

An Experimental Study on Temporary Portal or Superior Mesenteric-Femoral Vein Bypass at the Acute and Complete Interruption of the Portal Vein

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I. Introduction

If a method is established which enables temporary interruption of the portal vein for a certain length of time, it will largely improve the operability of extensive hepatectomy and pancreatoduodenectomy which generally accompany untractable hemorrhage.

Since ORÉ⁽⁶⁰⁾ carried out in 1856 an experiment of acute and complete interruption of the portal vein in rabbits, SCHIFF⁽⁷⁰⁾, BERNARD⁽³⁾, ECK⁽²⁵⁾, SOLOWIEFF⁽⁷⁸⁾ and, in this

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century, NEUHOF⁵⁷⁾, ELMAN and COLE²⁶⁾, BOYCE⁷⁾, BRUNSCHWIG⁸⁾, SCHAFER and KOZY⁷⁶⁾, MARKOWITZ and others have studied the acute and complete interruption of the portal vein in dogs, cats and rabbits, and they reported that the experiment invariably resulted in death when the interruption exceeds the permissible time. On the other side, ORÉ⁶⁰⁾, SOLOWIEFF⁷⁸⁾, NEUHOF⁵⁷⁾, BRUNSCHWIG⁸⁾ and others have demonstrated a possibility of survival at gradual occlusion of the portal vein.

In 1950, CHILD¹⁴⁾ carried out an experiment of acute and complete interruption in macaca mulatta monkey whose anatomical relationship much resembles to man, and observed many cases of survival, however, death of 8 per cent was directly due to the portal interruption. Judging from the result of CHILD¹⁵⁾ in monkeys, it is supposed that acute and complete interruption of the portal vein will be more safely carried out in man than in other animals. Considerable danger is predicted to adopt this procedure as an accomplished measure, requiring further studies. On the other hand, many studies have been carried out to prolong permissible time of temporary portal interruption. Namely, hypothermia, method to reduce blood amount draining into the splanchnic area by compressing the aorta¹³⁾, celiac²⁶⁾ or superior mesenteric artery⁵³⁾⁵⁵⁾, extirpation of the spleen and intestine, transfusion of blood and fluids, administration of antibiotics and steroid have been attempted experimentally and clinically. However, permissible time could be at most prolonged up to 60 minutes.

In 1952, PECK⁶⁶⁾ and in 1958 BARNETT²⁾ carried out various experiments of acute and complete portal interruption in dogs by setting an extracorporeal shunt of polyethylene tube from the portal to femoral vein in the former and from the splenic to femoral vein in the latter. After that, in 1960, DATE¹⁹⁾ studied external shunt from the mesenteric to femoral vein, in which the portal vein was interrupted for about 60 minutes, and reported 6 survivals out of 16 and 10 cases of hemorrhagic death due to infusion of anticoagulant. MAN⁴⁹⁾ reported, in 1961, that he could successfully carry out acute and complete interruption of the portal vein for 90 minutes by the use of bypass of plastic tube from the superior mesenteric to femoral vein.

However, there is no report concerning firstly what external shunt should be arranged and from what site of the splanchnic area the blood should be introduced to the systemic circulation, and secondly what management should be required to maintain normal coagulability in the body outside of the shunt, without forming clott mass in the shunt for certain length of time.

The author of the present paper experimentally studied in dog above mentioned 2 problems at the superior mesenteric-femoral vein temporary bypass in the aim of prolongation of permissible time in acute and complete interruption of the portal vein, and obtained some informations.

II. Mesenteric-femoral vein bypass.

(1) Preliminary experiment.

A. Prevention of coagulation by silicone coating.

1. Method.

Silicone KF 96 (SHINETSU Chem. Co. Ltd.) was dissolved in ether to 2 per cent.

Glass materials were thoroughly cleaned and dried for 30 minutes at 120°C. Before cooled out silicone solution was poured into and left for 1 minutes. Then the glass materials were left in room temperature for 24 hours in the situation so that silicone solution within the materials might flow down. Silicone coating was perfected by final heating of the materials for 3 hours at 250°C.

a. Static coagulation test.

Blood of dog was used and coagulation time was determined by modification of LEE-WHITE's method. Coagulation time in siliconized test tube was read at the moment in which 2 layers of plasma and blood corpuscle adhered to the wall and did not disassociate from it. Coagulation time in normally cleaned test tube was studied as control.

b. Trembling coagulation test.

The most important qualities of tube as a shunt circuit are less influence on coagulation of flowing blood and less adherency to the blood. Coagulation time was examined in siliconized test tube with siliconized rubber stopper which was turned upside down every 3 minutes. The same examination was also carried out in normally cleaned test tube for control. Blood of dog was similarly used. Blood withdrawn 180 minutes after intravenous injection of heparin of 2 mg/kg body weight in dogs No. 7, 8 and 9 was also subjected to comparative study.

2. Results

At static coagulation test, prolongation of 3 to 4 times of coagulation time was observed in siliconized test tube compared with that in normally cleaned one. Blood taken after administration of heparin showed prolonged coagulation time of more than 90 minutes ad infinitum, in siliconized test tube.

At trembling coagulation test also, although coagulation time was shortened to one third to one fourth of that in the above mentioned test, coagulation time was prolonged 2 to 2.5 times in siliconized test tube compared with that in control test. Blood taken after administration of heparin also showed, as in static test, coagulation time of more than 90 minutes in siliconized test tube (Tab. 1).

Tab. 1 Change in coagulation time caused by siliconization

Dog No.		2	4	5	7*	8*	9*
Siliconized test tube	Static test	13'36"	56'	42'	∞	∞	∞
	Trembling test	13'30"	12'	11'	∞	∞	∞
Ordinarily cleaned test tube	Static test	12'30"	14'	10'30"	21'	33'30"	27'
	Trembling test	5'	5'30"	5'	11'	16'30"	12'30"

∞ Means prolongation more than 90 minutes of coagulation time

* : Blood taken 180 minutes after intravenous injection of heparin of 2 mg/kg body weight

B. Influence of heparin on coagulation time.

1. Method.

Canine blood was used in vitro experiment. Blood of 1 ml was put in each of test tube of successive dilution of heparin, i. e. 1mg, 500γ, 400γ, 200γ, 100γ, 50γ, 10γ, 1γ,

$\gamma/2$ and $\gamma/4$, respectively contained in 0.1 ml of saline. As control, 1ml of blood was put in test tube containing 0.1 ml of saline. Coagulation time was determined by modification of LEE-WHITE's method.

For the experiment in vivo, 5 mongrel dogs weighing 9 to 11 kg were used. Coagulation time was determined by modification of LEE-WHITE's method with the lapse of time after single intravenous administration of heparin of 2 mg/kg body weight.

2. Results.

In vitro, blood of 1 ml showed prolonged coagulation time of more than 90 minutes ad infinitum in the test tube of 10 γ of heparin. Prolongation of coagulation time of 5 to 6 times was observed in 1 ml of the blood containing 1 γ of heparin, compared with that of control (Tab. 2.)

Tab. 2 Coagulation time of canine blood in various concentration of heparin (in vitro).

Dog No.	1	2	3	4	5
Amount of heparin	Coagulation time (min.)				
1mg	∞	∞	∞	∞	∞
500 γ	∞	∞	∞	∞	∞
400 γ	∞	∞	∞	∞	∞
200 γ	∞	∞	∞	∞	∞
100 γ	∞	∞	∞	∞	∞
50 γ	∞	∞	∞	∞	∞
10 γ	∞	∞	∞	∞	∞
γ	52'30"	78'	60'30"	63'	57'
$\gamma/2$	22'30"	32'	25'30"	21'30"	23'
$\gamma/4$	17'30"	19'30"	16'	18'	19'30"
Control Saline	10'	12'30"	10'30"	11'	12'

Prolongation of more than 90 minutes is represented by ∞ .

In vivo, coagulation time was prolonged more than 90 minutes in all the blood taken earlier than 150 minutes after the administration of heparin, and prolongation of coagulation time was 3 times of control in the blood taken 180 minutes after the administration of heparin (Tab. 3). Further prolongation of coagulation time of more than 90 minutes was observed for 1 hour by an additional intravenous administration of heparin of 0.5 mg/kg body weight 150 minutes after the initial administration of heparin of 2 mg/kg body weight (Tab. 3).

Tab. 3 Change in coagulation time with the lapse of time after intravenous injection of heparin of 2 mg/kg body weight.

Dog No.	6	7	8	9	10	11*	12*	13*
Time	Coagulation time							
Before	6'	7'30"	11'	8'30"	16'	15'	10'30"	9'
5 min. after administr.	∞	∞	∞	∞	∞	∞	∞	∞
10'	∞	∞	∞	∞	∞	∞	∞	∞
60'	∞	∞	∞	∞	∞	∞	∞	∞
90'	∞	∞	∞	∞	∞	∞	∞	∞
120'	∞	∞	∞	∞	∞	∞	∞	∞
150'	∞	∞	∞	∞	∞	∞	∞	∞
180'	19'30"	21'	33'30"	27'	35'	∞	∞	∞
210'	13'30"	18'30"	25'30"	18'30"	27'	∞	∞	∞

* : Additional intravenous injection of 0.5 mg/kg body weight 150 minutes after initial injection.

Prolongation of more than 90 minutes is represented by ∞

C. Heparin neutralizing effect of polybrene.

Heparin is usually used at extracorporeal circulation to prevent coagulation of blood. Here, it is required that the blood restores coagulability rapidly after the termination of experiment and postoperative bleeding is satisfactorily prevented. Lately it is reported by PRESTON, WEISS and others that in this purpose polybrene, a polymer of quaternary ammonium salt $(C_{13}H_{30}Br_2N_2)_x$, has an excellent heparin neutralizing effect. However, its optimal proportion of neutralization is reported variously by researchers. The author of the present paper studied the optimal proportion of heparin neutralization of polybrene from the aspect of coagulation time.

1. Method.

Canine blood was used in experiment. Polybrene of 100γ, 90γ, 80γ, 70γ, 60γ, 50γ, 40γ, 30γ, 20γ, 10γ and 1γ was respectively added to the mixture of blood of 1 ml and heparin of 100γ, and coagulation time was determined by modification of LEE-WHITE's method.

Five mongrel dogs weighing 8 to 11 kg were used for experiment in vivo. Polybrene of 1.4 mg/kg body weight was diluted with 5 per cent glucose solution to a concentration of 1 mg/ml and intravenously injected within 10 minutes, 30 minutes after the initial intravenous administration of heparin of 2 mg/kg body weight. Coagulation time was determined with the lapse of time after the injection of polybrene.

2. Result.

When polybrene was added to the blood containing heparin of 100γ/ml, optimal neutralizing proportion was found to be 1 amount of heparin to 1 to 0.7 amount of polybrene. When various concentration of polybrene was added to 100γ of heparin alone, white turbidity was observed in the mixture. Results obtained by adding blood to this mixture was, however, identical to that mentioned in the above. In vivo experiment,

coagulation time which was prolonged ad infinitum by heparin, was shortened already 5 minutes after the administration of polybrene at the proportion of 1 to 0.7. The effect of polybrene was stable and no prolongation of coagulation time was observed even 360 minutes after the administration (Tab. 4, 5).

Tab. 4 Coagulation time of 1 ml blood containing 100 γ of heparin in various concentration of polybrene (in vitro)

Dog No.	2	3	5	14	15	16
Amount of polybrene	Coagulation time					
100γ	18'	11'	15'30"	16'30"	16'30"	6'30"
90γ	19'30"	14'	25'30"	17'	23'30"	11'30"
80γ	19'30"	18'30"	27'	22'	26'	17'
70γ	20'	21'	32'	35'30"	16'30"	26'30"
60γ	∞	∞	∞	∞	∞	∞
50γ	∞	∞	∞	∞	∞	∞
40γ	∞	∞	∞	∞	∞	∞
30γ	∞	∞	∞	∞	∞	∞
20γ	∞	∞	∞	∞	∞	∞
10γ	∞	∞	∞	∞	∞	∞
0γ	∞	∞	∞	∞	∞	∞
Control Saline	12'30"	10'30"	12'	7'30"	13'	5'30"

D. Influence of ligation of the branches draining into the portal vein on organism, particularly on its survival.

1. Method.

Mongrel dogs of 6 to 11 kg were used and following experiments were carried out under intravenous anesthesia with Isozol.

a. The gastroduodenal and splenic

Tab. 5 Change in coagulation time with the lapse of time after administration of 1.4 mg/kg of polybrene after administration of 2 mg/kg body weight of heparin.

Dog No.	18	19	20	21	22
	Coagulation time				
30' after administr. of heparin	∞	∞	∞	∞	∞
5' after administr. of polybrene	15'30"	22'	13'30"	17'	9'
10'	12'	21'	14'	17'30"	11'
30'	13'30"	15'	13'30"	16'30"	11'30"
60'	14'	15'30"	13'30"	17'30"	8'30"
90'	11'30"	14'	12'	18'	9'
120'	13'30"	13'30"	12'	17'30"	8'30"
150'	12'30"	13'30"	12'30"	17'	8'30"
180'	12'	12'30"	12'	17'	8'
210'	13'	13'	11'30"	16'	7'30"
240'	12'	13'30"	12'	16'30"	7'30"
270'	11'30"	12'30"	11'30"	16'30"	8'
300'	11'30"	12'30"	11'	15'	8'
360'	11'	12'30"	11'	15'	7'30"
Control (Before)	10'30"	12'30"	12'	11'30"	7'

veins were ligated at the junction to the portal vein and simultaneously the spleen was removed.

- b. The first branch of the superior mesenteric vein of the liver side and the splenic vein were ligated at the junction with the portal vein, respectively, and splenectomy was performed.
- c. The gastroduodenal and splenic vein and the first branch of the superior mesenteric vein of the liver side were all ligated simultaneously at the junction with the portal vein and splenectomy was performed.
- d. The inferior mesenteric vein was solely ligated.
- e. One of the branches of the superior mesenteric vein was ligated at its bifurcation.
- f. The ileocolic vein and a branch of the adjoining iliac vein were simultaneously ligated at their bifurcation.

2. Results.

In group a, 4 dogs out of 5 survived the operation, and 1 dog died 2 hours after it. No abnormality was found in the abdominal cavity at autopsy and the cause of death was obscure.

In group b, all 5 dogs survived.

In group c, all 5 dogs died within 12 hours after the operation. At autopsy, considerable accumulation of bloody fluid was found in the abdomen in all cases. Numerous petechia was found on the pancreas, duodenum, antrum and corpus of the stomach and omentum. At the same time, massive bleeding was observed in the intestinal tract. The intestine, stomach and pancreas were slightly tintured grey violet, which was, however, obviously different from dark violet as observed at the portal ligation.

In group d, 3 dogs all survived.

In group e, 3 dogs all survived.

In group f, all 3 dogs died within 24 hours after the operation. At autopsy, outstanding dilatation and tortuosity of the ileocolic vein and numerous petechia on the ileocecal portion and mesentery of corresponding area and bleeding in the intestinal canal were observed.

E. Histological changes of intestine caused by the change of portal pressure.

1. Method.

Histological changes in small intestine and mesentery were studied with hematoxylin eosin double staining in dogs, in which portal pressure was kept for 3 hours in a level 2 times higher than in normal, by constricting the portal vein at the bifurcation with a cotton bandage. The same study was carried out in dogs, whose portal pressure was kept 3 and 4 times higher than in normal for 3 hours. Splenectomy was performed constantly.

2. Results.

At portal hypertension of 2 times for 3 hours, neither macroscopic change of color nor petechia on the intestinal tract and mesentery was observed.

Microscopically, no hemorrhage was found, although the mucous membrane of the intestine and mesentery were slightly edematous (Fig. 1, 2).

Neither change of the color nor bleeding in the intestinal canal was observed in the dogs of hypertension of 3 times for 3 hours. In these animals, however, slightly increased edema of the intestinal mucous membrane and hemorrhage in the top of the intestinal villi and mesentery were observed microscopically. Dilatation and edema of submucous vessels were characteristic (Fig. 3, 4). When portal pressure was elevated 4 times higher for 3 hours, intraluminal hemorrhage was observed in the intestine both macro- and microscopically. Desquamation of mucous epithel, edema of the mucous membrane, hemorrhage and marked production of mucous were observed, with outstanding increase in small mononuclear cells in the villi (Fig. 5).

(2) Portal-femoral vein bypass utilizing the pressure difference.

1. Experimental equipment.

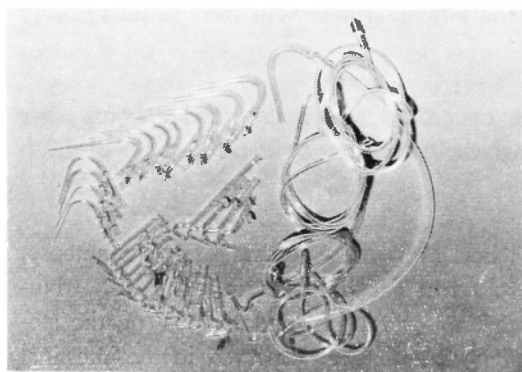


Fig. 6'. Cannulas and tubes of various sizes for bypass circulation.

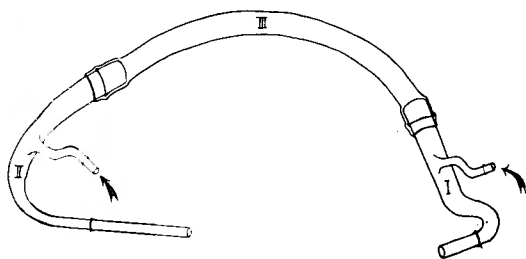


Fig. 6 Extracorporeal circuit

I : portal cannula

II : femoral cannula

III : N. F. Silicone-rubber tube

↘ : Perfusion set is connected.

Extracorporeal circuit was consisted of cannula for the portal and femoral veins and NF silicone rubber tube as is shown in Fig. 6 and 6'.

Cannula of 2 types for the portal vein were prepared, that is, one having caliber of portal end of 0.2 cm, 0.3 cm, 0.4 cm, 0.5 cm and 0.6 cm, respectively and caliber of another end of 0.6 cm, and another having caliber of both ends of 0.7 cm, 0.8cm, 0.9 cm and 1.0 cm, respectively. Cannula for the femoral vein was also designed in 2 types, that is, one having various caliber of femoral end of 0.1 to 0.6 cm with the difference of 0.1 cm, respectively and another having caliber of both ends of 0.7 cm, 0.8 cm, 0.9 cm and 1.0 cm, respectively. Cannula was made of hard glass. Wall of the both ends of the cannula was made as thin as possible, so that an occurrence of vortical flow might be prevented. Abrupt meandering and change in caliber of the cannula were at the same time avoided in order to minimize friction of the flow within the cannula.

The cannula was also so designed that fluid can be infused in the direction of blood flow.

NF silicone-rubber tube (NOGAMIKIKAI Co. Ltd.) of 3 sizes of 0.6 cm, 0.8cm and 1.0 cm was used in adequate length. Inside of the circuit was entirely coated with silicone and in all the junctions silicone KS 88 (SHINETSU Chem. Co. Ltd.) was used.

Prior to experiment, the equipment was filled with *sopa invertus* solution of 1 per cent for 2 hours for sterilization and rinsed well with aseptic saline solution.

2. Materials and method.

Eighteen adult healthy mongrel dogs of both sexes weighing 9 to 21 kg were used. Dogs were subjected to the experiment in the fasting state of 12 hours. Atropin sulfate of 0.3 to 0.4 mg was intramuscularly injected 30 minutes before the introduction of anesthesia. Isozol of 10 mg/kg body weight was intravenously injected and a tracheal tube was introduced. Anesthesia was maintained in 2nd plane of 3rd stage with ether and oxygen.

Operation was performed under aseptic condition.

Firstly, an incision was made in the right femoral region and the femoral artery and vein were adequately exposed. Mercurial manometer was connected to the femoral artery and blood pressure was monitored.

Secondly, abdomen was opened by upper median incision. The portal vein was ascertained by shoving the duodenum to the left side, was adequately exposed and was isolated from the bifurcation at the liver hilum to the junction of the 2nd branch of the superior mesenteric vein. The splenic vein was ligated and cut at its junction to the portal vein, and splenectomy was performed. The gastroduodenal and inferior mesenteric veins were also ligated and cut at the junction to the portal vein, 1st branch of the superior mesenteric vein preserved.

Thirdly, a small transverse incision was made on the femoral vein and the cannula was inserted and fixed. Fluid infusion was commenced from this cannula.

Fourthly, the portal vein was clamped at the hilum of the liver and at the level immediately above the bifurcation of the 1st branch of the superior mesenteric vein. A transverse incision was made on the portal vein between the junction of the splenic and

that of inferior mesenteric vein, and cannula for the portal vein was inserted and fixed. Interruption at the intestinal side was then released. At this procedure, cannula having approximately similar caliber to the vessels were used. With the start of bypass flow, heparin of 2 mg/kg body weight was intravenously infused and 150 minutes later 0.5 mg/kg body weight of heparin was added. During these procedures, a small polyethylene catheter was inserted from a small branch of the superior mesenteric vein up to a point a little below the cannula of this vein and connected to aquaous manometer for observation of mesenteric venous pressure.

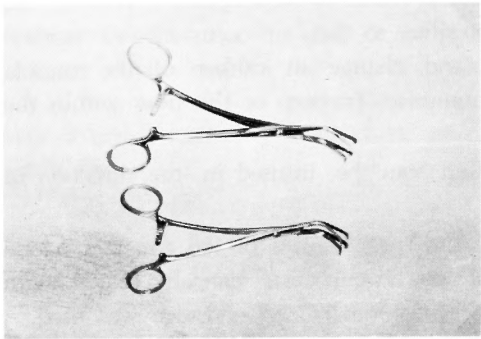


Fig. 7 Satinsky's vessel forceps modified by the author,

After bypass experiment for 180 minutes, blood flow was again interrupted at the intestinal side of the portal vein and the cannula was withdrawn and the protal vein was held with Satinsky's vessel forceps which was modified by the author of the present experiment as shown in Fig. 7 at the site of the small transverse incision. Then the interruption was released. The small incision in the portal vein was closed with continuous suture using No. 1 silk thread for vessel suture of Tatebe Co., blood flow to the liver being maintained. Protamine

Tab. 6 Result

Dog	No.	Sex	Body weight	Duration of portal inter- ruption	Cannula		Silicone rubber tube		Blood pressure		Sup. mesent. venous pressure		Outcome
					Caliber of portal end	Caliber of femoral end	Length	Caliber	Before interrupt.	After release	Before interrupt.	After release	
24	♂	18.5 kg	180 min	0.5cm	0.3cm	11.5cm	0.6cm	102 mmHg	85 mmHg	123 mmH ₂ O	130 mmH ₂ O	survival	
25	♀	10.3	180	0.5	0.2	10.6	0.6	110	52	110	148	death	
26	♂	16	180	0.6	0.3	13.0	0.6	113	93	137	134	survival	
27	♀	13.5	100	0.6	0.3	10.5	0.6	121	30	111	118	death	
28	♀	12	180	0.6	0.3	11.8	0.6	125	52	127	154	death	
29	♂	9	180	0.4	0.2	10.2	0.6	104	48	130	110	death	
30	♂	9.5	180	0.5	0.2	11.3	0.6	110	58	90	105	death	
31	♀	11.5	180	0.5	0.3	11.5	0.6	123	—	121	—	death during operation	
32	♀	12.5	180	0.6	0.3	12.0	0.6	105	65	125	120	death	
33	♂	13	180	0.6	0.3	12.0	0.6	112	40	132	240	death	
*35	♂	14	180	0.5	0.3	14.3	0.6	80	60	95	90	survival	
*37	♂	11.5	180	0.6	0.3	12.0	0.6	110	52	120	118	death	
*38	♂	15.5	180	0.5	0.3	14.2	0.6	126	—	122	—	death during operation	
*39	♀	18.6	180	0.6	0.3	11.9	0.6	110	60	133	108	death	
*40	♀	13	180	0.6	0.3	13.1	0.6	98	68	114	120	death	
*41	♂	17	120	0.6	0.3	13.4	0.6	118	—	—	—	death	
*42	♂	21	120	0.7	0.4	14.8	0.6	130	90	132	138	survival	
*43	♂	19	180	0.6	0.4	13.8	0.6	100	82	—	—	death	

Polybrene was used in astered animals and otherwise protamine sulfate.

sulfate of 1.5 amount or polybrene of 0.7 amount of heparin was solved in 100 ml of 5 per cent glucose and infused from the cannula of the femoral vein in order to neutralize anticoagulant effect of heparin.

The site of the suture was gently pressed with gauze until bleeding ceased and the abdomen was closed. The femoral vein was ligated after the inserted cannula was withdrawn.

3. Results.

Results of the extracorporeal circulation above mentioned is represented in Tab. 6. Four cases out of 18 survived for more than 72 hours.

Abrupt fall of arterial pressure and elevation of portal pressure, i. e. signs of congestion in the splanchnic area as is observed at simple portal interruption, were avoided by the use of the bypass after the portal flow was interrupted. However, gradual fall of arterial pressure during the bypass experiment was observed, which was due to untractable oozing from the site of portal dissection and operative wound caused by administration of anticoagulant heparin of 2 mg/kg body weight.

After bypass experiment, in 10 cases protamine sulfate and in 8 cases polybrene were used as anti-heparin agent. Coagulation time in these animals approached to preoperative level 5 minutes after the administration.

Blood pressure, however, did not recover readily and 11 animals died presumably of hypovolemic shock.

At autopsy of these animals, marked accumulation of bloody fluid was observed in the abdominal cavity. Congestion was not observed in the intestine, surface of which being pale. Hemorrhage into the intestinal canal was not observed.

III. SUPERIOR MESENTERIC-FEMORAL VEIN BYPASS WITH HEPARINIZATION CONFINED EXCLUSIVELY TO THE EXTRACORPOREAL CIRCUIT, DEVISED BY THE AUTHOR.

Since the cause of unfavorable results of above mentioned experiment II was considered to have consisted in untractable oozing from the operative wound which was due to administration of anticoagulant alone for long time of operation, some new device was required to prevent clott mass formation exclusively within the extracorporeal circuit, whereby coagulability otherwise being maintained to be normal.

Hence, the author of the present experiment, based on the preliminary experiments, devised method of portal or superior mesenteric-femoral vein bypass at portal interruption by the use of pressure difference or a mesenteric branch-femoral vein bypass by the use of pump, in which heparin is infused from portal cannula and anti-heparin agent polybrene from femoral cannula, in the proportion of 1 to 0.7.

(1) Preliminary experiment.

A. Influence of heparin-polybrene simultaneous infusion on coagulation time.

1. Method.

Polybrene of 1.4 mg/kg body weight was administered 30 minutes after administration of heparin of 2 mg/kg body weight in dogs. Blood was taken 60 minutes after the initial administration. One ml of the blood was put in each test tube containing 100γ, 50γ, 10γ, 5γ, 1γ, 0.5γ and 0.25γ, respectively, and change of coagulation time

was studied.

2. Results.

One ml of the blood taken 60 minutes after the administration of heparin and polybrene showed prolongation of coagulation time of more than 90 minutes in the test tube of 5γ of heparin. Five to six times' prolongation was observed in the test tube of 1γ compared with that of control, dog No. 22 alone showing 9 times' prolongation (Tab. 7).

Tab. 7

Change in coagulation time caused by heparin after heparin polybrene administration (in vitro).

Dog No.	18	19	20	21	22
Amount of heparin	Coagulation time				
100γ	∞	∞	∞	∞	∞
50γ	∞	∞	∞	∞	∞
10γ	∞	∞	∞	∞	∞
5γ	∞	∞	∞	∞	∞
γ	75'	82'30"	78'	88'30"	73'30"
0.5 γ	76'	57'	63'30"	52'30"	46'
0.25 γ	37'30"	32'30"	28'	32'30"	27'30"
Control	14'	15'30"	13'30"	17'30"	8'30"

Prolongation of more than 90 minutes is represented by ∞.

per cent was infused similarly from another catheter inserted proximally to the femoral vein by way of one of its branches.

Blood was taken from the femoral vein of the opposite side. Infusion of 0.02 per cent of heparin alone and that of 0.014 per cent of polybrene were performed respectively for control study.

Following studies were carried out with the lapse of time.

1. Change in red blood cell count.
2. Change in white blood cell count.
3. Change in platelet count, by direct counting method of REES-ECKER.
4. Change in coagulation time, by modification of LEE-WHITE's method.
5. Hematocrit ratio, by WINTROBE's method.
6. Electrocardiographic change, by standard limb lead and unipolar limb lead using a machinery equipped with heated stylus (FUKUDA Co. Ltd.) with the lapse of time before, during and after the infusion.

2. Results.

Change in red blood cell count was not observed in animals of heparin polybrene infusion and in those of heparin alone, while slight decrease was observed in animals of polybrene infusion alone (Fig. 8). Decrease of 23 per cent in white blood cell count was observed 30 minutes after infusion of heparin polybrene, and decrease of 21 per cent 1 hour after it, which then gradually restored. In 2 cases the decrease was only 4 per cent and 7 per cent 30 minutes after the infusion, respectively and cell count restored to the level before the infusion 1 hour after it, with no further fluctuation. White blood cell count decreased by 29 per cent in group of heparin infusion and by 41 per cent in

B. Influence of heparin polybrene simultaneous infusion on organism.

1. Method.

Heparin solution of 0.02 per cent was infused by way of the femoral vein in dogs at a rate of 1 ml/min. for 300 minutes through a polyethylene catheter inserted to the distal side in the leg. Simultaneously, polybrene solution of 0.014

Fig. 8 Red blood cell count

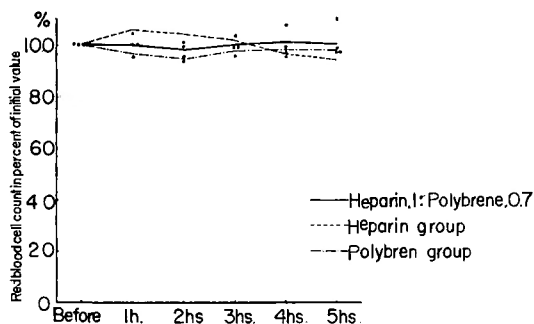
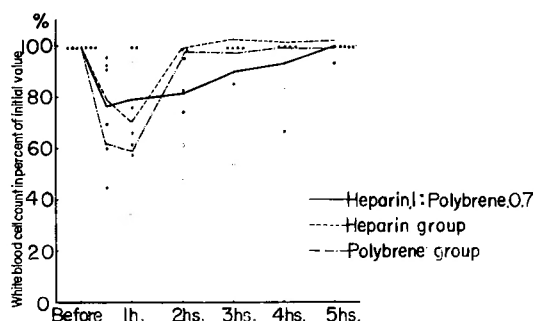


Fig. 9 White blood cell count



that of polybrene infusion 1 hour after it, and restored thereafter (Fig. 9).

Platelet count decreased in group of heparin polybrene infusion by 17 per cent 1 hour after the infusion and 21.5 per cent 2 hours after it, which gradually restored thereafter. In animals of heparin infusion, platelet count decreased by 43 per cent 1 hour after it and restored thereafter. In animals of polybrene infusion, platelet count decreased most markedly by 22 per cent 3 hours after it, which, however, returned to the value before the infusion, 4 hours after it (Fig. 10).

Coagulation time showed little change, remaining around the value before the infusion, in both the group of heparin-polybrene and that of polybrene. However, in animals

Fig. 10 Platelet count

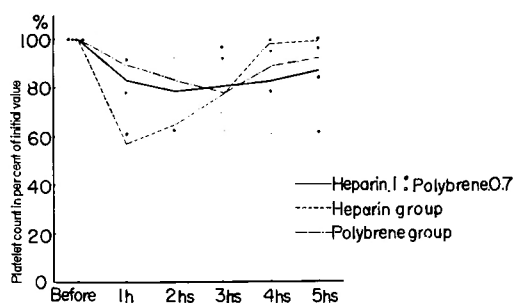


Fig. 12 Hematocrit ratio

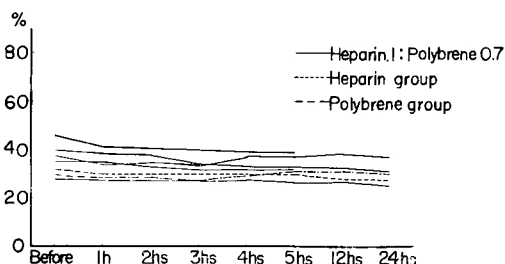
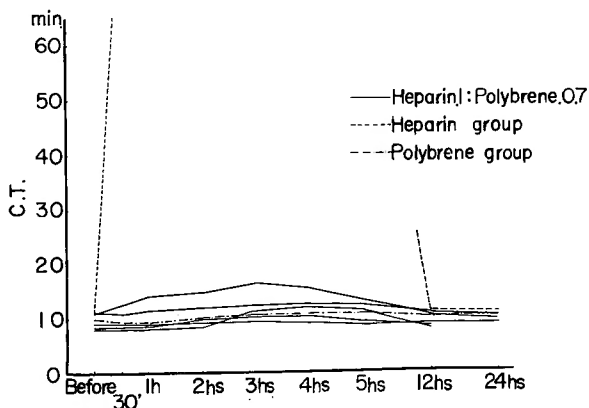


Fig. 11 Coagulation time

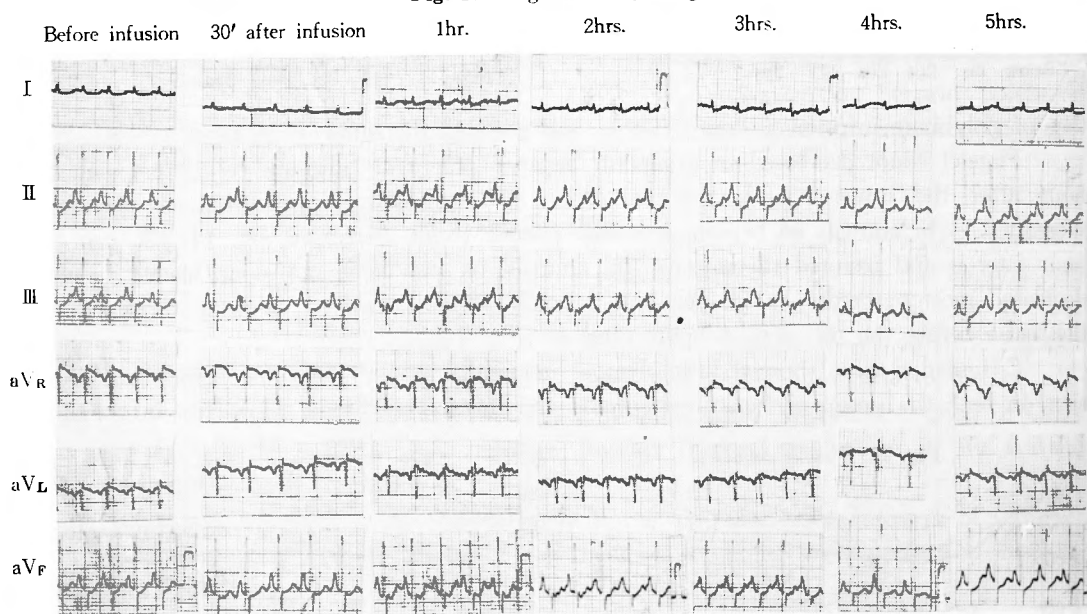


of heparin infusion, coagulation time was prolonged infinitely more than 90 minutes already 30 minutes after the commencement of the infusion, which returned to the value before the infusion 12 hours after its termination (Fig. 11).

Change was hardly observed in hematocrit ratio (Fig. 12).

No abnormality was found on electrocardiogram in animals of heparin polybrene infusion (Fig. 13).

Fig. 13 Dog No. 77 ♀ 10kg



(2) Bypass experiment.

1. Experimental equipment and method.

A. Portal or superior mesenteric stem-femoral vein bypass utilizing pressure difference.

Extracorporeal circuit used here was identical to the equipment in experiment II. Anticoagulant heparin was infused in portal cannula and at the same time antiheparin agent polybrene was infused in femoral cannula through a mechanism for adjusting number of drops of both solutions, as is shown in Fig. 14. Solution of heparin and polybrene was put in tightly closed vials and used. Number of drops was adjusted by a stopcock and negative pressure adjuster specially designed (Fig. 15).

Nozzle of drip tube was siliconized so that volume of 1 drop might become small owing to water repellent character of silicone. Moreover, in order to magnify the range of drip adjustment, a small tube of 20 cm in length was inserted into the drip equipment.

Anesthesia and operative procedure were similarly performed as in experiment II. Infusion of heparin polybrene was commenced as the portal flow was interrupted, and incision was made on the portal vein, from which the cannula was inserted. Then portal

Fig. 14 Illustration of extracorporeal bypass circulation utilizing pressure difference and heparin polybrene infusion.

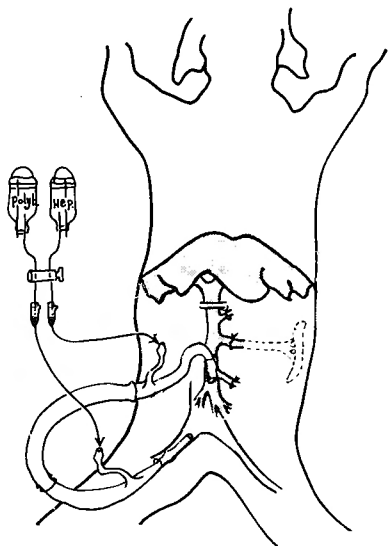
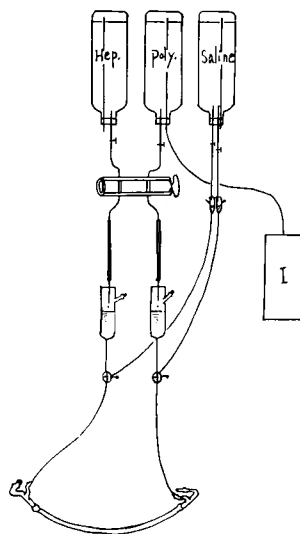


Fig. 15 Illustration of perfusion set and drip adjuster.

I : Negative pressure adjuster



interruption at the intestinal side was released and bypass flow was started.

Certain amount of heparin which corresponds in the term of γ to the minute volume of portal flow before the interruption in the term of ml was adjusted to be contained in 1 ml of saline and certain amount of polybrene which corresponds in the term of γ to 70 per cent of minute volume of portal flow before the interruption in the term of ml was adjusted to be contained in 1 ml of 5 per cent glucose solution. These solutions were adjusted to drop in 20 drops per minute and infused from portal and femoral cannula, respectively.

Complete interruption of the portal vein was performed for 180 minutes in 15 dogs with this equipment and method.

B. A superior mesenteric branch-femoral vein bypass with a pump in the extra-corporeal circuit.

Equipment was consisted of a small cannula, which could be inserted in a branch of superior mesenteric vein, pump, bubble trap, femoral cannula and equipment of heparin polybrene infusion (Fig. 16).

Cannula for the vessel of intestinal side was made of stainless steel ; 7 cm in length having caliber of 0.2 cm at the point. The cannula had side holes of 0.05 cm in width and 3.5 cm in length, on the both sides, 0.5 cm distant from the tip, further having a groove, 1.2 cm distant from the hole, for preventing the cannula to slip off from the vessel. Caliber of the cannula gradually increased finally to become 0.4 cm at another end connected to vinyltube.

At use, part of the side hole was covered with rubber tube and the end of the rubber tube was turned over for about 1 cm. As the cannula was inserted in the vessel, rubber tube turned was returned to the former state. Thus the vessel wall became to

Fig. 16 Illustration of extracorporeal bypass circulation by the use of pump.

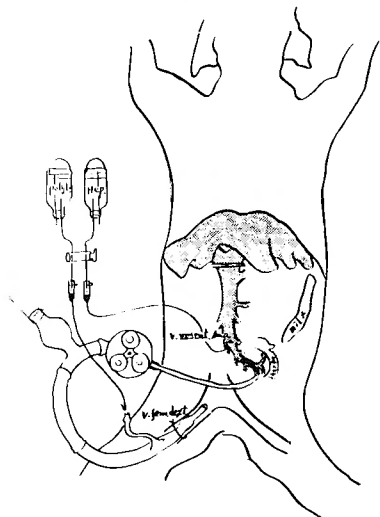
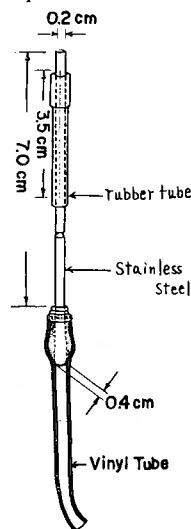


Fig. 17 Metal cannula for branch of superior mesenteric vein.



be tightly held all around between the cannula and the rubber tube, which enabled deeper insertion and fixation of the cannula without leakage of blood (Fig. 17).

This stainless steel cannula was connected to a pump through vinyl-tube of 0.4 cm in caliber.

For this experiment, a DE BAKEY²⁰⁾ roller pump was used.

Rubber tube of 5 mm in caliber, 2.5 mm in thickness of the wall and 60 cm in length was used within the pump. An A. C. series motor of 1/8 horse-power was used for the power source. Rotation was controlled by adjusting the position of brushes, and further finely controlled by a speed changer equipped with variable diametral pulley. Stroke volume was voluntarily and finely adjusted with the limit of 1500 ml per minute. Thick walled silicone rubber tube of 0.6 cm in caliber was used for outlet of the pump. In the midst of this outlet tube a bubble trap made of hard glass was placed.

All these equipments mentioned here were connected to the organism, total volume of extracorporeal circuit being 76 ml and inside being siliconized all over to minimize the change in blood character.

The same cannula for the femoral vein as in group A of experiment utilizing pressure difference was used.

In order to infuse heparin in the blood draining into the circuit from the splanchnic area, polyethylene tube of 0.1 cm in caliber was used.

Sopa invertus solution of 1 per cent was used for sterilization of the equipments. The equipments were filled with this solution for 2 hours, and rinsed with aseptic saline solution of 10 l. After the fluid was discarded, the equipments were again rinsed with aseptic saline of 2 to 3 l, and finally filled with this solution.

Adult mongrel 12 dogs were studied as control.

Chlorpromazine of 2 mg/kg body weight was intramuscularly injected 30 minutes before the operation. Anesthesia was introduced with intravenous injection of Isozol of

10 mg/kg body weight. Tracheal tube was introduced and oxygen alone was inhaled, depth of anesthesia being maintained with intermittent administration of Isozol. Prior to the operation, 100 ml of arterial blood from another dog was directly transfused from the left femoral vein.

Firstly, incision was made on the right femoral region and the femoral artery and vein was adequately exposed and isolated. A mercurial manometer was connected to the artery for observation of blood pressure. On the other hand, the cannula was inserted and fixed in the vein through a small incision, saline solution being infused from this cannula.

Secondly, the abdomen was opened by upper median incision and the portal vein was dissected at the hilum of the liver.

Thirdly, a polyethylene tube was inserted from a branch of the mesenteric vein, in a way not to be affected by the direction of the flow, up to the bifurcation of the splenic and portal vein for continuous observation of portal pressure.

Fourthly, a branch of the mesenteric vein in the end of small intestine was dissected up to its bifurcation and small incision was made on its bifurcation. It was already ascertained in preliminary experiment I, d, that the ligation of a branch of the mesenteric vein at its bifurcation did not influence on the intestine owing to existence of collateral anastomosis of the vessels. The metal cannula was introduced from the incision, turned over portion of rubber tube was returned as it had been and the vessel was covered. The cannula was further inserted gently and fixed without bleeding. At the same time, heparin infusion was started from a polyethylene tube inserted and fixed in a small branch of the mesenteric vein.

Then the DE BAKEY pump was let work slowly in occlusive setting and the portal flow was interrupted immediately before the bifurcation at the liver hilum. The rotation of the pump was immediately accelerated and adjusted to prevent the collapse of the vessel or the fall of the blood pressure accompanied by elevation of portal pressure.

At the same time, infusion from the femoral cannula was changed to polybrene infusion, and portal blood was introduced to the right femoral vein.

Amount and proportion of heparin polybrene infusion were similar to those in group A of experiment utilizing pressure difference.

After bypass circulation, metal cannula was withdrawn and the vessel was ligated. Portal interruption was released prior to withdrawal of the metal cannula. Entire blood remaining within the equipment was transfused by way of the femoral cannula.

Acute and complete interruption of the portal vein was performed for 300 minutes with above mentioned procedures, and following studies were carried out.

C. Examinations and method.

Here the experimental group utilizing pressure difference is called group A, and that using pump within the circuit group B.

1. Survival rate ; animals survived for more than 72 hours were regarded as survivor.
2. Pressure of blood, that of the portal or superior mesenteric vein ; continuously monitored before, during and after the operation.
3. Change in red blood cell count with the lapse of time.

- 4. Change in white blood cell count with the lapse of time.
- 5. Change in platelet count with the lapse of time, by direct method of REES-ECKER.
- 6. Change in hematocrit ratio, by method of WINTROBE.
- 7. Coagulation time ; by modification of LEE-WHITE's method.
- 8. Change in circulating plasma volume and circulating blood volume, by GREGERSON's method³²⁾.
- 9. Change in plasma fibrinogen, by LOSNER's method⁴⁶⁾. Heparin polybrene infusion was done in 4 dogs without bypass circulation for control taking their average value.
- 10. Plasma hemoglobin concentration ; by method of DRABKIN²⁴⁾ and calculated from following formula, extinction coefficient being set 11.4 and molecular magnitude of hemoglobin 16700γ.

$$\frac{1.67 \text{ Ed}}{\text{Em M}} \text{ g/dl,}$$

- whereby Em⁵⁴⁰M is 11.4, E represents extinction and d dilution number.
- 11. Serum protein ; with a refractometer (HITACHI Ind. Co.).
 - 12. Albumin-globulin ratio ; by method of AULL and McCORD¹⁾, and electrophoresis. Average value of 4 dogs of heparin polybrene infusion without bypass circulation was taken for control.
 - 13. B. S. P. test of 15th minute ; by ROSENTHAL and WHITE's method pre- and postoperatively in group A, and preoperatively and 48 hours after the operation in group B. Average value of 4 dogs of heparin-polybrene infusion without bypass circulation was taken for control.
 - 14. Electrocardiographic study ; by standard and unipolar limb lead before, during and after the operation.
 - 15. Histological studies of intestine and liver. Small intestine and liver immediately after operation were studied histologically by hematoxylin-eosin double staining. Macro-

Tab. 8 Results of bypass circulation utilizing pressure difference.

Dog No.	Body weight	Sex	External shunt	Duration of portal interruption	Outcome	Cause of death
46	13kg	♂	Sup. mesent.→right femoral vein	180 min.	survival	
47	12	♀	// → //	180	death	error of portal suture.
48	15.5	♂	// → //	180	survival	
50	12	♀	Sup. mesent.→both femoral vein	180	survival	
51	10	♀	Sup. mesent.→right femoral vein	180	survival	
52	15	♂	// → //	210	survival	
53	15	♀	Sup. mesent.→right jugular vein	180	survival	
57	9	♂	Sup. mesent.→right femoral vein	240	death	error of portal suture.
58	9.5	♀	// → //	180	survival	
59	19	♂	// → //	180	death	slipping off of vessel forceps.
60	21	♂	// → //	180	survival	
61	20	♂	// → //	120	survival	
62	13	♀	// → //	120	survival	
64	15	♀	// → //	180	death	portal injury
65	12	♂	// → //	180	survival	

scopic change in the intestine was also pursued during operation.

2. Results.

As is represented in Tab. 8 and 9, survival rate was 73 per cent in group A and 83 per cent in group B.

Clot mass formation was not found even in a single case within the circuit during the bypass circulation.

Tab. 9 Results of bypass circulation by the use of pump.

Dog No.	Body weight	Sex	Volume of flow per 1 rotation	Rotation of pump	Volume of flow	Duration of portal interruption	Outcome
74	10kg	♂	3.4cc	58/min	19.7cc/min/kg	180min	death (air embolus)
79	10	♀	3.4	46	15.6	300	survival
80	14	♂	3.6	90	22.0	300	survival
81	10	♂	3.6	62	21.0	300	survival
82	13	♂	3.6	78	21.9	300	survival
83	16	♀	3.6	96	21.3	360	survival
85	11	♂	3.9	75	26.5	300	death (hemorrhage)
86	15	♂	3.9	104	27.0	180	survival
88	10	♀	3.9	68	20.0	300	survival
92	14	♀	3.9	72	20.0	300	survival
*95	17	♂	3.9	57	13.0	90	survival
96	12	♂	3.9	83	26.9	300	survival

* In No. 95 dog interruption was carried out below the influx site of the splenic vein.

Cause of death was invariably hemorrhage from injury of the portal stem at vessel suture in group A, and in group B, dog No. 74 died of technical error and dog No. 85 died of hemorrhage from injury of the superior mesenteric vein at removal of the metal cannula, though the injury was repaired by suture.

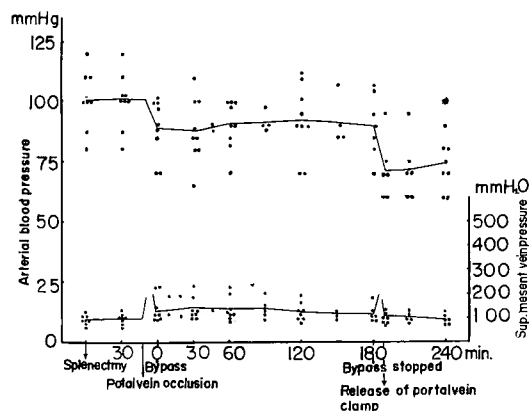


Fig. 18 Change in blood pressure and that of superior mesenteric vein in bypass circulation utilizing pressure difference.

Blood pressure and pressure in the portal or superior mesenteric vein in group A were as represented in Fig. 18. Sudden elevation of venous pressure and fall of the blood pressure were observed for 1 minute in which portal flow was interrupted at the liver hilum and the level of the trunk of the superior mesenteric vein. With the start of bypass circulation, superior mesenteric venous pressure restored to a level of 1.3 times of that before interruption which was stabilized and further returned to a level of 1.2 times of that before interruption.

On the other hand, blood pressure showed an abrupt fall of 12 mmHg on the average accompanied by sudden elevation of

portal pressure, and was stabilized thereafter.

As portal flow was interrupted at intestinal side at withdrawal of the portal cannula, superior mesenteric venous pressure elevated and blood pressure fell abruptly by 19 mmHg. As the portal interruption was released, superior mesenteric venous pressure returned to the level before interruption and blood pressure also restored gradually.

In group B, as shown in Fig. 19, portal pressure leapt up to a level of 1.5 times of that before interruption, by portal interruption for 1 hour, which, however, restored gradually during bypass circulation to the level before interruption.

Fig. 19 Change in blood and portal pressure in bypass circulation by the use of pump.

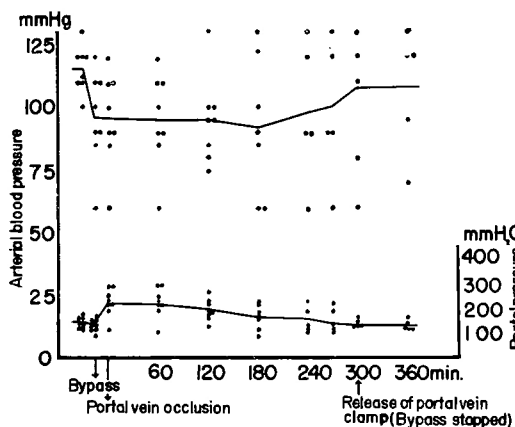
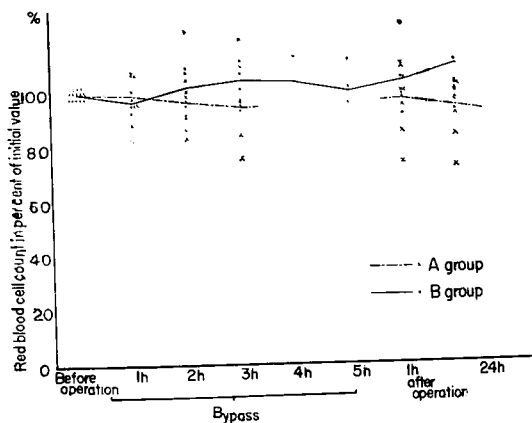


Fig. 20 Red blood cell count



On the other hand, blood pressure fell by 20 mmHg on the average, and showed gradual ascension later than 180 minutes. Both blood and portal pressures perfectly returned to the level before portal interruption by the release of it.

In red blood cell count, no change was observed in both group A and B (Tab. 10, Fig. 20).

White blood cell count decreased by 25 per cent 1 hour later in group A and gradually restored thereafter, while in group B, the decrease was 44.5 per cent 1 hour later and also gradually restored thereafter. A tendency of leucocytosis of 104 per cent was observed 1 hour after bypass circulation compared with the level before it (Tab. 11, Fig. 21).

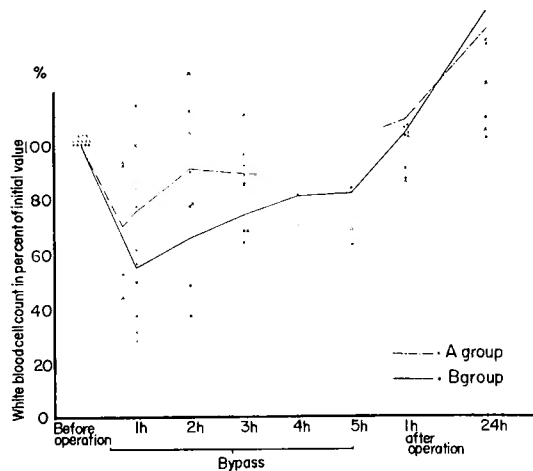
Platelet count in group A showed decrease of 12.4 per cent 1 hour later and 23.7 per cent 2 hours later and restored to 89.4 per cent of the value before bypass circulation 1 hour after the termination, and in group B, decrease of 38.9 per cent 1 hour later, 48.4 per cent 3 hours later and restored thereafter up to 74.9 per cent of the value before bypass circulation 24 hours after it (Tab. 12, Fig. 22).

In hematocrit ratio no marked change was observed both in group A and B (Tab. 13, Fig. 23).

Coagulation time in group A was not prolonged particularly, except that in dog No. 58 it was prolonged to 18 minutes and a half after bypass circulation of 180 minu-

Tab. 10 Red blood cell count

Dog No.	Before operation	60 min. after by-pass	120 min.	180 min.	240 min.	300 min.	60 min. after ope.	24 hrs.
A Group ($\times 10^4$)								
46	735	785	789	802	—	—	800	757
48	639	567	552	539	—	—	542	533
50	712	703	700	688	—	—	672	690
51	426	—	412	—	—	—	419	395
53	482	459	—	462	—	—	475	439
58	548	553	550	—	—	—	599	546
60	452	433	375	340	—	—	332	325
65	710	763	744	756	—	—	738	720
mean	588	609	589	598	—	—	572	551
B Group ($\times 10^4$)								
81	493	408	538	499	555	500	616	678
82	642	598	611	602	624	615	632	651
86	542	574	663	645	—	—	526	544
88	707	675	649	787	785	790	739	783
96	663	708	604	638	610	600	604	635
mean	609	593	613	634	644	626	623	659

Fig. 21 White blood cell count

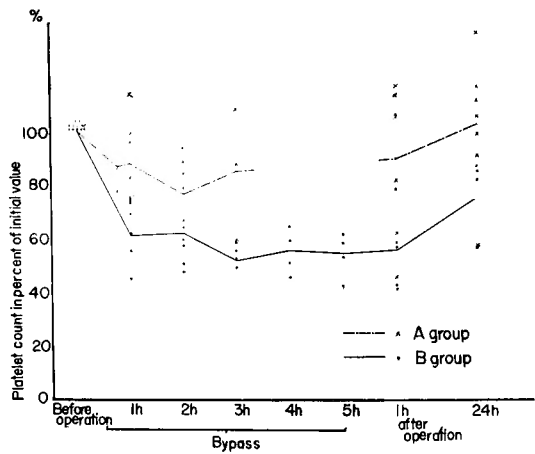
tes, which is 6 minutes and a half longer than that before it. While in group B, slight prolongation of coagulation time was observed in all cases during bypass circulation and in dog No. 82 it was prolonged up to 24 minutes after bypass circulation of 300 minutes, which is 10 minutes longer value compared with the value before it (Tab. 14, Fig. 24).

Circulating plasma volume decreased by 4 per cent in group A and 7 per cent in

Tab. 11 White blood cell count

Dog No.	Before operation	30' / 60' after by-pass	120'	180'	240'	300'	60' after ope.	24 hrs.
A Group								
46	15300	- / 4800	8400	10500	-	-	14000	188000
48	5400	5000/6200	-	-	-	-	-	-
50	19300	10200/10900	15000	17300	-	-	20100	20400
51	6400	- / 6400	6700	6200	-	-	6600	-
53	11000	- / 6800	8600	9300	-	-	11800	15200
58	7800	7300/-	9900	-	-	-	13100	14100
60	7700	3400/5200	6500	6600	-	-	6700	18200
65	6300	- / 6000	7100	7000	-	-	6700	11000
mean	9900	6500/6600	8900	9500	-	-	11300	16300
B Group								
81	4800	2400	1800	2800	3900	3800	6300	9200
82	15400	5800	12200	10600	9800	10000	12200	29600
86	12700	9800	11500	11700	-	-	13200	14000
88	7400	2100	3600	4800	5200	5100	6500	7600
96	7900	6700	5700	6800	7200	7600	9500	12100
mean	9600	5400	7000	7300	6500	6600	9500	14500

Fig. 22 Platelet count



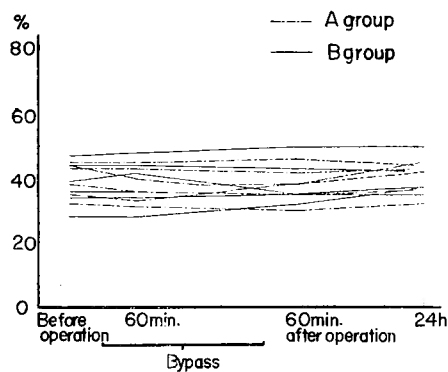
group B 24 hours after bypass circulation.

Circulating blood volume decreased by 3.5 per cent in group A and 4.52 per cent in group B 24 hours after bypass circulation (Tab. 15, Tab. 16, Fig. 25).

Plasma fibrinogen was estimated in only group B and it showed decrease of 21 per cent after 60 minutes' bypass circulation and 33.3 per cent 300 minutes after it, which restored to 62.2 per cent of the value before bypass circulation 1 hour after it

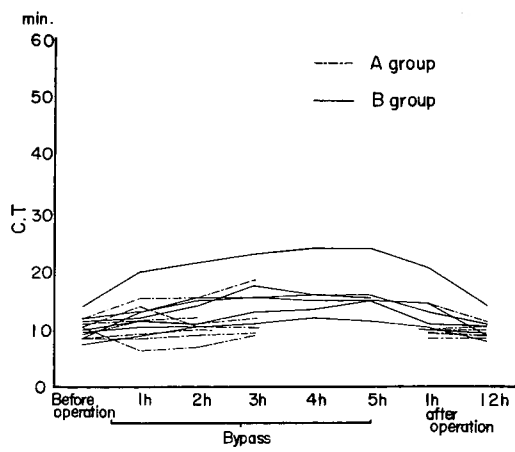
Tab. 12 Platelet count

Dog No.	Before operation	30'/60' after by pass	120'	180'	240'	300'	60' after ope.	24 hrs.
A Group ($\times 10^3$)								
46	294	-/216	196	174	—	—	134	168
48	106	-/120	—	114	—	—	122	110
51	330	-/272	260	—	—	—	204	298
53	224	-/211	—	—	—	—	234	248
58	112	96/84	72	—	—	—	126	152
60	160	124/120	134	140	—	—	130	158
65	181	180/182	162	—	—	—	194	212
mean	201	/172	165	143	—	—	163	192
B Group ($\times 10^3$)								
81	226	168	108	132	146	132	96	196
82	202	112	102	100	92	86	84	114
86	356	246	332	188	—	—	278	300
88	310	192	178	172	184	192	182	254
96	298	134	178	124	152	160	168	194
mean	278	170	180	143	144	143	162	212

Fig. 23 Hematocrit ratio**Tab. 13** Hematocrit-ratio

A Group					B Group				
Dog No.	Before operation	By-pass 60 min.	60 min after ope.	24 hrs.	Dog No.	Before operation	By-pass 60 min.	60 min after ope.	24 hrs.
46	45	45	45.5	44	79	44	44	43	42
48	43	43	42	43	83	28	28	32	37
50	32	31	30	32	85	36	36	—	—
53	35	33	38	42	88	39	41.5	35	37
58	38	36	35	36	92	34	34	35	35
65	42	40	38	45	95	47	48	50	50
mean	39.1	38.0	38.0	40.3	mean	38	38.5	39.0	40.2

Fig. 24 Coagulation time



Tab. 14 Coagulation time

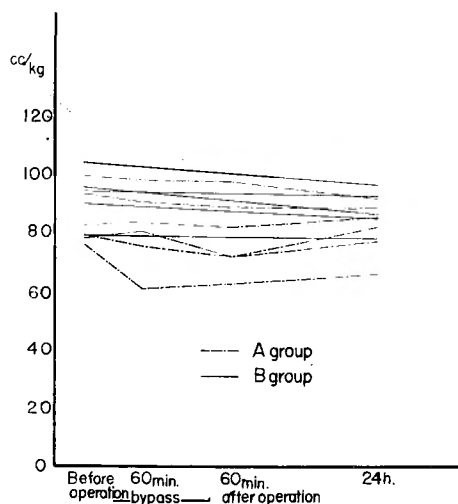
Dog No.	Before operation	Bypass 60 min.	120 min.	180 min.	240 min.	300 min.	60 min. after ope.	12 hrs.
A Group								
51	8'30"	—	10'	—	—	—	9'30"	9'
53	8'30"	8'30"	9'	9'30"	—	—	8'30"	8'30"
57	10'30"	11'	10'30"	10'30"	—	—	—	—
58	12'	15'30"	15'30"	18'30"	—	—	14'30"	11'30"
59	9'	11'30"	11'	12'	—	—	10'	16'
60	10'30"	6'30"	7'	9'	—	—	9'30"	9'
61	11'	11'30"	12'	—	—	—	10'	10'30"
B Group								
81	8'30"	15'	15'30"	15'30"	15'	15'	14'30"	9'
82	11'	20'	21'30"	23'	24'	21'	26'30"	14'
83	7'30"	9'	10'30"	11'	12'	11'30"	10'30"	8'
85	11'30"	12'	14'	17'30"	16'	15'30"	—	—
86	9'30"	10'30"	10'30"	11'	—	—	10'	9'30"
88	12'	13'	15'	15'30"	16'	16'	13'	11'
96	10'	11'30"	11'	13'	13'30"	15'	11'30"	16'30"

and 87.2 per cent 24 hours after it (Tab. 17, Fig. 26).

Plasma hemoglobin concentration was also studied in only group B. It showed lineal increase as time of bypass circulation went on, reaching 169.8 mg/dl on the average 5 hours later, which gradually decreased to 48.4 mg/dl 24 hours after it, 17.3 mg/dl 48 hours after it. In dog No. 81, the concentration was 252.3 mg/dl 5 hours later (Tab. 18, Fig. 27).

Slight decrease in serum protein was observed both in group A and B (Tab. 19, Fig. 28).

Fig. 25 Circulating blood volume



Tab. 15 Circulating plasma volume (cc/kg)

A Group					B Group		
Dog No.	Before operation	By-pass 60'	60' after ope.	24 hrs.	Dog No.	Before operation	after 24 hrs.
46	51.6	50.0	48.7	50.1	79	58.4	56.5
48	56.8	56.1	57.0	52.8	83	57.0	49.5
50	54.2	52.3	50.6	56.1	85	51.3	—
53	49.4	40.9	38.9	38.5	88	57.9	59.0
58	48.4	51.5	47.1	51.2	92	59.5	55.8
65	48.0	50.3	51.2	47.5	95	50.8	43.6
mean	51.4	48.5	48.9	49.4	mean	56.3	52.9

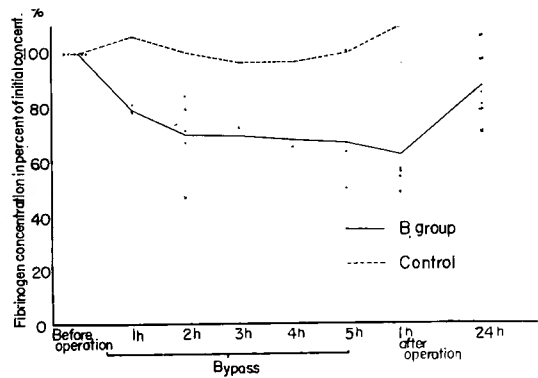
Tab. 16 Circulating blood volume (cc/kg)

A Group					B Group		
Dog No.	Before operation	By-pass 60'	60' after ope.	24 hrs.	Dog No.	Before operation	after 24 hrs.
46	93.8	90.9	89.3	89.5	79	104.3	97.4
48	99.6	98.4	98.2	92.6	83	79.2	78.7
50	79.7	75.8	72.3	82.9	85	84.8	—
53	76.0	61.0	62.7	66.3	88	94.9	93.7
58	78.1	80.4	72.4	77.5	92	90.2	85.7
65	82.8	83.8	82.5	86.3	95	95.8	87.2
mean	85.0	81.7	79.6	82.5	mean	91.5	88.5

In albumin-globulin ratio, no definite tendency was observed both in group A and B (Tab. 20, Fig. 29).

B. S. P. test as determined at 15th minute showed slight increase in retention 24

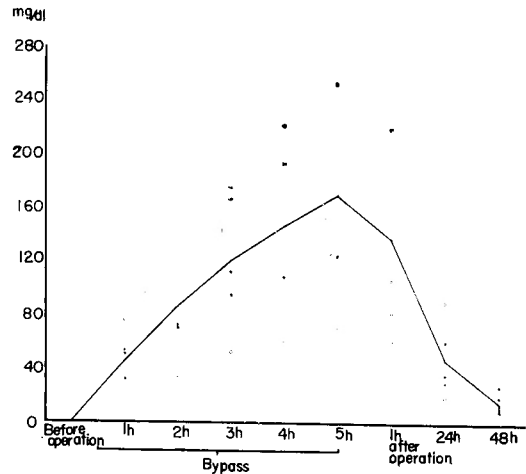
Fig. 26 Fibrinogen concentration in group B.



Tab. 17 Fibrinogen concentration in group B. (mg/dl)

Dog No.	Before operation	By-pass 60 min.	120 min.	180 min.	240 min.	300 min.	60 min. after op.	24 hrs.
81	462	363	390	240	237	232	260	327
82	633	394	300	354	336	336	309	498
86	394	372	264	237	—	—	213	334
88	435	341	311	462	444	437	415	457
96	570	462	455	415	372	360	322	551
mean	499	386	324	342	347	341	304	433
control	534	566	534	512	516	511	580	—

Fig. 27 Plasma Hb concentration in group B.

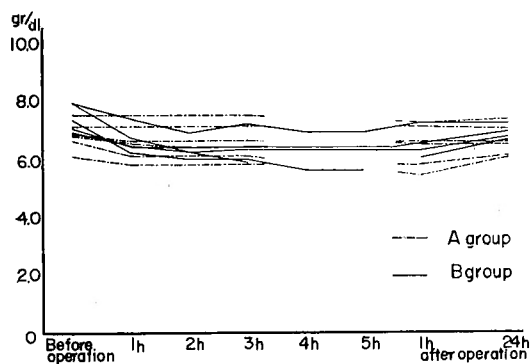


hours after bypass circulation in group A and 48 hours after it in group B (Tab. 21, Fig. 30).

By portal interruption, slight bradycardia was observed electrocardiographically in

Tab. 18 Plasma Hb. concentration in group B. (mg/dl)

Dog No.	By-pass 60 min.	120 min.	180 min.	240 min.	300 min.	60 min. after ope.	24 hrs.	48 hrs.
81	53.6	117.1	175.7	221.7	252.3	219.7	90.8	29.2
82	77.8	138.0	167.0	193.4	230.7	221.0	61.9	20.1
86	32.5	72.5	112.5	—	—	82.2	31.2	11.7
88	21.9	35.6	53.6	61.5	71.2	62.8	20.7	12.1
96	52.7	71.6	95.8	109.9	125.2	107.6	37.3	13.3
mean	47.7	86.9	120.9	146.6	169.8	138.7	48.4	17.3

Fig. 28 Serum protein**Tab. 19** Serum protein

Dog No.	Before operation	By-pass 60'	120'	180'	240'	300'	60' after ope.	24 hrs.
A Group								
51	6.84g/dl	6.64 g/dl	6.64 g/dl	6.64 g/dl	—	—	6.60g/dl	6.60g/dl
52	7.51	7.51	7.51	7.51	—	—	7.21	7.34
53	6.81	6.61	6.41	6.41	—	—	6.61	6.71
60	6.62	6.12	6.12	6.12	—	—	5.42	6.04
61	6.12	5.82	5.82	5.82	—	—	5.82	6.12
62	7.12	7.12	7.12	7.12	—	—	7.12	7.02
mean	6.84	6.64	6.60	6.60	—	—	6.46	6.64
B Group								
81	7.04g/dl	6.44g/dl	6.44 g/dl	6.44g/dl	6.44 g/dl	6.44g/dl	6.54g/dl	6.94g/dl
82	7.92	6.72	6.22	6.32	6.32	6.32	6.32	6.77
85	7.31	6.21	6.01	6.01	5.61	5.61	—	—
86	6.87	6.47	6.27	5.87	—	—	6.07	6.67
88	7.91	7.41	6.91	7.21	6.91	6.91	7.21	7.21
mean	7.21	6.65	6.37	6.37	6.32	6.32	6.54	6.90

Tab. 20 A/G Ratio

A Group				B Group			
Dog No.	Before operation	After operation	24 hrs.	Dog No.	Before operation	After operation	24 hrs.
53	0.78	0.73	0.69	81	0.92	1.0	1.1
58	0.87	0.77	0.91	82	1.21	1.02	0.90
60	0.98	0.96	0.94	86	0.92	0.97	0.90
61	1.05	0.96	0.98	88	1.08	0.72	0.92
62	0.91	0.87	0.76	96	1.14	1.16	1.19
mean	0.92	0.86	0.86	mean	1.05	0.97	1.00
control	0.97	0.94	0.96				

Fig. 29 A/G ratio

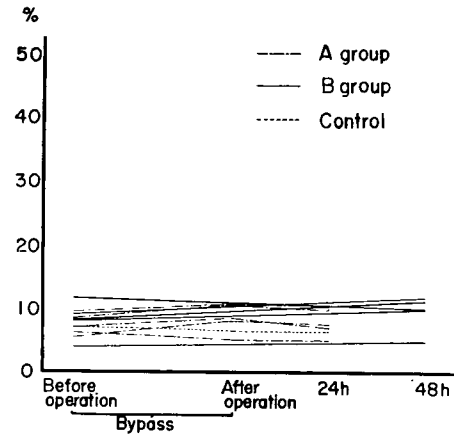
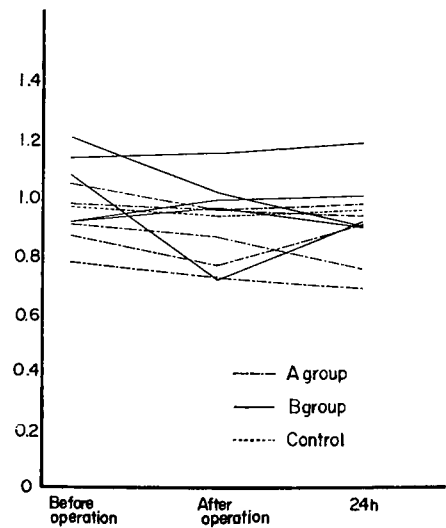
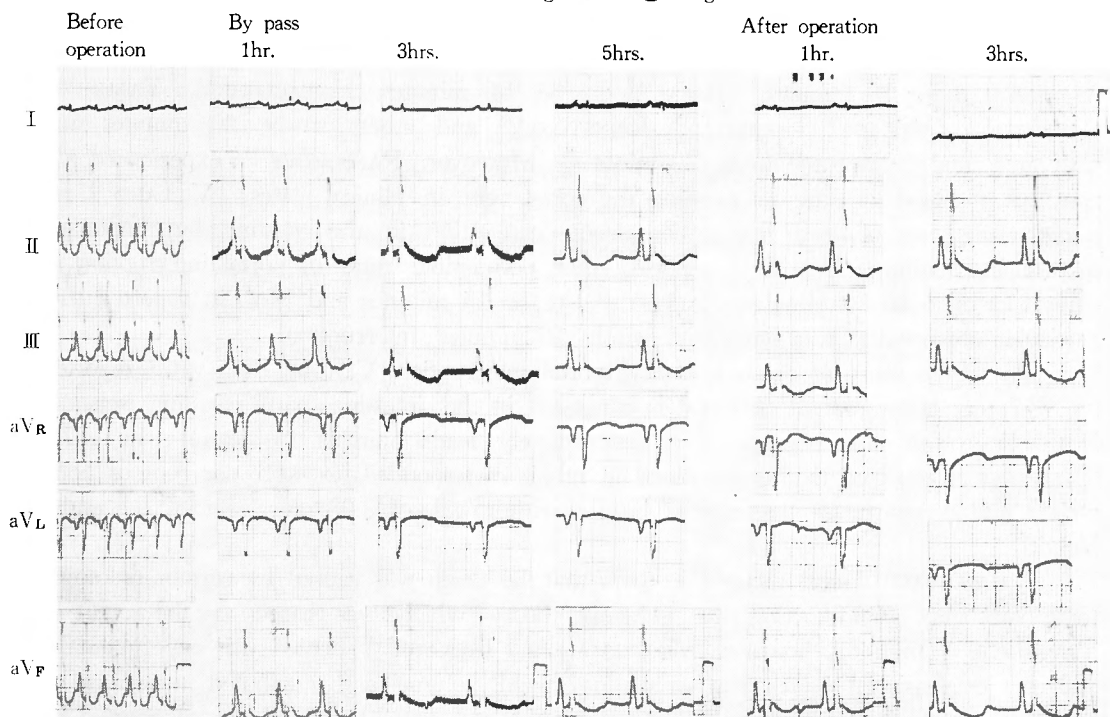


Fig. 30 BSP test



Tab. 21 BSP-test

A Group				B Group		
Dog No.	Before operation	After operation	24 hrs.	Dog No.	Before operation	48 hrs.
51	7%	8.5%	7%	80	8%	10%
52	6.2	5	5	81	8.2	11
60	8.5	10.5	10	82	4	5
61	5.5	8	7.5	86	9	11.5
62	9.4	10.5	10.5	96	11.5	10
mean	7.3	8.5	8.0	mean	8.1	9.5
control	7	6.5	6.5			

Fig. 31 Dog No. 82 ♂ 13kg

all cases, except a dog of No. 86. Slight prolongation of P-Q time and increase in the amplitude of P wave were also observed, which, however, restored to normal as time elapsed during bypass circulation. Neither appearance of myocardial infarction nor change in S-T segment and T wave was observed (Fig. 31).

Macroscopically, there was no change such as hemorrhage, petechia or edema in the mesentery and intestine during bypass circulation and there was no change in tincture of the intestine compared with that before bypass circulation both in group A and B.

Histological study of intestine revealed no abnormality in group A, with some exceptions of edema in the villi and hemorrhage in its apices, while in group B intestinal bleeding was observed in no case, villi and epithelium revealing no change (Fig. 32, 33).

Histological study of liver revealed slight congestion around central vein 24 hours after bypass circulation both in group A and B. No change was observed in liver cells, showing no thrombus and glycogen content being normal (Fig. 34, 35).

IV. DISCUSSION

It has long been known that animals are led to death by acute and complete interruption of the portal vein. Since ORE⁶⁰⁾ reported in 1856 that death resulted very early in rabbits after acute and complete interruption of the portal vein, survival time of the portal interruption has been variously reported by SOLOWIEFF⁷⁸⁾ to be 4 to 22 hours, by SCHIFF⁷⁹⁾ and CLAUDE BERNARD³⁾ to be 3 hours, by NEUHOF⁵⁷⁾ to be 50 to 90 minutes, by ELMAN and COLE²⁶⁾ to be 66 minutes, by BOYCE⁷⁾ to be 87 minutes, by PECK⁶⁶⁾

to be 60 minutes, by JOHNSTONE⁴⁰⁾ to be 79.7 minutes and by TANTURI⁸³⁾ to be 125 minutes.

On the other hand, concerning permissible time of portal interruption, BURDENKO⁹⁾ reported it to be 10 minutes, DANIEL¹⁸⁾ to be 14 minutes, HATAGOSHI³³⁾, YABUKI⁹²⁾, RAFFUCCI⁷³⁾, CSILLAG¹⁷⁾, GOODALL³¹⁾, JOHNSTONE⁴⁰⁾ and others to be 20 minutes and CARTER¹²⁾ and OYANAGI⁶³⁾ to be 30 minutes. Moreover, RANSOHOFF⁷¹⁾ experienced abrupt fall of blood pressure by pressing the portal vein in clinical cases. VILLARD⁸⁶⁾ reported some cases of death due to conspicuous congestion in the intestine by tamponade in the liver hilum. WARVI⁸⁷⁾ reported that permissible time of portal interruption in clinical cases to be 30 minutes, RAFFUCCI⁷³⁾ to be 15 minutes and MIKAMI reported that particular abnormality was not found within 15 minutes' interruption.

As to the cause of death following portal interruption, CLAUDE BERNARD³⁾ reported in 1877 that large amount of blood is congested in the intestine with resulting ischemia in the brain and other organs, which immediately leads animals to death. In 1872, TAPPEINER⁸⁴⁾ reported that entire blood in rabbit corresponded to 4.68 per cent of body weight and demonstrated that rabbits survive withdrawal of 3.08 per cent of the entire blood.

LAUTENBACH⁴⁴⁾ also thought in 1877 that the death was caused by certain unknown toxic substance, contradicting the ischemia theory which was based on the report of TAPPEINER. In 1885, however, MOSSELMAN and LIENAU⁵⁴⁾ denied this experimentally and put emphasis on decrease in circulating blood volume and attributed the cause of death to insufficiency of oxygen and carbonic gas content, which was supported by CASTAIGNE and BENDER¹³⁾.

As the toxic product in the intestinal tract is not decomposed in the liver, NETTER⁵⁶⁾ thought in 1884 the cause of death to be due to this toxin. In 1913, NEUHOF⁵⁷⁾ considered that death was not caused by acute ischemia or intoxication, but caused by shock secondary to intense and rapidly developing congestion in the intestine and swelling of this organ. In 1929, KRYMHOLZ⁴³⁾ attributed the cause of death to debility of cardiac function, based on the facts that blood amount pooled in the splanchnic area is not so large to affect general circulation and further to lead animals to death, and that animals sometimes die gradually being emaciated, whereas animals sometimes die with convulsion as is usually observed in cerebral anemia or intoxication.

In 1934, ELMAN and COLE²⁶⁾ determined circulating blood volume and concluded that death of portal interruption was caused by decrease in circulating blood volume due to rapidly developing congestion in the splanchnic area, which was of the same mechanism as in hemorrhagic shock. He reported that the decrease in circulating blood volume was 5.2 per cent of body weight as determined by weighing abdominal organs. BOYCE⁷⁾ and others repeated in 1935 the experiment of ELMAN and COLE and observed increase of 3.05 per cent in weight of the intestine following portal interruption. They further reported that death did not result by withdrawal of 4.56 per cent blood of body weight, on the average, but animals died of shock by blood withdrawal of at least 5.8 per cent. From these findings, they implicated a neurogenic factor in the cause of death. In 1950, MALLET-GUY⁴⁸⁾ observed at portal interruption decrease of 49.3 per cent in circulating blood volume, which corresponds to 4.9 per cent of body weight as determined by

CHICAGO-blue method.

CHILD¹⁴⁾ also is of opinion that the death is caused by shock induced by abrupt decrease in circulating blood volume. In 1957, JOHNSTONE⁴⁰⁾ observed decrease of 57.9 per cent in circulating blood volume by the use of radioactive ³²P. He, however, presumed a participation of some other unknown etiologic factor in the cause of death, although admitting the importance of decrease in circulating blood volume. In 1960, CARTER¹²⁾ reported that anoxia in the tissues and accumulation of metabolic products play an important role in intestinal hemorrhage and cause of death. In 1962, TAKAMATSU⁸²⁾ reported that the cause of death was shock secondary to the decrease of 40.3 per cent in circulating blood volume as determined by Evans-blue method.

As has been surveyed in numerous literatures concerning the cause of death of portal interruption, no acceptable theory is established yet. However, congestion in the splanchnic area following portal interruption is the most attracting phenomenon, which has been regarded by many researchers widely as an important factor of the death.

At this acute and complete portal interruption, devices and experiments have been carried out to prolong permissible time of the interruption based on the cause of death.

Namely, CASTAIGNE and BENDER¹³⁾, ELMAN and COLE²⁶⁾, BOYCE⁷⁾, NELSON⁵⁵⁾, OYANAGI⁶³⁾ and others tried to reduce blood flow into the splanchnic area by simultaneous interruption of the aorta, celiac or superior mesenteric artery. ELMAN and COLE, PECK and GROVER⁶⁶⁾ intended to retrench the area of congestion and hemorrhage with resulting prevention of abrupt decrease in circulating blood volume by removing the intestine and spleen, and performed blood and fluid transfusion to fill up the decrease in circulating blood volume. RAFFUCCI⁷³⁾, NELSON⁵⁵⁾ and others intended to inhibit growth of anaerobic flora in the liver and intestinal flora by the administration of antibiotics such as penicillin, aureomycin and streptomycin. RAFFUCCI and PECK⁶⁶⁾ also intended to strengthen adrenocortical defence reaction against stress by the administration of ACTH, and to prolong survival time by the vagus block in the aim of lessening initial fall of blood pressure, which is caused by stimulation of subserous endings of the vagus and sympathicus in the intestine due to circulatory disorder brought about by portal interruption. Experiments have been made to reduce blood flow and oxygen consumption in the tissues by the aid of hypothermia by RAFFUCCI, CSILLAG¹⁷⁾, BERNHART⁴⁾, GOODALL³¹⁾, CARTER¹²⁾ and TAKAMATSU⁸²⁾, and by the aid of vagus block by THÖLE⁸⁵⁾.

In either of these experiments, permissible time was at most prolonged up to 60 minutes.

On the other hand, ORE⁶⁰⁾, in 1856, was the first to demonstrate the feasibility of gradual interruption of the portal vein in dogs, which was ascertained by BRUNSCHWIG⁸⁾ in 1945. SOLOWIEFF⁷⁸⁾ showed in 1875 that animals may be saved by ligation of the branches of the portal vein in stages, and ITO and OMI³⁹⁾ approved of this observation in 1902. NEUHOF⁵⁷⁾ demonstrated in 1913 that animals survived the complete interruption after constricting the lumen of the portal vein gradually. POPPER⁶⁸⁾ also reported the similar results.

In 1960, HOFFMAN³⁶⁾ prevented death of the animals by preliminary transposition of the spleen into the thoracic cavity, thus creating collateral circulation.

In 1877, ECK²⁵⁾ reported that dogs do not die after portal interruption by the establishment of portocaval anastomosis which makes portal blood drain into systemic circulation regardless of development of collaterals. SCHAFER⁷⁵⁾ and KOZY reported also survivals of portal interruption by establishing end-to-side anastomosis using BLAKEMORE's tube.

In 1950, CHILD¹⁴⁾¹⁵⁾ demonstrated in his experiment of acute and complete portal interruption in macaca mulatta monkey, that 59 cases out of 76 survived for long without any disorders, although 6 cases out of 76 died of congestion as ascertained by autopsy. He attributed the cause of favorable survival rate in monkeys to the fact that portal blood streams into systemic circulation chiefly through the intrapelvic collaterals after the interruption.

Hereupon, he performed simultaneously pancreatoduodenectomy and portal resection in the above mentioned animals. However, all the animals died of utterly untractable massive bleeding from the site of the operation caused by necessarily accompanying portal hypertension. At this point, he postulated so-called two stage operation in which the portal vein is initially ligated, and after adequate development of collaterals with resulting lowering of portal pressure, pancreatoduodenectomy and portal resection are performed. However, HONJO³⁷⁾ pointed out in 1962 that this operative measure is constantly accompanied by various difficulties, and now CHILD himself does not adopt this measure.

On the other hand in 1926, COLP¹⁶⁾ performed acute portal interruption in 3 clinical cases of pylephlebitis and all the patient died ultimately, but he concluded that the cause of death did not consist in the interruption itself. In 1945, BRUNSCHWIG⁸⁾ reported that death resulted 8 days after portal resection in a patient of pancreatic cancer with invasion to the portal vein, and he considered that the cause of death was not portal interruption, but bile peritonitis, since they observed adequate development of collaterals already at initial laparotomy. In 1950, PARSONS⁶⁴⁾ and PERSON and DEVINE⁶⁷⁾ respectively reported successful cases of simultaneous resection of pancreatic cancer and the portal vein in a single stage. They predicted that serious bleeding would not occur by portal interruption in these cases because the collaterals had already developed at the time of laparotomy owing to partial occlusion of the portal vein. In 1960, PATTON and JOHNSTONE⁶⁶⁾ reported 2 cases of post-traumatic portal and splenic ligation, in which, however superior mesenteric-caval anastomosis was necessary due to portal hypertension after the operation.

In 1952, McDERMOTT²²⁾ postulated an operative measure of one stage resection with establishment of an ECK's fistula, contradicting the concept of the two stage operation from the reason that two stage operation should be avoided particularly in cancer and hemodynamics of the portal system must be maintained in normal state as much as possible. This operation of one stage resection with establishment of an ECK's fistula was performed thereafter by ZIMMERMAN⁹³⁾ in 1 case and by Hubbard in 2 cases. It is reported that all these patients died of ammonia intoxication, hypoalbuminemia and fatty infiltration of the liver 20 months after in McDERMOTT's case and 3.5 months and 7 months after in 2 cases of HUBBARD³⁸⁾, respectively. Establishment of ECK's fistula has some different influence from that in portal hypertension. Namely, it suggests that possibility of ECK's fistula syndrom or liver failure is larger at establishment of ECK's

fistula in the cases of normal liver function without portal occlusion and necessarily deprived of development of collaterals. This fact was already proved by animal experiment of BOLLMAN⁶⁾.

On the other hand, STARZL and KAUPP⁸⁰⁾ established temporary ECK's fistula in order to avoid congestion in the splanchnic area at hepatic blood flow interruption for total liver resection in the experiment of liver transplantation in animals and the fistula was reconstructed to the previous state after the transplantation. Thus, several trials were carried out to make portal blood flow into the systemic circulation in the aim of preventing congestion in the splanchnic area with resulting shock at portal interruption. In 1952, PECK⁶⁹⁾ reported experiment of portal-femoral vein bypass in dogs and in 1958 BARNETT²⁾ performed portal interruption for 60 minutes with splenic-femoral vein bypass through external shunt of polyethylene tube. After that in 1960, DATE¹⁹⁾ performed portal interruption of 60 minutes in dogs, by the aid of mesenteric-femoral vein external shunt and transfusing the portal blood bled from the mesenteric vein using pump and 10 out of 16 animals died. In 1961, MAN⁴⁹⁾ reported that portal interruption was safely carried out for 90 minutes without fall of blood pressure by splenic-femoral vein bypass using MAYON plastic tube. Anatomical relationship of the portal vein, however, much differs in man from that in dog, the splenic vein usually draining into the portal trunk behind the head of the pancreas. Accordingly, the portal vein of this region is naturally included in resection at the surgery of the pancreatic head, and it is assumed to be difficult to apply MAN's method in clinical cases.

From the consideration of literatures it is assumed that acute and complete interruption of the portal vein is always lethal in dogs, and even though it is not fatal, judging from the experiment in monkey of CHILD, considerable danger is prospected at surgery around the portal vein in man, being associated with various disturbances accompanying to it.

In addition, it is suggested that congestion in the splanchnic area and resulting various disturbances can be prevented by adequate development of collaterals or positive establishment of those.

Hence, the author of the present experiment carried out to make portal blood flow temporarily into the femoral vein at portal interruption by the use of pressure difference between the portal and femoral veins or the use of pump intervening between a branch of the mesenteric vein and femoral vein, as a clinically applicable method.

The results were utterly unfavorable in the experiment of anticoagulant administration of 2 mg/kg body weight, survivals being only 4 cases out of 18 in portal interruption for 180 minutes, which approximately corresponds to the results of DATE. This was presumably due to hemorrhagic shock caused by untractable oozing from the operative field. Subsequently, polybrene was infused as antiheparin agent from the outlet cannula simultaneously with bypass circulation. Polybrene has an advantage over protamine sulfate in the respect that it is stable itself as chemical material.

Concerning heparin neutralizing effect of polybrene, PRESTON⁶⁹⁾ reported that neutralizing proportion was 0.7 to 0.5 as estimated from in vivo coagulation test, WEISS⁸⁹⁾ reported it to be 1 to 0.7 at extracorporeal circulation, SAEGUSA⁷⁴⁾ and SHIMIZU⁷⁷⁾ also

to be 1 to 0.7 or 1, LILLEHEI⁽⁴⁵⁾ and NILSEN⁽⁵⁸⁾ to be 1 to 1 and the author of the present experiment obtained optimal proportion of 1 to 0.7, though determined only from the observation of coagulation time in vitro and in vivo.

As to the method of administration, KEATS⁽⁴²⁾ and others administered intravenously within 15 to 60 seconds in a concentration of 1mg/ml at the end of bypass circulation, SAEGUSA adopted intravenous injection within 30 to 120 seconds or intra-auricular injection on the right side and WEISS stated that it is preferable to administer within 5 minutes.

From an original idea, the author of the present experiment infused heparin and polybrene during bypass circulation simultaneously in the proportion of 1 to 0.7 so that the heparin infused from inlet of the circuit might be neutralized at its outlet. By this device, bypass circulation was successfully achieved without formation of clot mass within the circuit, on the other hand maintaining normal coagulability within the organism, without unfavorable side effect such as oozing or rebound phenomenon of heparin.

It is necessary to minimize head loss as possible at the arrangement of extracorporeal circuit by the use of pressure difference. Accordingly, small vessel is not suited for this purpose, but a vessel as large as possible is required. As the splenic vein has a large caliber as the stem of the superior mesenteric vein, it can be used most favorably. It is, however, impossible to use this vessel when the operative procedure involves this vessel.

From this point, external bypass circulation was carried out from the portal trunk to femoral vein using pressure difference. By this method, 73 per cent of survival rate was obtained in portal interruption of 180 minutes. On the other hand, as it was necessary to interrupt portal flow at the insertion and withdrawal of the cannula, though for a while, initial fall of blood pressure was inevitable as was pointed out by SOLOWIEFF⁽⁷⁵⁾, RANSOHOFF⁽⁷¹⁾, KRYMHOLZ⁽⁴³⁾ and PECK⁽⁶⁶⁾. Blood pressure was, however, stabilized thereafter and portal pressure was maintained during bypass circulation in the level of 1.3 times of that before it. Another problem at this procedure was that there was a possibility of fluctuation in the volume of blood flow owing to interference of the circuit to the operative field with resulting transition of the cannula and circuit. At this point, bypass was arranged from a branch of the mesenteric vein, distant from the operative site, to the femoral vein. In order to transport the same amount of portal blood as that before interruption to the femoral vein, it is necessary to annex energy corresponding to loss of energy due to resistance within the small vessel and head loss. Consequently, a power source of pump is required, and the author of the present experiment used a DE BAKEY roller pump, which is said to destroy less blood cells.

As it was ascertained in dog that the ligation of a branch of the mesenteric vein has no unfavorable influence, a branch of the mesenteric vein at the end of the ileum was used. Aspiration and transfusion of blood of 21.2 ml/kg body weight per minute, on the average, was achieved by equipping slender side holes on the both sides of metal cannula for a branch of the mesenteric vein. MAN reported that aspiration and transfusion of portal blood of 15 ml/kg body weight per minute was possible by way of the splenic vein.

Concerning the amount of portal flow in dogs, BURTON-OPITZ⁽¹⁰⁾ observed it to be 18.8 ml/kg body weight per minute, FISCHER⁽²⁸⁾ 30.8 ml/kg body weight per minute,

STEWART⁷⁹⁾ 24.6 ml/kg body weight per minute and HEIMBURGER⁸⁴⁾ 30.1 ml/kg body weight per minute and HEIMBURGER calculated it to correspond to 23 per cent of stroke volume.

According to BLALOCK and MASON⁵⁾, it was 21.6 ml/kg per minute. At the transfusion volume of 21.2 ml/kg per minute, on the average, in the present experiment, there was observed no fall of blood pressure, portal pressure restored gradually to the level before interruption, although initially elevated to the level of 1.5 times of normal, and the intestine showed normal tincture, without petechia on the mesentery and hemorrhage in the intestinal tract, furthermore, decrease in circulating blood volume being checked as little as 4.5 per cent.

Initial fall of blood pressure of 20 mmHg is obviously due to the fact that the pump is let work in critical occlusive setting in the moment of cannula insertion before the portal vein is interrupted and accordingly blood is aspirated from the splanchnic area in a moment to fill up the bulk of 76 ml of the circuit.

At the portal interruption of 300 minutes under above mentioned procedures, blood pressure was stable throughout the experiment and survivals were obtained in 83 per cent.

Electrocardiographically, slight bradycardia and increase in amplitude of P wave were merely observed in the both groups of bypass circulation using pressure difference and pump, without showing unfavorable findings such as marked lowering of S-T segment or T wave and negative T as reported by TANTURI⁸³⁾ and RAUL⁷²⁾ to appear at portal interruption.

No particular change was found in cell component of blood, except those due to influence of heparin and polybrene, in the group of bypass circulation using pressure difference, while in the group using pump, although no change was observed in red blood cell count, lineal increase in hemoglobin concentration due to the disintegration of erythrocytes was noticed as the time of bypass circulation extended, reaching 169.8 mg/dl 300 minutes later. This is assumed to be due to physical impingement to blood and hemoglobin concentration increases naturally as rotation of the pump is accelerated with the increase in the amount of blood flow.

MALLONEY⁴⁷⁾ and McCAUGHAN⁵¹⁾ made comparative study on roller pump and metal finger pump and reported that hemolysis was more pronounced in metal finger pump on the condition of the similar amount of blood flow. CAPPELLETTI¹¹⁾ also reported that blood cell destruction was in the most slight degree in roller pump.

HODGES⁵⁵⁾ studied on the influence of degree of pressure at latex tube in the pump on hemolysis and reported that hemolysis was more conspicuous in occlusive setting than in non-occlusive setting, although amount of blood flow is maintained constant in the former.

Hemoglobin concentration restored up to 48.4 mg/dl 24 hours after bypass circulation and hemoglobin was hardly observed in plasma 48 hours after it.

According to GILLIGAN³⁰⁾ and OTTENBERG⁸²⁾, hemoglobin is taken and destructed by the reticuloendothelial system, until plasma hemoglobin concentration exceeds the kidney hemoglobin threshold, it is excreted from the kidney in the rate of 5 mg per 100 ml of plasma every minute.

In the present experiment, symptom such as anuria due to hemolysis was not

observed even in a case, which suggests that hemolysis of this extent alone has no influence upon organism.

FIDLER²⁷⁾ and QUICK⁷⁰⁾ observed in dog amazing decrease in platelet count, though temporarily, caused by heparin, and DOMINGO²³⁾ also reported decrease of 40 per cent in platelet at 1st hour of heparinization for 4 hours with constant concentration of heparin in dogs. The author of the present experiment observed decrease of 43 per cent in platelet at 1st hour of heparinization for 5 hours using heparin solution of 0.02 per cent, and decrease of 21.5 per cent in platelet was observed temporarily by the administration of polybrene. PRESTON⁶⁹⁾ and WEISS⁸⁸⁾ also reported temporary decrease in platelet.

Moreover, it is presumed that physical destruction by the pump might participate to some extent in this decrease in platelet, since the decrease is obviously larger in bypass circulation than the decrease caused simply by heparin and polybrene. OSBORN⁸¹⁾, DE WALL²¹⁾ and NILSSON⁵⁹⁾ reported decrease in platelet count in cardiac bypass.

GANS²⁹⁾ reported close correlation between the time of cardiac bypass and the decrease in platelet count.

Plasma fibrinogen decreased by 33.3 per cent after the experiment of 5 hours in the present experiment, which was presumed to be essentially due to bypass circulation. WRIGHT⁹¹⁾ and KAULLA⁴¹⁾ also reported decrease in plasma fibrinogen concentration in cardiac bypass, and they thought that the decrease was caused by pronounced fibrinolysis. On the contrary, GANS considered that this decrease is not caused by dilution of blood, increase in fibrinolytic activity or blood transfusion, but caused by intravascular clotting.

Concerning the liver function, SUGIURA⁸¹⁾ reported that it showed abrupt decay until 1 month and a half after ECK's operation and showed no further change as determined from hepatic efficiency.

In the present experiment, no change was found in liver function, which was presumably due to the fact that portal mesenteric vein bypass was performed temporarily within the period of time required for operation and the blood from the splanchnic area drained into the liver normally thereafter.

Histological studies of the liver revealed no change in liver cells, without showing any findings as reported by SOLOWIEFF⁷⁸⁾. Such findings as atrophy of liver cells in the central area of lobules, fatty degeneration and degeneration or necrosis of liver parenchyma as reported by BOLLMAN⁶⁾ and SUGIURA⁸¹⁾ were not observed.

In the intestine, congestion or edema could not be observed during bypass circulation, and microscopically congestion or hemorrhage was not demonstrated, or submucous edema as was observed by MORINO⁵³⁾ was not found in the group using pump.

As has been reported in the present paper, acute and complete interruption of the portal vein could be performed for long time without serious influence upon organism by the temporary use of portal-mesenteric vein bypass.

V. SUMMARY

1. Congestion in the splanchnic area during acute and complete interruption of the portal vein could be favorably prevented, by transporting portal blood to the systemic circulation through external bypass equipped with cannula originally devised by the author.

2. Survival rate of acute and complete portal interruption for 180 minutes using external bypass with single intravenous administration of heparin of 2 mg/kg body weight was 22 per cent, which was presumably due to untractable oozing from the operative field during the operation.

3. By infusion of heparin of 1 per 1 ml of blood flow in the portal cannula and silicization of external circuit, clot mass formation was not observed in the circuit, and by infusion of polybrene of 0.7 per 1 of heparin from the femoral cannula, coagulation time was well maintained within the range of normal, without showing oozing from the operative field.

4. Survival rate was 73 per cent in the portal interruption of 180 minutes using pressure difference and 83 per cent in the portal interruption of 300 minutes with a branch of the superior mesenteric-femoral vein bypass using pump.

5. No particular change was observed in circulating blood volume, liver function and electrocardiogram both in the group using pressure difference and pump.

As to the influence on blood components, plasma fibrinogen concentration, platelet count and white blood cell count returned to normal after bypass circulation and hemoglobin concentration also returned to normal 48 hours after it. Thus, acute and complete interruption of the portal vein could be carried out for long time without serious influence on organism.

At accomplishing the present experiment, the author wishes to express the greatest gratitude to Prof. Dr. ICHIO HONJO for his continuous and kind guidance, at the same time the author is deeply debted to Assistant Prof. Dr. KIGOSHI for his kind advices and to the member of our clinic for their kind helps.

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- (* Written in Japanese)

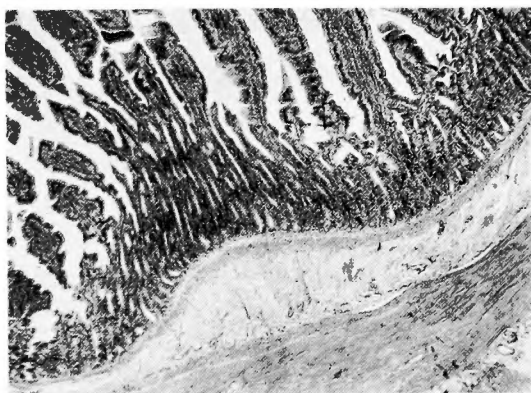


Fig. 1

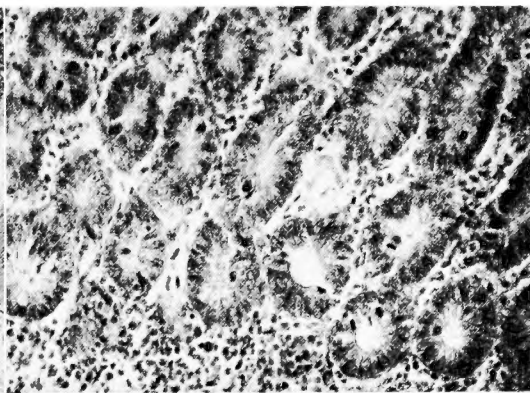


Fig. 2

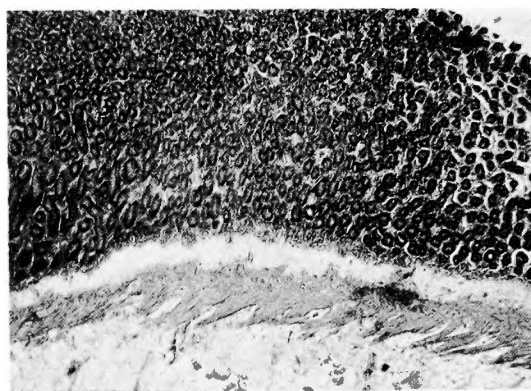


Fig. 3

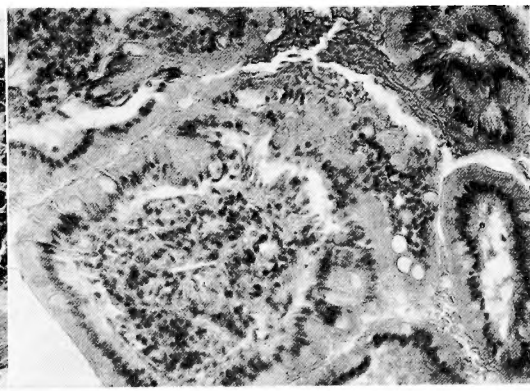


Fig. 4

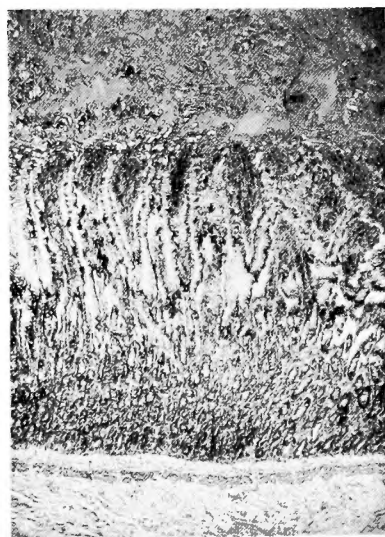


Fig. 5

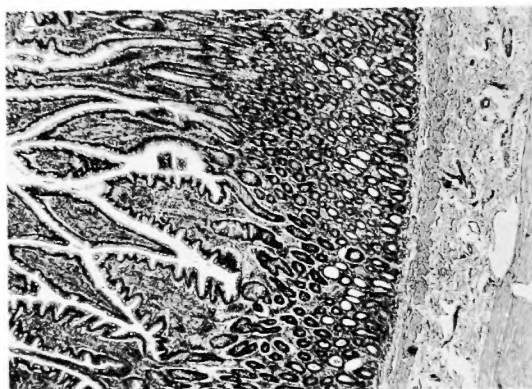


Fig.32

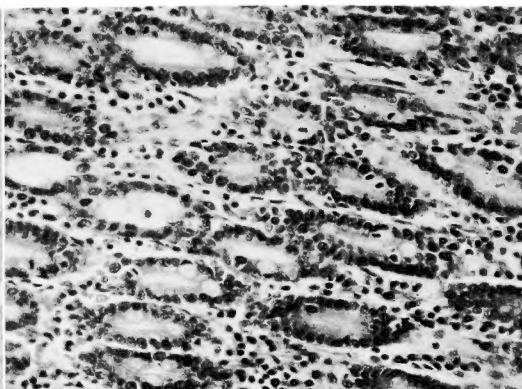


Fig.33



Fig.34

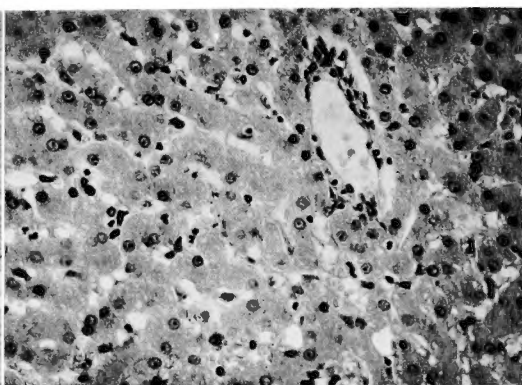


Fig.35

Fig. 1. Histological change of small intestine at portal hypertension of 2 times higher level for 3 hours. ($\times 50$)

Fig. 2. ($\times 300$)

Fig. 3. Histological change of small intestine at portal hypertension of 3 times higher level for 3 hours. ($\times 50$)

Fig. 4. ($\times 300$)

Fig. 5. Histological change of small intestine at portal hypertension of 4 to 5 times higher level for 3 hours.

Fig. 32. Small intestine after 300 minutes' bypass circulation by the use of pump in dog No. 96. ($\times 50$)

Fig. 33. ($\times 300$)

Fig. 34. Liver after 300 minutes' bypass circulation by the use of pump in dog No. 96. ($\times 50$)

Fig. 35. ($\times 300$)

和 文 抄 録

急速門脈完全遮断に対する一時的門脈、或は上腸間膜
静脈—股静脈 Bypass に関する実験的研究

金沢大学医学部第2外科学教室（指導：本庄一夫教授）

北 川 勲

門脈血流の一時的遮断が一定時間可能となるような方法が確立されたならば、本法を出血量の多い肝広汎切除、脾頭十二指腸切除に応用し得る。

著者は犬を実験対象として、急速門脈完全遮断時、門脈血流を体循環系へ Bypass する方法、即ち門脈圧と股静脈圧との圧差を利用する体外回路造設法、及び腸間膜静脈の1分枝よりポンプを使用する事による体外回路造設法を著者の考案したカニューレを用いて検討し、次の結果を得た。

(1) 門脈流域のうつ血をさける事が出来た。

(2) ヘパリン2mg/kg静注1回投与による体外回路造設に際しては、180分急速門脈完全遮断で22%の生存率を得た。この際、術中術野から多量の異常出血が見られた。

(3) 体外回路内シリコン処置によつて、門脈カニューレ内血流量1ccに対して、1γ量のヘパリン点滴投与

で回路内凝血形成なく、股静脈カニューレ内に、ヘパリン1に対してポリブレン0.7の比で同時にポリブレンを点滴投与する事により回路外生体においては、血液凝固時間は略正常値を保っており、同時に術野からの異常出血は全く認めなかつた。

(4) かゝる方法により、圧差利用群では、180分門脈遮断に対して73%の生存率を、ポンプ使用群では、300分間門脈遮断に対して、83%の生存率を得た。

(5) 圧差利用群、ポンプ使用群共に循環血液量、肝機能に著変を認めず、心電図学上にも著変を認めなかつた。

血液成分に及ぼす影響も、フィブリノゲン量、血小板数、白血球数は術後回復しており、溶血度も術後48時間で略術前値にまで回復している。

かゝる方法により、全身的影響少なく、長時間にわたる急速門脈完全遮断を施行し得た。