EXPERIMENTAL STUDY ON HEPATO-ENTEROSTOMY

By

Susumu Shibagaki

From The 1st Surgical Division, Kyoto University Medical School
(Director: Prof. Dr. Chisato Araki)
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CONTENT

INTRODUCTION

When some persistent stenosis or when occulusion takes place within the extrahepatic billary tract due to various causes, namely when the discharge of the bile towards the intestine is apparently reduced or when it absolutely fails, surgeons carry out various reconstruction of the biliary tract. But when tumor develops centered around the porta hepatis, or when the development of tumor commences from the adjacent tissue of the porta hepatis and extends to that region, or in the case of congenital obstruction of the bile duct, surgeons cannot utilize the extrahepatic bjliary tract.

For the treatment of severe jaundice in such cases, several operative procedures utilizing the intrahepatic biliary tract have been considered.

"Hepato-cholangio-eenterostomie" by Laméris in 1912 and "Intrahepatic Cholangio-jejunostomy with Partial Hepatectomy" by Longmire in recent years were reported, and Honjo originated a report on "Hepato-enterostomy" in 1952. This report by Honjo seems to be the most simple and efficacious procedure as compared

with the other two.

It is my intention to evaluate experimentally the hepato-enterostomy in dogs, and produce jaundise operatively and then to perform hepato-enterostomy in experimental dogs.

1. GROSS-ANATOMY OF THE BILE DUCT

The liver of a dog is divided into lobes, namely the left, right and middle lobes each of which consists of two minor lobes, and the caudate lobe (the left minor lobe of the middle lobe is popularly called the quadrate lobe).

The two minor lobes of the left lobe is partly connected with each other by the hepatic parenchym and the two minor lobes of both the right and the middle lobes are respectively connected by hepatic parenchym to a comparatively large extent. The right minor lobe of the left lobe and the quadrate lobe are barely connected, and there is almost no mutual connection of the parenchym between the left minor lobe of the right lobe and the middle lobe.

As for the bile duct, intrahepatic ducts come from the intrahepatic biliary one in the various lobes and join themselves to the choledochus. The gallbladder is located between the middle lobe and quadrate lobe and, contrary to human cases, the cystic duct opens into the begining part of the choledochus, and almost all of the hepatic ducts join the choledochus more distally between the cystic duct and the duodenum.

The anatomy of both intra-and extra-hepatic ducts varies considerably according to each individual dog. I injected a contrast medium into the choledochus of 22 experimental dogs and took X-ray pictures of their bile ducts. I also poured

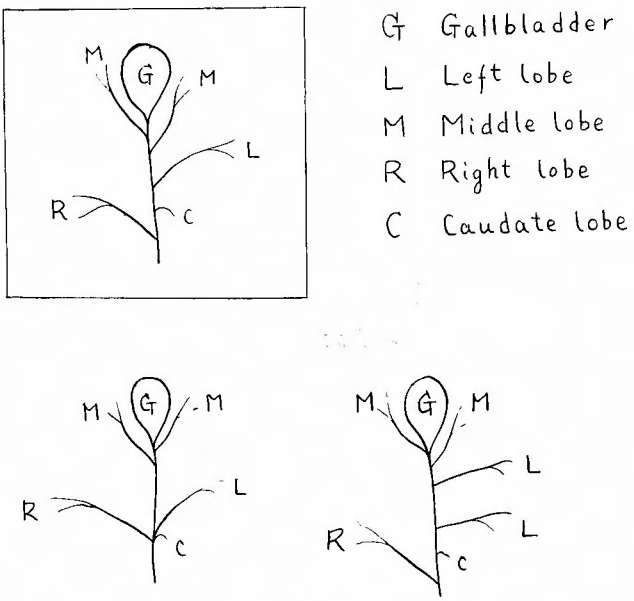


Fig. 1 Type I

plastic medium into the choledochus and made casts of the bile ducts, and thus I was able to roughly classify the varieties of the bile ducts into the following three types.

TYPE I: No communication is found between the hepatic ducts of the respective lobes except for the choledochus acting as an intermediate. (Fig. 1)

TYPE II: Immediate communication is found between the bile duct of the middle or the quadrate lobe and the bile duct of the left lobe. (Fig. 2)

TYPE III: Direct communication is recognized between the bile duct of the middle or the left lobe and the bile duct of the right lobe. (Fig. 3)

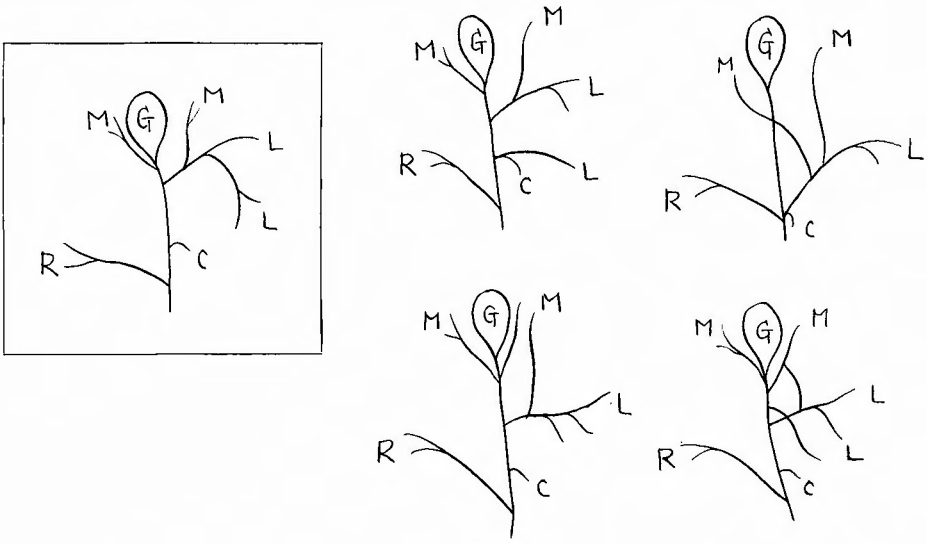


Fig. 2 Type Ⅱ

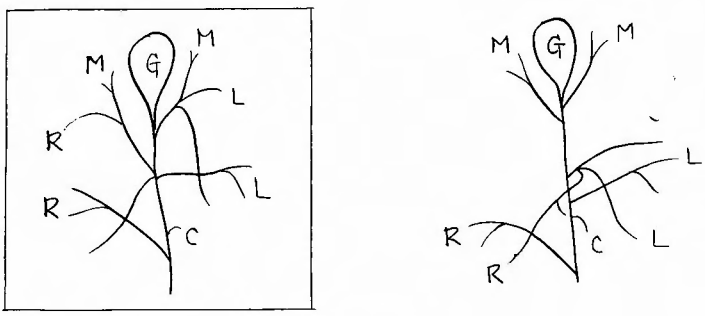


Fig. 3 Type Ⅲ

In any types, the bile duct of the caudate lobe independently enters the choledochus. The ratios of these types in 22 cases of experimental dogs are 6 cases for TYPE I or 27 per cent, 14 for TYPE II or 64 per cent, and 2 for TYPE III or 9 per cent. (Table 1) It is natural to find a MIXED TYPE, though very rare.

By the study of pouring Indian ink into the choedochus, no orifice of the choledochus into the duodenum was found except that of VATER'S papilla.

2. CHOLEDOCHUS LIGATED AND DIVIDED DOGS

Table 1

	Number of cases	%
Type Ⅰ	6	27
Type Ⅱ	14	64
Type Ⅲ	2	9
Total	22	100

(1) Method of Producing Choledochus Ligated and Divided Dogs.

All experimental dogs were fasted on the day of operation and less than 0.05 g of Isomital soda was administered intravenouly per kg body weight.

The choledochus in ligated dogs, according to the report made by HIRABAYASHI was found to re-communicate several weeks after ligation. In my experiment of ligated dogs, though I had ligated the choledochus at two places, re-communication was found as early as about 10 days after ligation. Therefore, I divided the choledochus under double ligature about 2 cm distant from the duodenal orifice.

(2) Changes in the Value of Total Serum Bilirubin in Choledochus Divided Dogs.

Bilirubin in serum was determined by the Evelyn-Malloy method using a photoelectric colorimeter. In choledochus ligated and divided dogs the value of total serum bilirubin reached its highest from 1 week to 10 days after the operation. (Fig. 4)

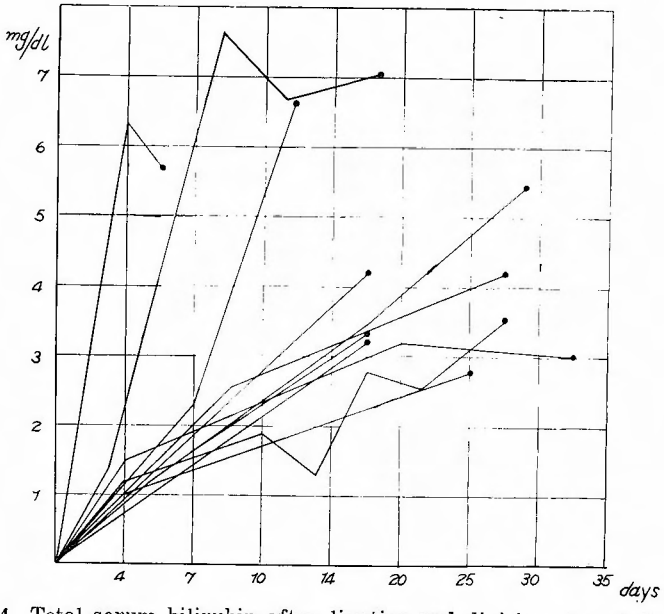


Fig. 4 Total serum bilirubin after ligation and division of choledochus.

In some experimental dogs the highest value was over 9 mg/dl whereas in others it was approximately 3 mg/dl. In all cases the value of total serum bilirubin showed no prominent changes after reaching its highest value.

(3) Symptoms and Life Expectancy of Dogs with Jaundice.

Choledochus ligated and divided dogs several days after the operation began to excrete dark-brown urine with the conjunctive becoming yellow and the mucous

membrane in the mouth becoming yellowish.

When total serum bilirubin ranged from 3 to 5 mg/dl, these dogs had absolutely no appetite and upon reaching 7 mg/dl, they refused to drink water. Some that did threw it up later.

Out of 11 cases, one was found to accumulate ascites approximately 3 weeks later (ascites 3000 cc.).

Thus, normally after 3 to 5 weeks and regardless of the value of total serum bilirubin, the dogs died. Generally speaking, it was found that when the value of total serum bilirubin ascended at a rapid rate, death occured in an early stage.

The average length of survival of the 11 cases was 22.6 days. According to the experiment carried out by Ito et al., they reported a life expectancy extended from 30 to 40 days.

(4) Histological Findings.

There has been, hitherto, various reports as regards histological findings of choledochus ligated and divided dogs, and I carried out histlogical examinations to make a comparison with these findings after hepato-entarostomy.

Hepatic cells became atrophied, the spaces between the hepatic cells widened; and findings of serous inflammation were present. Hepatic cells cords became distorted, and bile thrombus of the central zone was found. The expansion of bile ducts was noticed in Glisson's sheath. Degeneration was found in cells in the cenral zone. (Fig. 5).

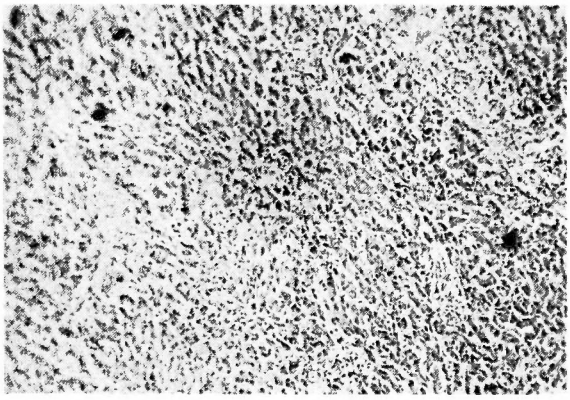


Fig. 5 27 days after ligation and division of the choledochus.

3. HEPATO-ENTEROSTOMY.

As the liver of a dog, in comparison to that of a human being, is much thinner and much softer, it would be difficult or impossible to suture it if no preparation is made to the liver which is to be anastomosed prior to hepato-enterostomy. The question as to how to simplify anastomosis of the dog's liver with the intestine, or, in other words, how to tranform a portion of hepatic tissue (which is to be anastomosed) into the hard elastic substance is the key in producing hepatoenterostomized dogs.

In choledochus ligated and divided dogs, even when death is about to occur due to billary cirrhosis, the liver does not become hardened. Whatever the case, if hepato-enterostmy is not accomplished during a period when the dog is comparatively vigorous, it will die, being wakened by operative injuries.

To have a simple and easy method of hepato-enterostomy, I performed the following experiments.

(a) A Method by Mechanical Stimulation.

5 per cent tincture of iodine and solution of penicillin were applied to the surface of the liver and though the greater omentum and the intestine adhered to the liver and the liver itself became somewhat hardened, it was still impossible to perform an anastomosis between the cut surface of the liver and the intestine.

(b) A Method by Using Plastic Medium.

I devised a method to harden the hepatic parenchym by aseptic inflammation caused by heat during polymerization of plastic medium which was injected directly under the capsule of the liver. Thereafter I succeeded in performing hepato-enterostomy with ease.

The plastic medium used consisted of monomer and benzol peroxide. The latter was the catalizer and when added to the former at an approximate ratio of 1 to 2, the medium became hard and heated after maintaining its fluidity for several minutes.

(1) Preparations for Hepato-enterostomy.

Adult dogs approximately 10 kg in weight were used for hepato-enterostomy before which they were given the following preperations. When the choledochus was ligated and divided, the plastic medium was injected directly under the hepatic capsule (at a depth of 2 or 3 mm) and 2 or 3 cm apart from the edge and surrounding the peripheral protruded potion of the bile. (Fig. 6)

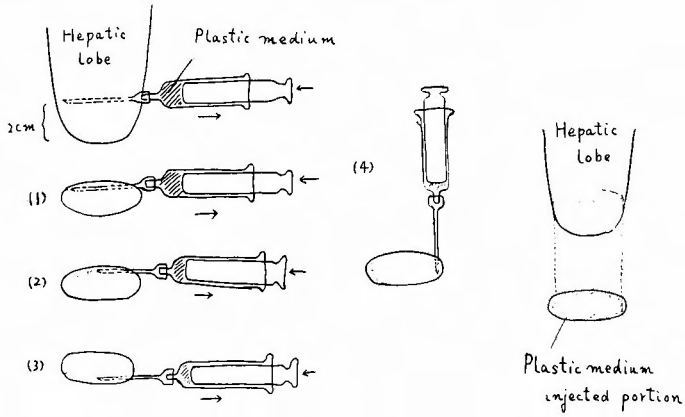


Fig. 6

The injected medium under the capsule of the liver commenced to disperse in several minutes and producing a heat over 60 degrees C., it became indurated and plapable from the surface of the liver.

The value of the total serum bilirubin of the dogs 1 or 2 weeks after receiving these preparation reached its highest and it was thus maintained. Experimental dogs of this period were used for performing hepato-enterostomy.

When jaundice was maintained over such a period, the dogs become so emaciated that they were not able to tolerate anesthesia bofore the operation, or even if the hepato-enterostomy was successful, they became extremely weak postoperatively that they died before any sufficent examination could be made.

(2) Method of Hepato-enterostomy.

Approximately half of the amount of anesthetic used in the preliminary operation was administered. The upper median incision was done along the wound made in the prior operation.

Hepato-enterostomy was accomplished according to Roux's Y shaped anastmosis. In other words, the jejunum was divided at a place approximately 15 cm from the Treiz's ligament on the side of the anus and an end-to-side anastomosis was made between the cut end of the oral side of the jejunum and the jejunal loop on the anal side and the latter was used for hepatoentoromy. The distance between the two anastmosises should be approximately 40 cm.

The peripheral part of the hepatic lobe about 0.5 cm apart from the place where the plastic medium was first injected during the preliminary operation, was removed. At this instance, a flow of blood and bile from the cut surface of the liver was noticed. Arterial bleeding from the cut end of the liver was conrolled by small tipped forceps and was ligated. Cautery or Thrombin powder might be locally used to check the parenchymatous bleeding or if let alone, the bleeding would stop by natural coagulation at the cut end.

The area of the cut end was usually 1×2 cm. There was no need to acquire a larger area than this because the larger the area the more apt it was to cause insufficiency of the anastmosis. The size of an opening of the anastmosis when completed was usually less than 0.7×1.5 cm.

In using the middle lobe, opening of the anastmosis, in most cases, was far narrower due to its shape. As the cut end of the liver and the opening of the anastmosis played an important role in the results of the experiment, they shall be discussed later.

The anastmosing technique is to anastmose the cut end of the liver to the

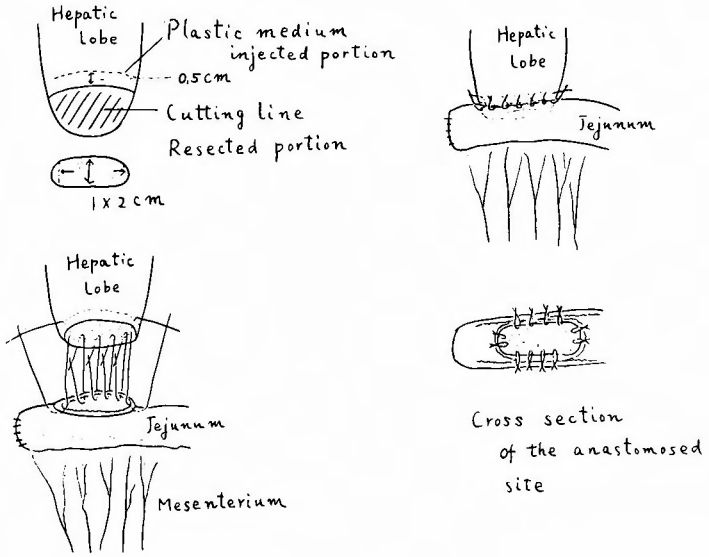


Fig. 7

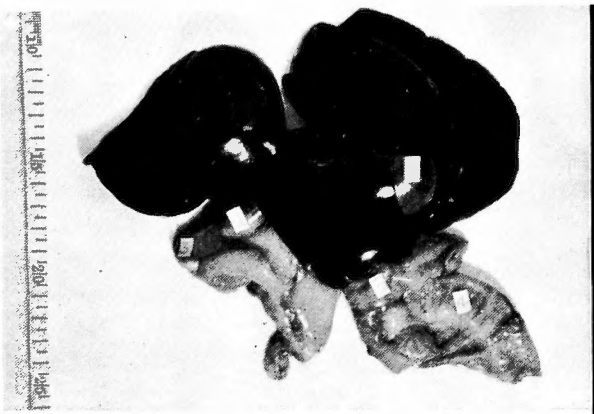


Fig. 8
(1) Choledochus (2) Gallbladder
(3) Duodenum (4) Jejunum
(5) Hepato-enterostomy

Fig. 9 Intraluminal view of hepato-enterostomy

wall of the intestine or directly to anastomose the former to the stump of the intestine. (Figs. 7, 8 and 9)

Interrupted sutures were made between the posterior hepatic margin and the entire layer of the posterior wall of the jejunum. At this time, it was necessary for the suture thread, on the side of the liver, to go over or, in other words, to bridge above the the zone where the plastic medium was injected. Similarily, interrupted sutures of the entire layer were made between the anterior hepatic margin and the anterior jejunal wall, and the anastmosed part was then coverd

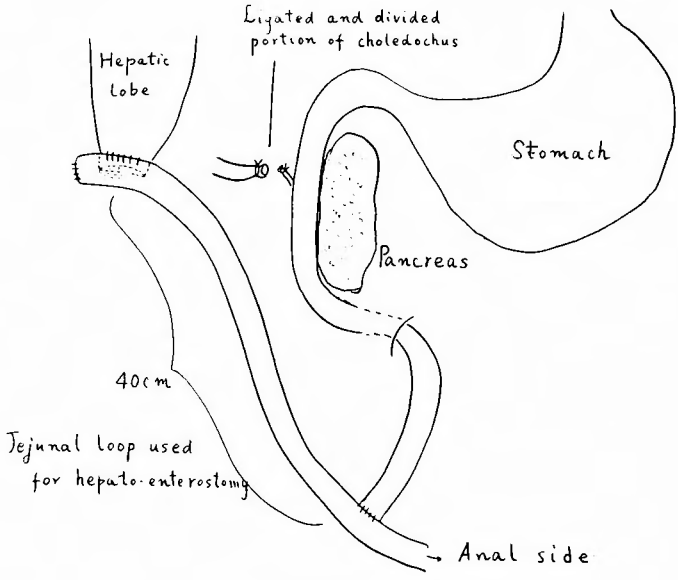


Fig. 10

by the greater omentum. (Figs. 10, 11 and 12)

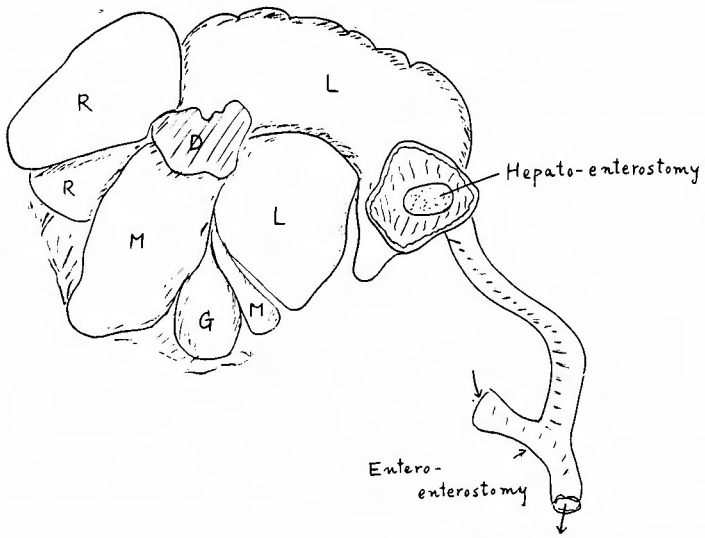


Fig. 11

According to this method, I succeeded in hepato-enterostomy in dogs and was able to observe the postopeative courses in 14 cases. (Table 2)

The left hepatic lobe was used in 6 cases, the middle lobe in 4 cases, and the right lobe in 4 cases.

(3) Changes of Total Serum Bilirubin after Hepato-enterostomy.

Prior to hepato-enterostomy, the total serum bilirubin was as shown in Fig. 13. It was generally known that total serum bilirubin hardly dropped in value 3 to 4 days after hepato-enterostomy or even one week after hepato-enterostomy, but on the contrary, it was sometimes proven that it slightly rose over the value before hepato-enterostomy.

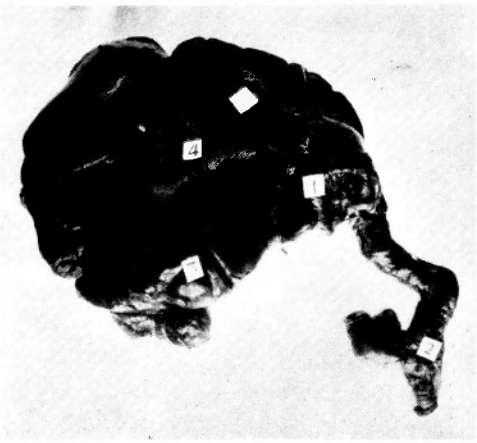


Fig. 12
(1) Hepato-enterostomy
(2) Jejuno-jejunostomy
(3) Gallbladder
(4) Diaphragm
(5) Left lobe

These phenomena could be considered as the bile duct was also ligated together with the blood vessel in checking the bleeding from the cut surface of the liver at hepato-enterostomy, or as the adherence of coagulated blood substances to the cut surface obstructed the leakage of bile through the anastmosed surface until it was shed. In such cases in which a rise of total bilirubin was seen, it could be considered that jaundice had not yet reached its maximum value, but had been increasing.

Table 2 Hepato-enterostomy

Dog No.	Weight (kg)	No. of days before hepato-enterostomy	Length of survival (day)	Lobe used for anastomosis	Effect on total bilirubin in serum	Presence of liver abscess	Cause of death
6	12.6	10	20	R	##	−	Emaciated (Sacrificed)
10	9.8	10	12	R	##	−	Emaciated
23	10.5	15	24	R	##	−	Distemper
40	8.5	11	17	R	+	−	〃
4	12.	8	11	M	±	−	Jaundice
11	9.6	17	20	M	+	Anastomosed region (+)	(Perforation peritonitis Duodenal-ulcer)
18	9.5	10	13	M	+	−	Jaundice
30	10.8	12	12	M	##	−	Distemper
9	7.3	10	14	L	##	−	〃
13	7.2	17	32	L	+	−	Emaciated
16	7.5	15	57	L	##	Anastomosed region (+)	〃
26	13.4	10	114	L	##	The greater part of the left lobe (+)	Abscess of liver Distemper (Sacrificed)
37	12.5	9	29	L	##	−	Distemper
57	8.	9	21	L	##	−	(Perforation-peritonitis (Duodenal ulcer)

After about one week, total serum bilirubin commenced apparently to drop, and in approximately 2 weeks it eventually reached the lowest value. This lowest value did not regain their normal value but sustained approximately 1 mg/dl thereafter in almost all cases. No jaundice symptom was shown by a dog that sustained this value of approximately 1 mg/dl, and the dog had a good appetite and became refreshed; in other words, no difference was noticed when compared with normal dogs. These cases are acknowledged as effective cases.

(a) In dogs in which the right lobe was used for hepato-enterostomy, 3 out of 4 cases were effective whereas, in one case, though the value had dropped at one time, it commenced to rise again, and the dog died. (Fig. 14)

An autopsy of this case revealed that the anastmosed part was covered with mucous membrane of the jejunum which obstructed the bile flow.

(b) In dogs in which the middle lobe was anastmosed to the jejunum, except for one case that was an effective one, the other 3 cases did not reveal any apparent drop in total serum bilirubin. (Fig. 15)

(c) In dogs in which the left lobe was anastomosed to the jejunum, all cases indicated a marked drop in total serum bilirubin. (Fig. 16)

In Fig. 17, the average values of total serum bilirubin in groups (a), (b) and (c) were shown. In general, 10 out of 14 cases revealed an apparent drop in total serum bilirubin. In analysing these values, the group using the left lobe was effective in 100 per cent, the group using the right lobe in 75 per cent, and the

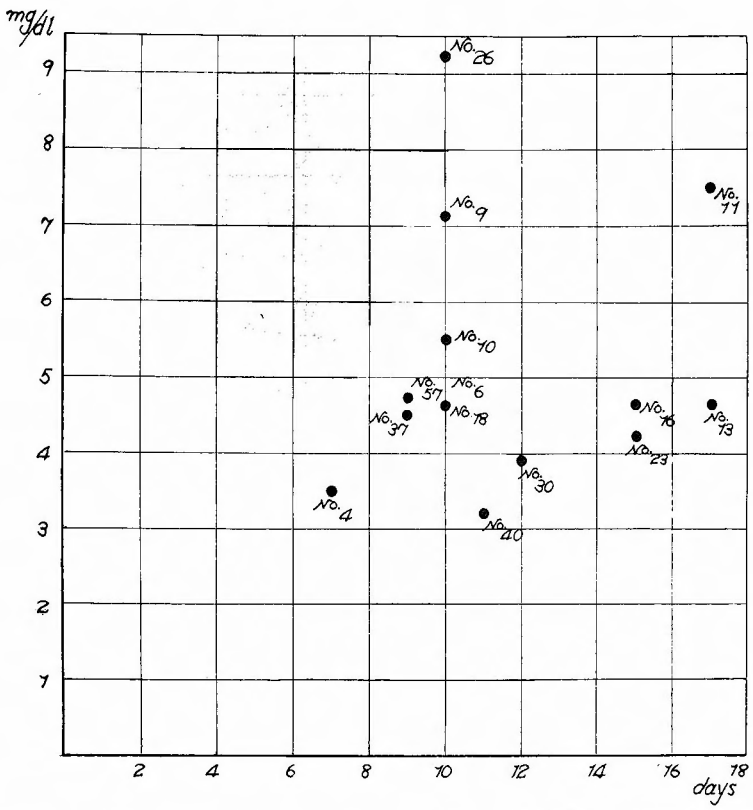


Fig. 13 Total serum bilirubin after ligation and division of choledochus. (directly before setting hepato-enterostomy)

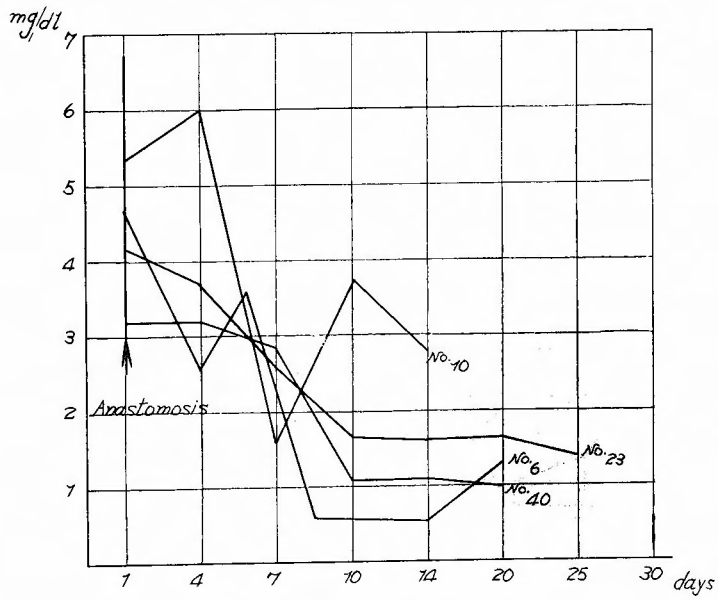


Fig. 14 Changes of total bilirubin in serum after hepato-enterostomy (right lobe)

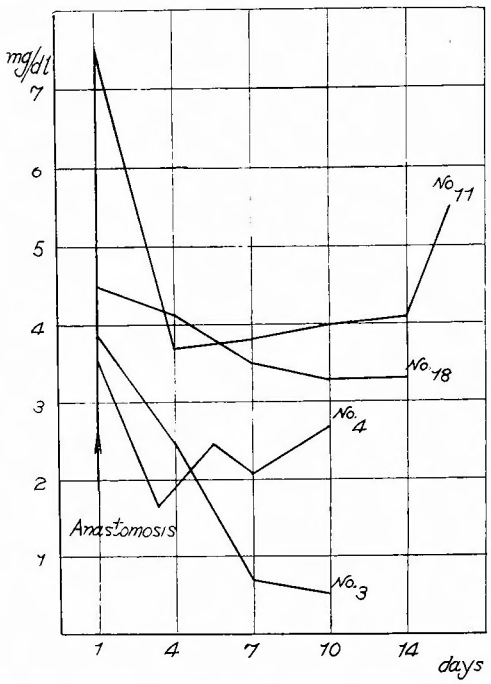


Fig. 15 Changes of the total bilirubin in serum after hepato-enterostomy (middle lobe)

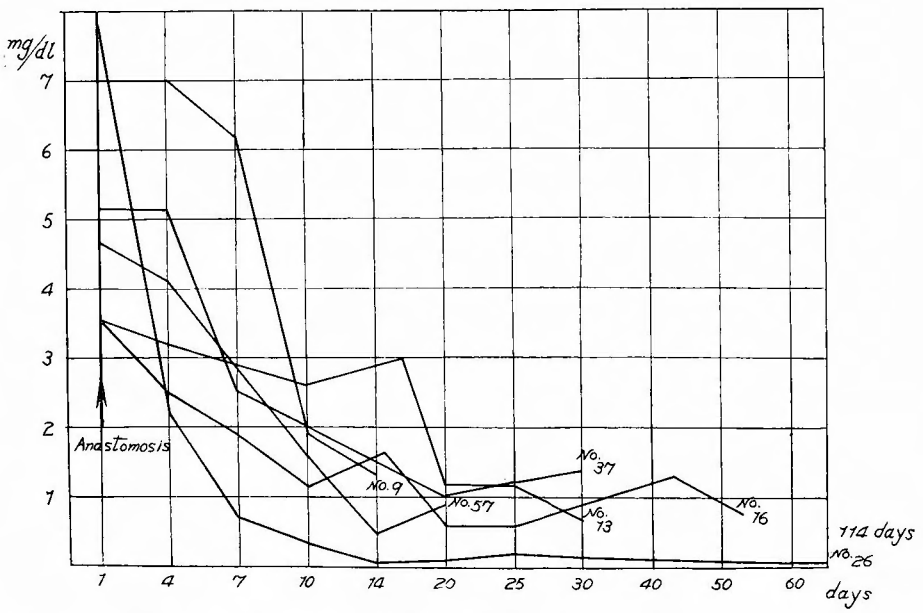


Fig. 16 Changes of the total bilirubin in serum after hepato-enterostomy. (left lobe)

group using the middle lobe in 25 per cent.

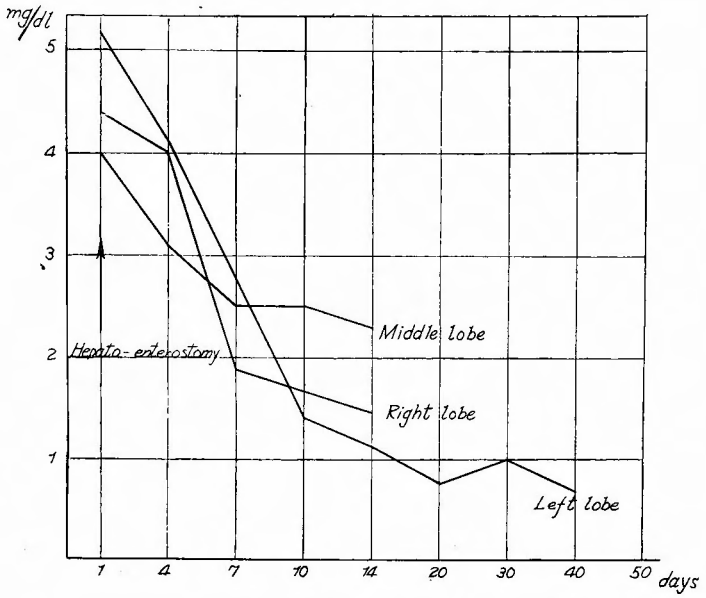


Fig. 17 Average value of total serum bilirubin after hepato-(left, right or middle lobe) enterostomy.

4. SEVERAL PROBLEMS RELATED TO HEPATO-ENTEROSTOMY.

(1) Insufficiency of Hepato-enterostomy.

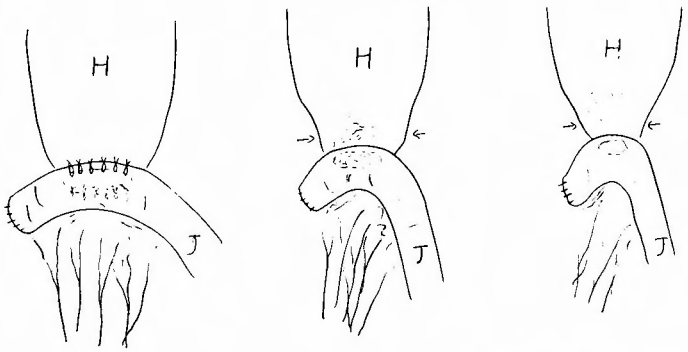
As mentioned previously, hepatic lobes of a dog do not have such a strong capsule as that of a human liver and when an injection of plastic medium is administered unskillfully, it will easily bring about insufficiency of hepato-enterostomy. During the elary stage of this experiment, there were many cases that died due to biliary peritonitis caused by insufficiency.

(2) Differences in the Size of Anastmosis.

The fact that majority of the experimental dogs revealed only a small drop in total serum bilirubin after a lapse of a definite period meant that the anastmosed area at the time of operation was made to be narrow or small-sized, or that it became narrow or small-sized due to some other sources.

The narrowing of the anastmosis were often found in cases when the middle lobe was used. Anatomically, the thickness of the middle lobe of the liver was thin, and at the time of anastomosis, the cut end was not round or not square-shaped, but was oval or rectangular in shape so that when anastmosis was done, it further became narrower and in extreme cases the area of the section became less than 0.5×1 cm.

Moreover, with the lapse of time after anastomosing, the hepatic parenchym near the anastomosed site was destroyed and shed, and became cicatricial, and it took the form as shown in Fig. 18, which caused the anastmosed section to be narrow. The mechanism of decreasing jaundice by our hepato-enterostomy was not



H. Hepatic lobe
J. Jejunum

Fig. 18 The hepatic parenchym near the anastomosed site was destroyed and shed, and became cicatrical with the lapse of time after anastomosing.

with an object to perform an anastomosis on the main bile ducts within the liver as in LONGMIRE's method, but was a method by which we could expect excretion of the bile from minute bile ducts within the liver of which internal pressure became high because of the obstruction of the bile flow. Therefore, the larger the area of the anastomosed section, the greater number of minute bile ducts it would contain.

However, there was no necessity to enlarge the anastomosed section more than necessary because this would necessitate the use of many suture threads so that much risk arose which was apt to bring about insufficiency.

An ideal size of the anastomosed section was not in its length but in the width of the section itself. From my experimence in 14 cases, the area of 1×1.5 cm was enough to obtain unobstructed bile flow. Incidentally, the avarage liver weight of the 14 cases was 316 g.

(3) Problems of Bleeding.

We found in the clinical report of Laméris and others many cases of large bleeding into the intestine, but according to Dr. Honjo of our laboratory, none was found at all. In my experimental dogs also, though there were several cases where the threads with which the the blood vessel had been ligated were found to have shed at autopsy, none was found to have died of bleeding from the cut end of the liver. The use of cautery for temporary stoppage for bleeding in order to avert ligation of the bile duct running parallel to the blood vessel was thought better not to be practiced because of the fact that there was a risk of rebleeding due to early shedding of the coagulated tissue.

(4) Postoperative Course of Experimental Dogs after Hepato-enterostomy.

On the first day after the operation, dogs were deprived of food; on the second day they were given liquid food (water or milk), and thereafter ricegruel and eventually ordinary food. In cases in which the value of bilirubin did not sufficiently decrease, their appetite did not improve but in cases where the effect of hepato-enterostomy was apparent, those which had had no appetite and had symptoms of vomitting due to severe jaundice were completely devoid of such symptoms

and regained a healthy appetite.

Feces which were of a light yellowish color or of witish gray prior to the operation turned to a dark brownish color for a certain period after it, and by 2 weeks after the operation the color became quite normal.

The color of urine turned from a dark brownish color to that of light yellow, and regained its normal color from 3 to 4 weeks after the opertion.

Many cases indicated no resolution in the yellow tint of the skin and mucous membrane, but in effective cases of long survivals the yellow tint disappeared about five weeks after the operation.

(5) Results of Liver Function Tests.

(a) Urine Urobilinogen Test.

The urine urobilinogen test according to EHRLICH's aldehyd reaction did not turn out to be the object of the test due to the fact that it maintained a negative finding in all cases before and after the operation. A negative result prior to the operation was due to no discharge of bile within the intestine whilst a negative after the operation suggested that bile was being well discharged into the intestine and, at the same time, the liver function was not so apparently disturbed.

(b) Cephaline Cholesterol Flocculation Test (C. C. F. T.)

Of the experimental dogs, there were some that revealed positive before operation (nomal dogs), and there were those that also showed positive after ligating and dividing the choledochus; there were those that revealed absolutely no changes in the extent of their positiveness after hepato-enterostomy, while others of the experimental dogs showed somewhat of a fall in the extent of their positiveness. But, generally speaking, though the overall physical condition of experimental dogs became good and their body weights increased, this reaction did not necessarily bring about good results. Namely, in other words, even in an experimental dog (Nn. 26) which survived a long time and showed no different points from normal dogs, C. C. F. T. revealed a strong positive finding. Thus, within the scope of my experimental method in dogs, I could not obtain any definite results as far as the liver function tests were concerned.

(c) Blood Serum Protein.

The total protein in serum of experimental dogs ranged from 4.8 g/dl to 7.6 g/dl. In those cases in which jaundice was noticed to decrease and the general condition became better after the operation, a certain increase of blood serum protein was observed.

(6) Fate of Dogs after Hepato-enterostomy.

Of the 14 cases, 2 cases died of perforative peritonitis resulting from an ulcer of the duodenum, and 5 other cases died due to causes unrelated directly to the experiment. Increase in jaundice caused the death of 2 other cases, whereas in the remaining 5 cases, physical conditions were greatly impaired by the formation of abscesses in the liver and other causes, and they were eventually sacrificed. The average length of survival was approximately 40 days. In comparing this figure with that of choledochus ligated and divided dogs, namely with the average of

Table 3

The Length of survival of the choledochus ligated and divided dogs.		The length of survival of hepato-enterostomized dogs.	
No. 1	34 (day)	No. 6	30 (day)
2	18	10	22
3	17	23	39
4	13	40	28
5	28	4	19
6	8	11	37
7	32	18	23
8	35	30	24
9	29	9	24
10	17	13	49
11	18	16	72
		26	124
		37	38
		57	30
Average length of survival	22.6	Average length of survival	40

22.6 days, we can note that the former had an average prolongation of 17.4 days, but when we consider the fact that if distemper or other accidents had not occurred in experimental dogs, it is believed that the average length of survival would have been prolonged much more. (Table 3)

(7) Hepato-enterostomy and Ascending Infection.

During approximately 5 days after hepato-enterortomy, 1,500,000 unit penicillin and 3 g. of streptomycin were used and even if the 40 cm jejunal loop was established between the hepato-enterostomy and the entero-enterostomy according to the Roux's method, infection of the liver due to bacillus within the intestine could not be prevented because the hepatic parenchym and the intestine directly communicated when anastomosis was accomplished. In the case of experimental dog No. II, a small abscess was discovered near the site of the anastomosis macroscopically on the 20th postoperative day, but ordinarily, it was usual that abscess could not be found macroscopically within the first month.

In the case of a long survival of 114 days after hepato-enterostomy, many small abscesses were found in the entire left liver which was used for anastomosis, but even in this case, it was affirmed roentgenologically with injection of a contrast medium into the choledochus at the time of autopsy, that sufficient amount of bile could still flow out from the anastomosed section.

(8) Roentgenogram of Intrahepatic Bile Ducts after Hepato-enterostomy.

A dog which underwent hepato-enterostomy 10 days after ligation and division of the choledochus was sacrificed and the liver was extracted 14 days after hepato-enterostomy. By injecting a contrast medium into the choledochus, a roentgenogram of the intrahepatic bile ducts was taken as shown in Fig. 19. The choledochus apparently was still dilated, and the gallbladder was also enlarged though the

dilatation of the bile ducts did not reach the anastomosed portion, and findings were observed in which the contrast medium reached into the intestine by way of the minute bile ducts in the anastomosed site. In this case the total serum bilirubin had apparently dropped from 7 to 10 days after hepato-enterostomy.

Fig. 19 The entrance of contrast medium into the intestinal canal via hepato-enterostomy is shown roentgenologically. (↓)

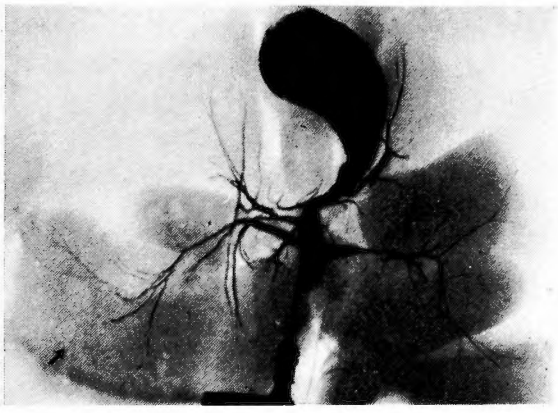


Fig. 20 Numerous small transparent patches (abscesses) are shown. (↓)

As shown in Fig. 20 which is the roentgenogram of experimental dog No. 26, numerous small transparent patches were found in the anastomosed liver lobe when compared with other lobes. These findings showed the abscesses of the liver. Moreover, it was found that the contrast medium flowed into the jejunum over the anastmosis. I believed that the contrast medium was able to reach the intestine through the abscesses.

As the thickness of the bile duct had returned to that of a normal bile duct, it was confirmed that the stagnation of bile within the liver was reduced and the anastomosis was functionally effective. Moreover, as a result of the abscess formation, the size of the hepato-enterostmized part was gradually reduced as shown in Fig. 14, and the anastomosed area of this case was approximately 0.5 cm^2.

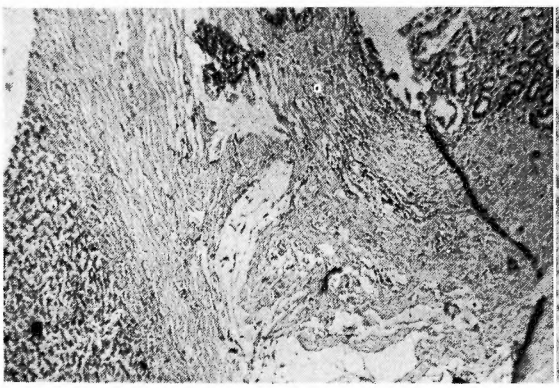


Fig. 21

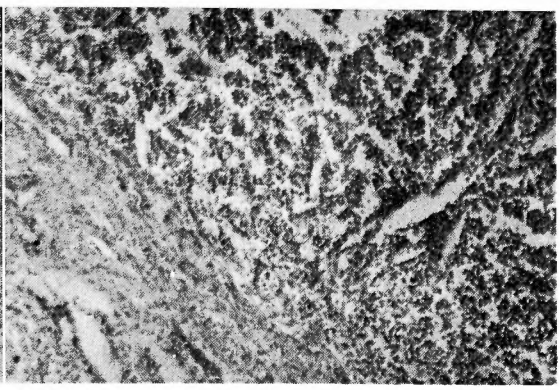


Fig. 22

(9) Histological Findings.

Histopathological study was done on the liver of experimental dog No. 26. In the vicinity of the anastmosed region of the left lobe atrophy of the hepatic cells and serous inflammation were indicated. Though infiltration of the cells was found in the sinusoid, there was no noticeable inflammatory reaction. (Fig. 21) The other part of the left lobe possessed signs of inflammation and atrophy of the hepatic cells, and abscesses were noticed in several parts. (Fig. 22) The middle lobes were free from inflammatory findings and, though minute particles of the contrast medium (Barium) were found, there was no evidence of bile thrombus, that is, the evidence of jaundice. (Fig. 23)

Another example was taken from the dog No. 16. In this case inflammation was found in the surroundings of bile ducts, and atrophy of the hepatic cells also were noticed. In several parts, abscesses due to ascending infection were proven, but findings of jaundice were not recognized. The bile ducts near the hepato-enterostomized part were distinctly enlarged, the connective tissues around the bile duct were proliferated and thickened, and Indian ink was found which filled the enlarged bile ducts. (Fig. 24) As the stagnation of bile within the liver was

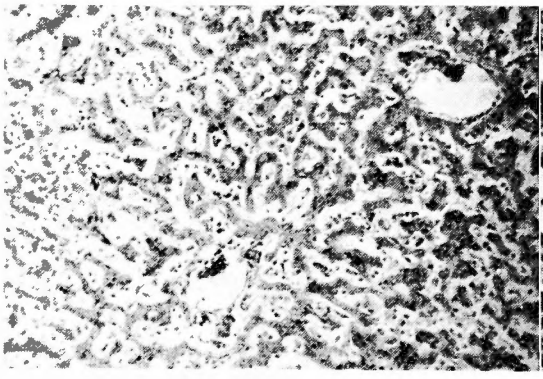


Fig. 23

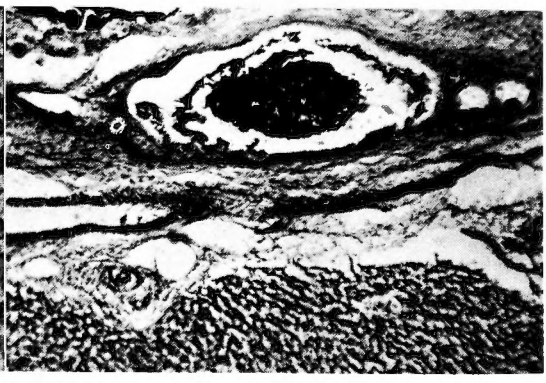


Fig. 24

not noticed and as the proliferation and thickening of the connective tissues around the bile ducts and the dilation of the bile ducts were recognized, it was believed that the excretion of bile through the anastomosed part from the dilated bile duct was satisfactory.

(10) Comparison of Total Serum Bilirubin after Hepato-enterostomy with that after Cholecystojejunostomy.

In the case of cholecystojejunostomy, an apparent drop in total bilirubin was already found on the fourth day after the operation. In the first week, it approached its normal value and by the end of the second week, all cases returned to normal value. (Fig. 25) In this regard, when making a comparison with hepato-enterostomy, the drop in total serum bilirubin or, namely, the disappearance of jaundice was more apparent. In the case of hepato-enterostomy, total serum bilirubin did not drop to its normal value, because the bile within the liver had to be

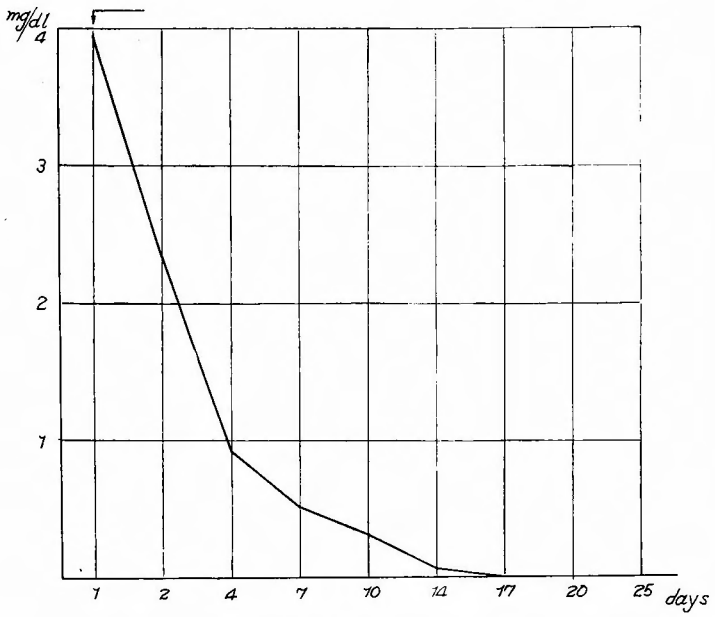


Fig. 25 Cholecystojejunostomy. Changes of total serum bilirubin of choledochus ligated and divided dogs after cholecystojejunostomy.

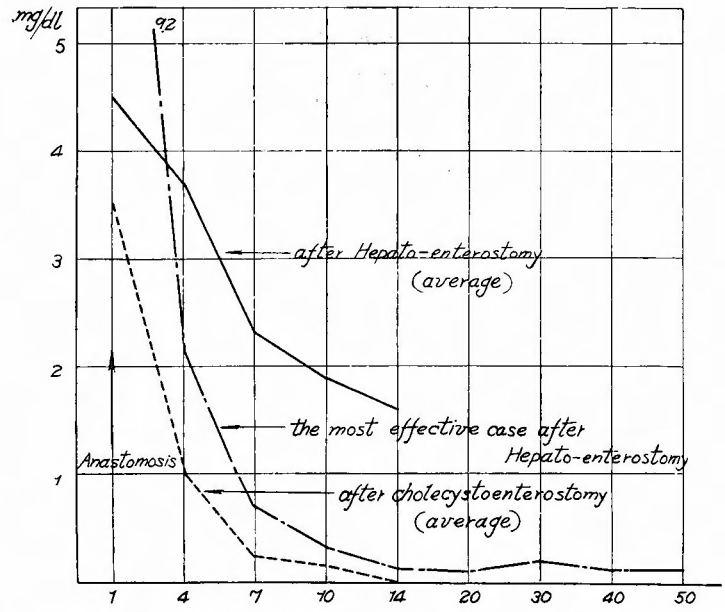


Fig. 26 Comparison of changes in the value of total serum bilirubin after hepato-enterostomy with those after cholecystoenterostomy.

congested to a certain degree in order that the anastomosed part display its function, and after the rise of internal pressure of intrahepatic bile ducts, the bile was forced to flow out from the anastomosed part of low pressure. It is believed, that when the pressure exceeded a certain degree, the bile commenced to flow back from the capillary bile duct and when the pressure dropped, the bile stopped its flow so

that total serum bilirubin never dropped below a certain level.

But in the one case of hepato-enterostomized dog which was a long survival case of 114 days after anastomosing the left lobe, satisfactory results were obtained almost comparable to that of cholecystojejunostomized dogs. (Fig. 26)

5. MINIMAL EFFECTIVE AMOUNT OF LIVER IN ORDER TO PREVENT JAUNDICE.

What amount of hepatic tissue performing bile excretion is required in order to avoid the occurrence of jaundice?

The following experiment was performed with an intention to find out this limitation, that it, minimal effective amount of the liver in order to prevent the animals from jaundice.

In this experiment, I excluded experimental dogs which had such bile duct types that would have hindered the object of my experiment.

(1) The values of total serum bilirubin evaluated after cholecystojejunostomy were as mentioned previously in Section II of Part 4. Namely, when bile which originated from all the hepatic lobes was excreted into the intestine from the gallbladder, the total bilirubin perfectly returned to its normal value 2 weeks after the operation.

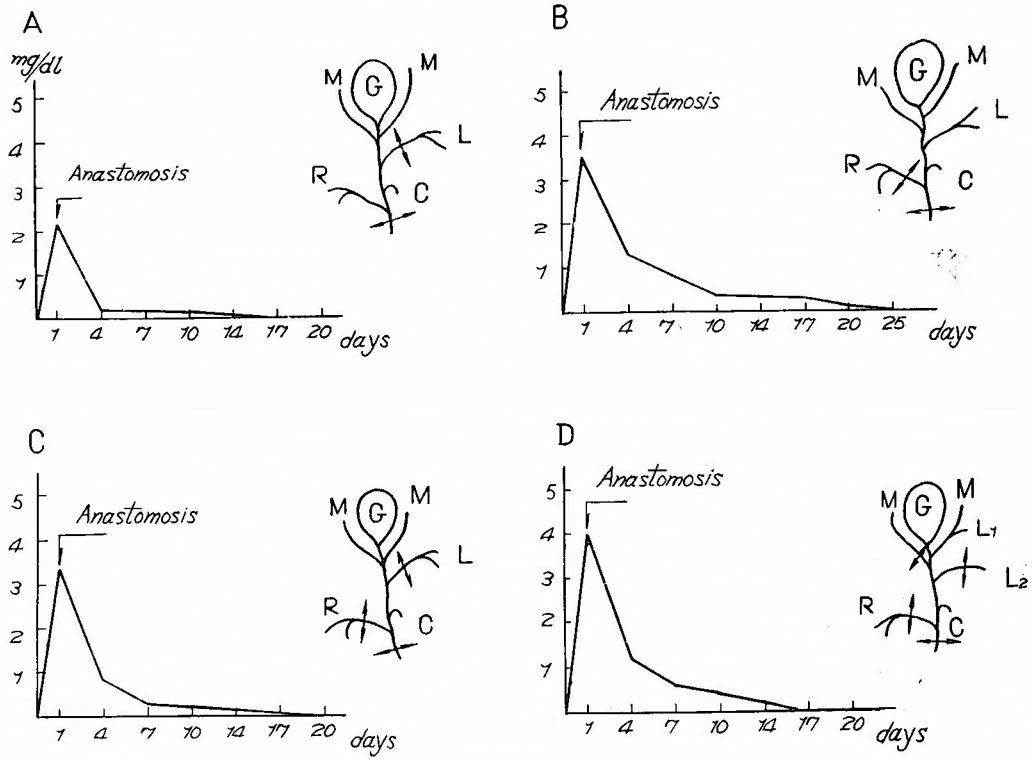


Fig. 27 Changes of the value of total serum bilirubin after cholecystojejunostomy (↔ ligated and divided portion of extrahepatic bile duct.)

(2) In an experimental dog, the choledochus and the bile duct of the left lobe were ligated and divided (in this case, bile duct TYPE II could not be used as the left bile duct was anastomosed with other ducts), and two weeks after the operation, cholecystojejunostomy was performed. The bile stream from the lobes of which bile ducts were not ligated and divided passed through the choledochus, the cystic duct, the gallbladder and entered the jejunum. (Fig. 27A)

In this case, it was thought that the bile were able to escape from the right and middle lobes which were about 2/5 or 1/3 of the entire liver in weight. Changes of the total serum bilirubin after this operation did not differ so much from the values in the case of the above (1) group.

(3) Changes of total serum bilirubin in a dog which had received cholecystojejunostomy about 2 weeks after ligation and division of the choledochus and of the bile duct of the right lobe were examined. The hepatic lobe of this dog which had bile outflow capability was 2/5 or 3/5 of the entire liver in weight. This experimental group did not differ greatly from those in the case of the above (1) group. (Fig. 27B)

(4) When performing cholecystojejunostomy after approximately 2 weeks in dogs in which the choledochus and the bile ducts of the right and left lobes were ligated and divided, the weight ratio of the lobe having possible outflow capability was 1/4 or 1/3. In this case, however, there was no noteworthy difference when compared with the case of (1) group. (Fig. 27C)

(5) In dogs in which the choledochus, the bile ducts of the two right lobes, the left minor lobe of the left lobe and the right minor lobe of the middle lobe were ligated and divided and to which cholecystojejunostomy was performed after two weeks, the weight ratio of the lobe in which bile was able to escape was only 1/5 or 1/6. The period in which total serum bilirubin retured to normal value was

Fig. 28 Barium injected from the gallbladder did not reach any other parts than the right minor lobe of the left lobe and the quadrate lobe.

only somewhat prolongated than the groups above mentioned. (Fig. 27D, Fig. 28)

Autopsy of these experimental dogs revealed that in all cases of hepatic lobes of which bile ducts were ligated and divided, they took on a jaundice color and became somewhat hardened, and the bile ducts were dilated. These findings were apparently recognized expecially in Group (5), and the bile which filled the dilated ducts revealed a more markedly light color compared with normal bile. In certain bile ducts, whitish mucous fluid was only found.

As a contrast to the above mentioned experimental groups, the choledochus was not ligated but only the right bile duct and the left lobe bile duct were ligated and divided in 3 cases. In these experimental dogs jaundice was not noticed, and total serum bilirubin of 0.2mg-0.5mg/dl within 2 weeks after the operation was proven, and then it disappeared. The experiment of this kind proved to be almost similar in results to the experiment already performed by Ito in Japan.

The focus of my experiment was not to search for the extent of jaundice in normal dogs by allowing a part of the normal liver to remain, but was to study the conditions of the experimental dogs in which the liver was more or less in a damaged state due to obstructive jaundice, and to find out to what extent such damaged hepatic lobes had a share in the excretion of bile in order to reduce jaundice. Due to the aforementioned experiment, I was able to attain my purpose. Namely, even in experimental dogs with obstructive jaundice and, with more or less damaged liver, if bile from the hepatic tissue of an approximate 1/6 of the entire liver in weight can be excreted into the intestine, jaundice will disappear.

6. COMMENT

As operative treatments for injury, constriction and obstruction of the choledochus and intrahepatic bile ducts, various methods have been conceived and performed from approximately 1900. Kehr, Maylard, Smoler and others anastomosed a bile duct in the hepatic lobe with the stomach or the intestine, expecting excretion of bile. Almost all of the cases died within 1 or 2 days due to insufficiency of anastomsis or to hemorrhage into the intestine from the cut surface of the liver (Kollaps). Bobbio in 1907 carried out experiments similar to the above method on cats and dogs but failed to succeed. In 1912, Capelle, Laméris, Kanich and others had made reports successively. Expecially Laméris reported a case by resecting a part ($2\frac{1}{2} \times 6$ cm) of the right lobe edge and by anastomosing a part of the jejunum to it, he was able to keep his subject alive for approximately 8 months, and he named this method "hepatocholangio-enterostomie." But such a case like this was exceptional and, moreover, no systematic data was reported. Thereafter, except for Auschuts (1913), Gottstein (1922), and Haberland (1921), hepato-cholangio-enterostomie was not only considered effective but also dangerous and complicated and it was not performed ever since.

A procedure of intrahepatic cholangio-jejunostomy with partial hepatectomy (for biliary obstruction) was reported in 1948 by Longmire and Sanford, followed by Lippmann. In this method they did not use the intrahepatic bile ducts near the

liver edge but performed a large resection on the left hepatic lobe, securing a large bile duct from its cut surface and then anastomosing the intestine to this duct. The procedure was complicated, and operative injury was comparatively great.

However, the procedure reported in 1952 by Honjo which he had named as "hepato-enterostomy" is simple with little operative injury but with wide applicability and little danger so that it is being followed by others.

Through my experiments hepato-enterostomy can be proven as a useful and effectual procedure for certain obstructive jaundice.

7. SUMMARY AND CONCLUSIONS

1) I had originally devised the procedure for hepato-enterostomy in experimental dogs.

2) The course of the intra-hepatic bile ducts was investigated, and I have classified them into three types.

3) Most cases of the failures in hepato-enterostomy (disturbance of the bile flow) were due to the narrowing of the anastomosed section. If the anastomosed section was maintained at 1.0×1.5 cm in dogs, the disappearance of jaundice would certainly be acquired.

4) Though ascending infection could not be, more or less, avoided in hepato-enterostomy, in survival cases of 4 months and over in which multiple minor abscesses in the liver were proven, the effectiveness of hepato-enterostomy was sustained.

5) In comparing hepato-enterostomy with cholecystojejunostomy, its effectiveness was somewhat inferior to the latter but there were some cases in which effectiveness was almost comparable.

6) It was made possible to prolong the average life span of 22.6 days of choledochus ligated and divided dogs to a further 17.4 days or more by hepato-enterostomy improving their general conditions at the same time.

7) There is a possibility to reduce jaundice by hepato-enterostomy if comparatively healthy hepatic tissue 1/6 of the entire weight of the liver still exists.

From the above results, I am convinced that hepato-enterostomy can be safely and easily performed and, moreover, widely applied for clinical cases.

In concluding my report, I wish to express my deepest gratitude and sincere thanks to prof. Dr. Chisato Araki, my honored director, and to Assist. Prof. Dr. Ichio Honjo for their continuous guidance and kind encouragement and supervision. Pertaining to histological findings, I am greatly indebted to Instructor Dr. Fumihiro Ichida of the First Division of Internal Medicine of Kyoto University Medical School for his kind guidance.

LITERATURE

1) Ehrhardt, O.: Hepato-Cholangio-Enterostomie bei Aplasie aller Grossen Gallenwege. Zentralbl. f. Chirurg. 1226. 1907.
2) H. J. Laméris: Hepato-Cholangio-Enterostomie; Zentralbl. f. Chirurg. **39**, 1665. 1912.
3) W. Kausch: Über Gallenweg-Darmverbindungen. Archiv f. Klinische Chirur. **XCVII** 575. 1912.
4) Auschütz, W.: Beitrage uber Gallengang-Darmverbindungen. Zentralbl, f. chirurg. **36**, 1407, 1913.
5) Auschütz, W.: Über Cholecystenterostomie und Hepato-Cholangio-enterostomie. Zentralbl, f.

chirurg. **48**, 1757. 1922.
6) H. F. O. Haberland: Studien an den Gallenwegen. Archiv, f. Klnische Chirurg. **CXXX**, 492, 1924.
7) Longmire, W. P. and M. C. Sanford: Intrahepatic Cholangio-Jejunostomy with Partial Hepatectomy for Biliary Obstruction: Surgery. **24**, 264. 1948.
8) Harwell Wilson a C. E. Gillespie: Partial Hepatectomy with Intrahepatic Cholangio-jejunostomy. Ann. Surgery. June; 756. 1949.
9) W. P. Longmire and M. C Sanford: Intrahepatic Cholangio-jejunostomy for Biliary Obstruction. Ann. Surgery. Sept; 455. 1949.
10) Sanders, R. L.: Hemihepatectomy with Hepaticojejunostomy for Irreparable Defects of the Bile Ducts. Arch. Surg. **58**, 752. 1949.
11) Harvey, N. Lippmann and Longmire, W. P.: Intrahepatic Cholangiojejunostomy for Biliary Construction. Surg. Gynec. & Obst. **98**, 363. 1954.
12) Oka, T.: Research of Mechanical Jaundice. Tokyo Iji Shinshi (in Japan). 2552. 1936.
13) Ito, T.: Results of Bile Duct Ligation, Partial and Complete. Chiba Igakkai (in Japan). **13**, Book I; 742. 1935.
14) Hieda, K.: Experimental Research of Jaundice (Vicissitude of Bilirubin in Serum Value after Choledochus Ligature in Rabbits and Dogs.) Nisshin Igaku (in Japan). **15**, 1113. 1926.
15) Hirabayashi, T.: Choledochus Ligation Tests of Guinea Pigs, Rabbits and Dogs. Nisshin Igaku (in Japan). **28**, Book II; 1409. 1939.
16) Toyoshima, H.: Surgical and Anatomical Research of Hepatic Construction by Plastic Medium Injection. Arch. Jap. Chir. (in Japan). **23**, 476. Sept. 1954.
17) Honjo, I.: Hepato-entersotomy Rinsho Geka (in Japan). Aug. 129. 1953.
18) Honjo, I. and Araki, C.: Hepato-Enterostomy. J. International Coll. Surg. **20**, 775. 1953.
19) Ohno, S.: No Liver Obstacle, No Jaundice. Nagai Shoten (in Japan) 1954.
20) Kusui, K.. Jaundice. Igaku Shoin (in Japan) 1952.

和 文 抄 録

肝腸吻合の実験的研究

京都大学外科第1講座 (主任 荒木千里教授指導)

柴 垣 進

肝外胆道の機械的狭窄，或いは，閉塞に対して外科医は種々の胆道再建術を行つて来た．しかし，先天性の胆道欠損症や，胆道の狭窄，閉塞の原因が肝門部にある場合，もはや，肝外胆道は利用価値が無くなる．これらの症例に対しても，肝内胆道を対象とする外科手段が古くから，一部の外科医により考慮されていた．

すなわち，Ehrhardt, Laméris, Kausch, Auschütz 等で，時に，Laméris の Hepato-Cholangio-enterostomie (1912) が代表的である．

しかし，これらの手段も当時の医学としては相当に危険な，しかも効果の期待し難い方法とみなされて一般化しなかつた．

近年，Longmier, Sanford 等が intrahepatic cholangio-jejunostomy with partial hepatectomy なる術式を発表し，教室の本庄博士が Hepato-enterostomy の術式を本邦最初に発表するに至つて，再び，肝内胆道応用の問題が注目された．

私は本庄博士の臨床例に平行して，実験犬で黄疸を作成し，次で肝腸吻合を試み，之に成功して以下の種々の実験を行い次の如き結果を得た．

1) 胆管の解剖

合成樹脂を総胆管より注入して，その鋳型を作成し又は，造影剤の注入によるレ線像より，22例の実験犬の胆管走行 (主として肝内胆管) を3型に分類し得た．この内わけは，第2型が普通型で14例，64%，第1型は6例，27%，第3型は最も稀で2例，9%であつた．

2) 総胆管結紮切断犬作成，その血中ビリルビン

（以下「ビ」と略す）値の変動，生存日数

総胆管結紮切断犬は術後1週間より10日過ぎる頃には，血中「ビ」値は最高となる．「ビ」値の高低，最高値に至る時期は犬の個体に相当の差がある．11例の平均生存日数は22.6日であつた．

3) 肝腸吻合

犬の肝は人体の肝に比較すると相当軟かく，結合織の薄弱の為に肝腸吻合は困難であるので，合成樹脂液を肝被膜下に注入して，肝組織を強靱にして吻合に便ならしめ肝腸吻合に成功した．

4) 肝腸吻合の吻合口の大小に関する問題

14例の肝腸吻合犬の吻合口面積は1cm×1.5cm で充分であつた．吻合口の大きさは吻合口の長さでなく，巾のあるものが良く，この目的の為には左葉肝が応用し易く，中葉は厚みも薄く成績も不良であつた．なお14例の肝重量の平均値は316gである．

5) 出血に関する問題

Laméris 等の臨床例には相当数に，腸管内への大量出血による死亡の記載がみられるが，教室の本庄博士の例では1例も認められない．実験犬に於ても肝切面（吻合口）よりの出血は放置していると自然に凝固止血される事が多い．

6) 肝腸吻合後の臨床症状

術前高度の黄疸で食思不振，嘔吐を来した例も，術後は一般症状も好転し，糞便は術前，淡黄色又は，灰白色より術後1週間は黒褐色となり，2週間頃には正常便となる．尿色も4週間頃には正常尿色に，皮膚及び粘膜の黄染は遂に消褪しない例もあつたが，長期生存例では5週間後には完全に消失した．

7) 肝腸吻合犬の運命

肝腸吻合犬14例の内2例は十二指腸潰瘍による穿孔性腹膜炎で，5例は実験に直接関係のない疾患により死亡した．2例は黄疸症状悪化の為に死亡した．他の5例は肝膿瘍その他で全身衰弱を来したので薬殺した．以上の平均生存日数は約40日余である．

今かりに，この生存日数を総胆管結紮切断犬が死亡に至るまでの生存日数22.6日に比較すると，平均17.4日余生命の延長をみた．

8) 肝腸吻合と上行感染の問題

肝腸吻合術後，ペニシリン150万単位，ストマイ3gを使用したが，たとえ，Roux 氏法により，40cm空腸吻合脚を設置しても，吻合に際して肝実質と腸管とが直接連結するので，必然的に吻合直後から腸内細菌による感染はさけられない．吻合術後約4ヵ月長期生存例では吻合左肝葉全般に小膿瘍多数を認めたが，剖検時，なお，吻合口より充分量の胆汁流出が可能なることを造影剤注入レ線像により確認し得た．

組織像からも，上行感染により肝変化が認められるが黄疸所見なく，肝腸吻合口附近の胆管は著明に拡大し周囲の結締織は増殖肥厚し拡大した胆管には，総胆管切断端の肝側より注入した墨汁が認められる．

9) 肝腸吻合犬と胆嚢空腸吻合犬の術後血中「ビ」値の比較

胆嚢空腸吻合では，術後4日目で著明な下降をみる．更に，1週間目には殆んど正常値に近づき，術後2週間で全例共血中「ビ」値は正常となる．この点，肝腸吻合では，たとえ，術後2週間を経ても正常値まで下降しない事実は，肝内に胆汁がある程度鬱滞して胆管内圧が高くなつた後に，圧の低い吻合部を通り流出する．すなわち，一定の圧を越えた時，初めて毛細胆管より逆流し，圧の下降と共に流出も停止する為に常に一定度以下には血中「ビ」値が下降しないものと思われる．しかし，肝腸吻合犬に於ても長期生存例では胆嚢空腸吻合の場合に匹敵し得る良果を得ている．

10) 肝の黄疸阻止有効量の限界

黄疸発生肝に如何程，胆汁排泄機能のある肝組織が残存すれば黄疸が消褪するかを知る為に，先に述べた肝内胆管の解剖により実験目的を妨げる様な胆管型の実験犬は除外して次の実験を行つた．

総胆管結紮切断と同時に，各葉よりの胆管を種々の組合せで結紮切断し（総胆管と交流のある肝領域を2/5あるいは，1/3を残して），黄疸発生後，胆嚢空腸吻合を行つても約2週間以内に黄疸は完全に消失する．最後に右葉2葉，左葉左，中葉右の胆管を結紮切断して後に総胆管を結紮切断し，黄疸発生後一定時日を経て胆嚢空腸吻合を行つても，この際は胆汁流出可能な肝領域は肝重量比の1/5～1/6に過ぎないが，血中「ビ」値の下降は多少延長するが正常値に復する．

すなわち，この実験より，比較的健康な肝組織が肝全体の1/6も残存しておれば肝腸吻合により黄疸を消褪せしめ得る可能性がある．