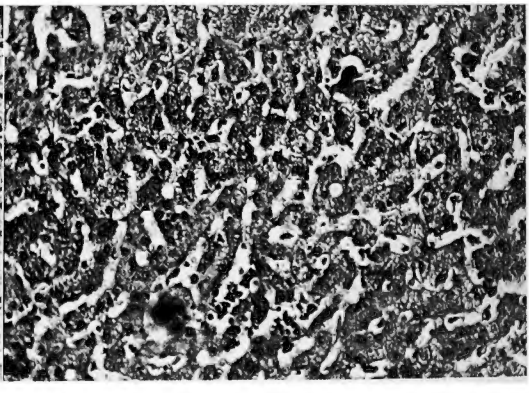

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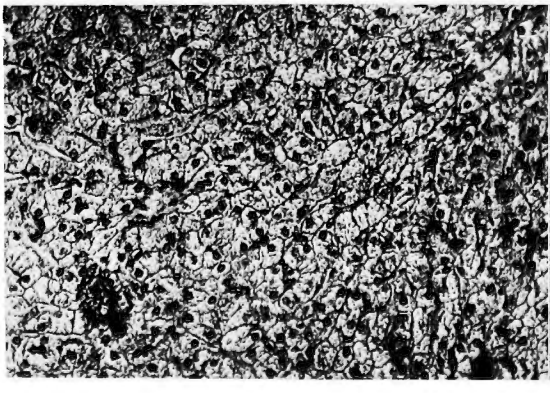

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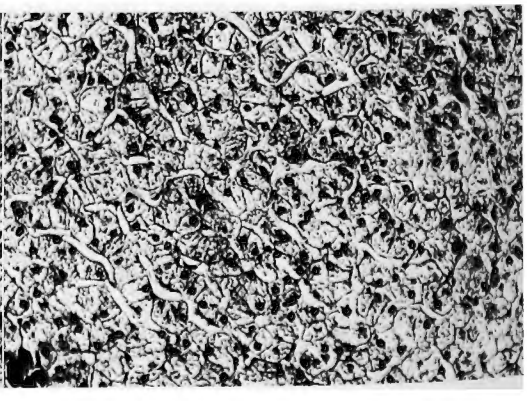

P. 停滞値は 2.5%から 12.5%まででであつた. 門脈犬 5 例の肝再生率平均は92.8%, B. S. P. 停滞値は2.5%から15.0%まででであつた. Eck 氏瘻犬に就ても, 肝切除を行なつた所, 術後生存し得た 1 例も17日で死亡したが, 肝再生率は21.2%であつた.

正常犬群と門脈犬群との各肝再生率平均値に就て, t-検定を行ない, 両群の間に有意の差が無い事を明らかにした.

Eck 氏瘻犬は唯 1 例であるが, Child, Grindlay 等の実験成績とも一致し, 肝再生能の著明な低下は明らかである.

又, 再生肝の組織学的検索の結果は, 肝の再生が単なる鬱血による増大でもなく, 間質のみの増殖によるものでもない事を証明し得た.

以上の実験成績によつて肝は動脈血のみでは肝切除後の肝再生を営み得ないが, たとえ肝動脈は遮断されても門脈血のみで肝再生能を維持し得る事を明らかにする事が出来た.