W. L. OLSZEWSKI, S. SZYFELBEJN, J. NIELUBOWICZ

EXPERIMENTAL PORTAL HYPERTENSION AND ASCITES FOLLOWING PARTIAL STRICTURE OF THE COMMON BILE DUCT

Department of Experimental Surgery, Polish Academy of Sciences, Warsaw

SUMMARY

The constriction of the common bile duct by 50—70 per cent causes in dogs apart from cholestasis a complete picture of portal hypertension. The changes were observed mostly in the 13th week after the operation. The increase of the portal pressure, development of the abdominal collateral circulation and ascites were the characteristic signs. The authors suggest the method of partial constriction of the common bile duct as a model for studies on portal hypertension.

* *
*

The experimental stricture of the common bile duct is followed by considerable bile stasis, and very often by disturbances in the portal circulation. These abnormalities consist in the increase of the portal blood pressure, development of the collateral circulation and ascites. They usually appear six weeks following surgical procedure.

The finding of complete picture of changes considered typical for portal hypertension was fully unexpected. Some experiments were undertaken therefore to explain following problems:

1. How far are the developed disturbances of the portal circulation similar to those observed in liver cirrhosis?
2. What is the degree of the portal hypertension developed in these conditions?
3. What is the mechanism of ascites formation?
4. Could the partial constriction of the common bile duct be used for the experimental production of portal hypertension and ascites?

MATERIAL AND METHODS

The experiments were performed on 15 dogs, weighing 13 to 16 kg. The laparotomy was performed under eunarcone narcosis. A plexiglas ring, with inside diameter of 2—3 mm, was inserted on the common bile duct. As the average diameter of the normal duct in the dog is 4 mm, its lumen was thus narrowed by 50% to 75%. The animals were examined every two weeks and their general conditions, degree of cachexia, dilatation of the superficial veins and formation of ascites were studied. Next, laparotomy was performed after a full development of these abnormalities. Special attention was paid to visceral veins and collateral circulation. The condition of lymphatic vessels, lymph nodes and spleen was evaluated. The liver and bile ducts were inspected and the amount of ascitic fluid was measured. The pressure in the portal vein and in the inferior vena cava below and above the diaphragm was measured using the water manometer. The pressure in the biliary tracts was also estimated. The samples of ascitic fluid and the lymph from the intestinal and hepatic ducts and from the thoracic duct were examined. Subsequently the splenoportography was performed with a seriograph „Odelca" using 50% triuropan. At autopsy attention was paid to see if the portal vein was narrowed or occluded. Liver sections were taken for histopathological examination.

RESULTS

Six to thirty-one weeks were needed for the formation of distinct symptoms of portal hypertension and ascites. Out of 15 dogs, these abnormalities developed in 12, that is in 80% of the examined animals.

The dilated superficial venous vessels and vessels of the omentum adhered to the scar remaining after the initial laparotomy and usually caused a serious bleeding. After the laparotomy the first thing we noticed were the markedly dilated omental and mesenteric veins, the multiple tortuous vessels of the collateral circulation between the mesenteric veins and the inferior vena cava and the left renal vein in the falciform ligament of the liver and periesophageal veins. In the intestinal mesenterium dilated lymphatic vessels could be seen. At the basis of the intestines significantly enlarged lymph glands were found and around them in the retroperitoneal space there were large pools of transparent, straw-colored fluid. Markedly dilated vessels of *cisterna chyli* could be noticed in the retroperitoneal space on the anterior surface of vertebral column.

Ascites was found in 11 dogs. The fluid was transparent, straw-colored and did not coagulate after it was removed from the peritoneal cavity. The circumscribed pools of similar fluid were seen many times in the omentum and in the gastrocolic ligament.

The liver was usually of normal size, had a smooth surface and brownish-green color. There was no exudation of liquid on its surface. The extrahepatic

bile ducts and the gall bladder were usually distended. The bile had black-green color and was very thick. In each case markedly distended lymphatic vessels could be noticed in the hepatic hilus, and the outflowing lymph was yellow. The lymph nodes in the hepato-duodenal ligament were markedly enlarged and greenish-brown. The spleen was of normal size. At autopsy no narrowing or thrombosis of the portal vein were seen. The pressures found in the portal vein and in the biliary ducts are presented in Table I.

Table I

Dog's number	Time of observation in weeks	Collateral circulation	Pressure in the portal vein in cm of H_2O	Dilatation of the lymphatic vessels	Amount of the ascitic fluid in ml	Pressure in the biliary tracts in cm of H_2O	Presence of bile in duodenum
126	6	++	19	+++	30	18	—
165	10	+++	29	+++	1000	13	+
136	10	++	23	+++	500	14	+
134	11	+	15	+++	1000	16	—
125	11	+	19	+++	50	—	—
133	11	+++	18	+++	100		+
128	12	+++	20	+++	700		+
135	12	+++	20	+++	50	13	+
133/A	12	++	22	+++	2000	21	—
155	15	+++	41	+++	700	21	—
176	16	++	22	++	—	7	+
587	31	+++	24	++	3000		+
Average	13		22·6		760	15·1	66·6%

The results of the chemical analysis of blood, peritoneal liquid, hepatic lymph, intestinal lymph and the liquid from the thoracic duct are presented in Table II. The splenoportograms revealed the dilatation of the ramifications of the portal vein in the liver, also the collateral circulation through the Retzius system was visualized: the rectal, periesophageal and umbilical veins (Fig. 1, 2 and 3). In some pictures a distinct dilatation of veins could be seen. They were similar to the esophageal varices observed in human.

On histological examination of the liver a tendency to the formation of the biliary cirrhosis of liver was found (Fig. 4). It was expressed by the proliferation of the connective tissue and of the biliary canaliculi in the portal areas. This connective tissue proliferation encroached upon the hepatic parenchyma. In many slides the distension of the ramifications of the portal vein was noticed (Fig. 5).

Table II

Dog number	Blood						Ascitic fluid				Intestinal lymph			Hepatic lymph			Thoracic duct lymph		
	Bilirubin in mg.	Alkaline phosphatase in Bodansky's units	SGPT transaminase in Umbreit's units	protein			Specific weight	protein g%			protein g%			protein g%			protein g%		
				total g%	albumin in g%	globulin in g%		total	albumin	globulin	total	albumin	globulin	total	albumin	globulin	total	albumin	globulin
126	6·0			4·13	1·07	5·06		1·34	0·28	1·06				5·75	1·43	4·30	4·78	1·24	3·54
165	1·3	8·2	402	8·03	1·77	6·26		3·09	0·8	2·29	1·9	0·3	1·6	5·54	1·47	4·07	3·59		
136	2·6	28·8	668	6·31	1·26	5·05	1008	0·38			1·34	0·7	1·17				2·29	0·5	1·79
134	2·3	16·5	388	5·78	0·95	4·78	1018	0·15	0·02	0·13	0·38	0·04	0·34	3·11	0·59	2·52	3·49	0·66	2·83
125	2·1	18·0	604	5·24	1·21	4·03		0·57	0·17	0·40	0·3			4·48	1·05	3·43	3·04	0·73	2·31
133	0·4	—	40	5·35	0·8	4·55	1012	1·15	0	1·15	0·57						1·72	0·15	1·57
128	0·6	4·5	60	5·73	1·09	4·64	1010	0·5						4·01	0·88	3·13	2·48	0·52	1·96
135	0·6	11·2	98	7·26			1007	0·42						4·13	1·12	3·01	3·82		
133 A	1·1	32·5	492	5·11	1·53	3·58	1010	0·4			0·88								
155	6·9	60·0	1500	6·67	1·67	5·00	1012	1·15	0·29	0·86									
176	2·0	17·25	820	6·3	1·64	4·66								3·6			3·75		
587	0·2	26	300	5·73	1·78	3·95	1008	0·3											
Average	2·18	22·2	488	5·97	1·34	4·50	1010	0·86	0·31	0·95	0·89	0·17	1·04	4·37	1·09	3·41	3·22	0·63	2·3

DISCUSSION

Snell (22) in 1927 noticed in two dogs during the fifth and eighth week following ligation of the common bile duct ascites and a collateral circulation in the portal system.

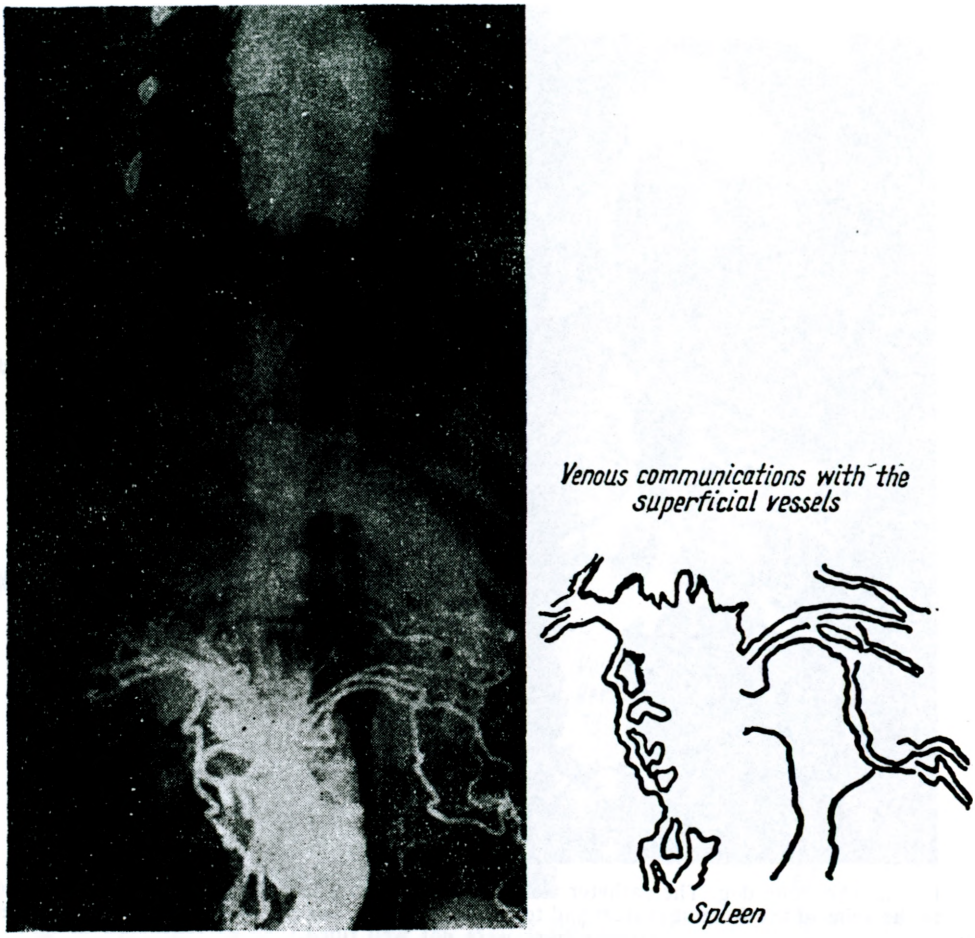

Fig. 1. Splenoportography. The contrast passed fast to the omental veins adhered to the scar.

In 1957 *Aronsen* stated that sometimes ascites appears after the ligation of the common bile duct of a dog. These were, however, casual observations and none of these authors tried to explain the mechanism of these abnormalities.

Our observations indicate that disturbances of the portal circulation and ascites developed in dogs after an average of 13 weeks following the stricture of the common bile duct by 50% to 75%. The abnormalities developed in 80% of the animals.

The collateral circulation of the portal system developed first of all through the anastomoses of the mesenteric veins with the left renal vein and the inferior vena cava and also through the umbilical, periesophageal and rectal veins. In some cases the esophageal varices could be well visualized in the rentgenograms. The described picture of the collateral circulation is similar then to the changes

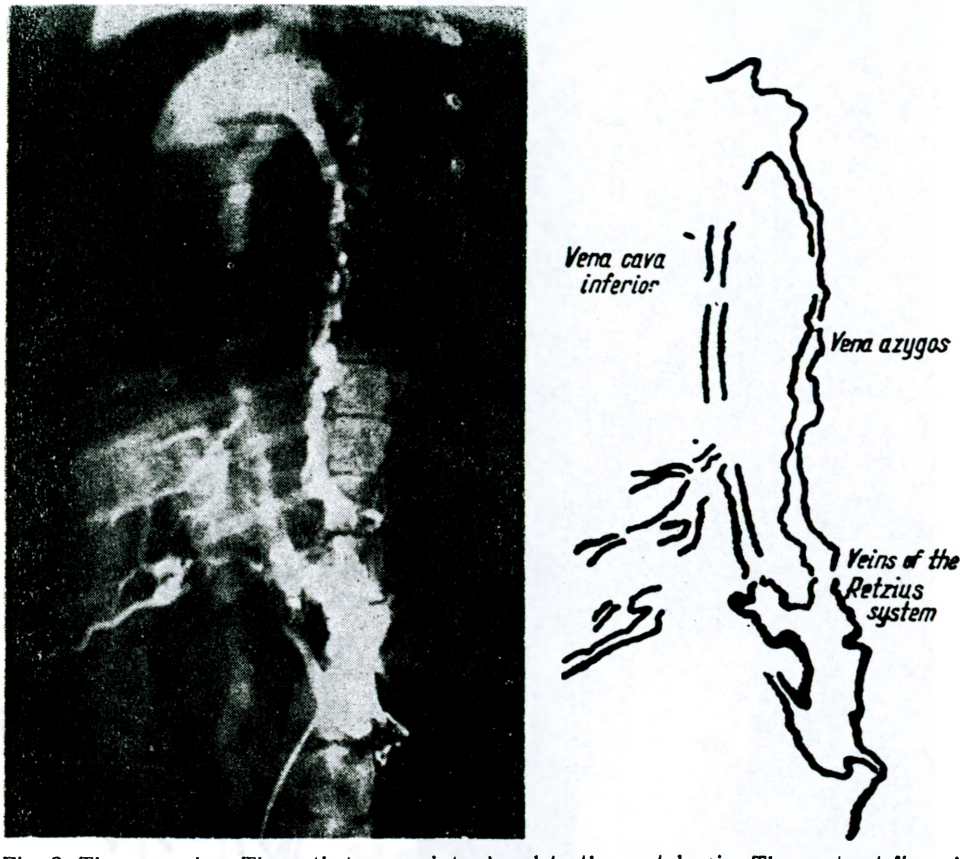

Fig. 2. The same dog. The catheter was introduced to the portal vein. The contrast flowed to the veins of the Retzius system and to the azygos vein. The ramifications of the portal vein in the liver were not well filled.

of this type observed in human (5). The average portal pressure was 22·6 cm of H_2O. The normal values of this pressure estimated in healthy animals using the same manometer were 11·5 cm of H_2O. The average pressure in the inferior vena cava was 7·5 cm of H_2O, and hence the pressure gradient between the portal vein and the inferior vena cava was 15·1 cm of H_2O. The normal pressure values in the portal vein in dogs vary according to different authors from 6 to 15 cm of H_2O (9, 16, 17, 21, 23) and the pressure in dogs with experimental hypertension of various types (23, 26) can range from 13 to 25 cm of H_2O. In hyper-

tension and ascites which were provoked using the most popular method of narrowing the inferior vena cava above the diaphragm, the pressure gradient between the portal vein and the inferior vena cava was only 1·5 cm of H_2O (19).

A considerable dilatation of the lymphatic vessels of the intestinal mesenterium, hepatic hilus and *cisternae chyli* and also the thoracic duct was striking

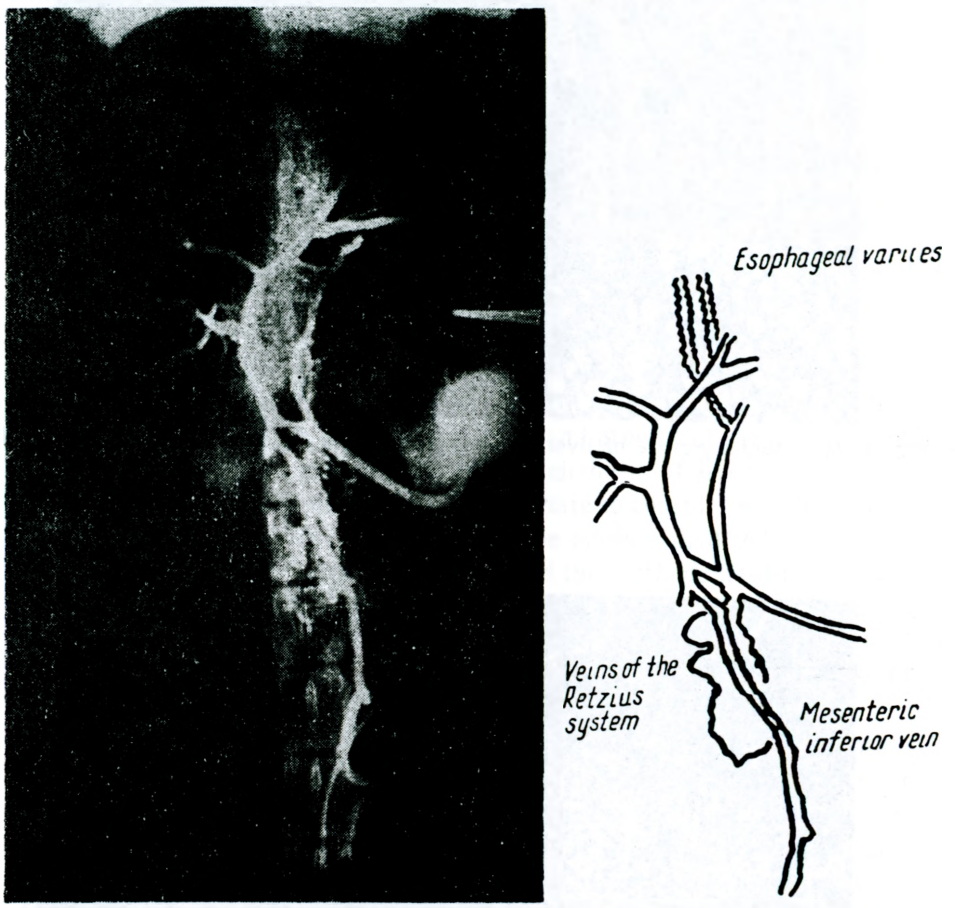

Fig. 3. Splenoportography. The contrast passes slowly to the liver. The Retzius veins, esophageal varices amend senteric inferior vein are already well filled.

in all instances. The accumulation of fluid similar to the lymph obtained from the lymphatic vessels was seen in the retroperitoneal space around the enlarged lymph nodes. The specific weight of the fluid obtained from the peritoneal cavity was low, average 1·010. The level of protein was also low, average 0·86 g%. The values obtained by us, corresponded approximately to the composition of the ascitic fluid in the human; its specific weight is about 1·010 and the protein content ranges from 0·1 to 3·8 g% — average 1·11 g% (18, 27). The fluid obtained by us differed from the peritoneal fluid of animals with ascites, caused

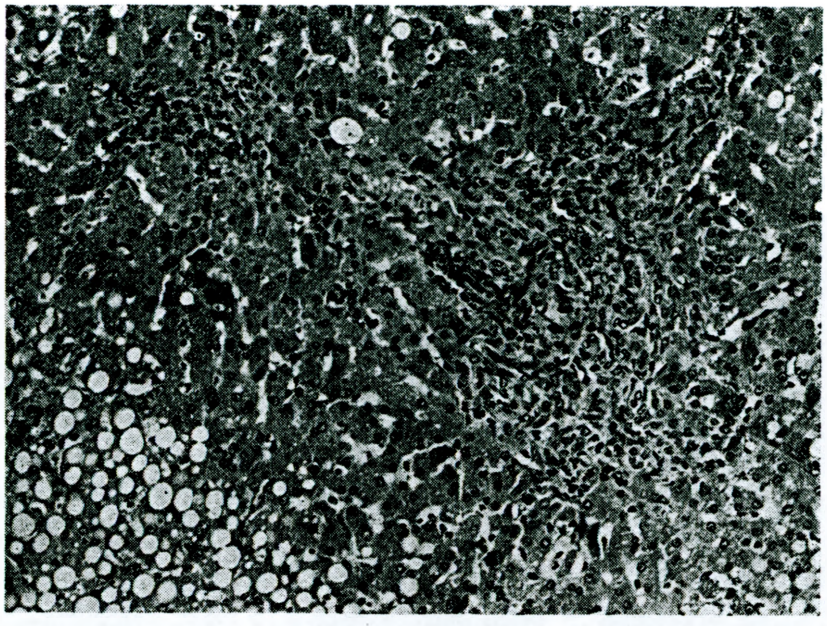

Fig. 4. Microscopic picture of liver changes. Fibrosis in the portal areas. H. E., × 150.

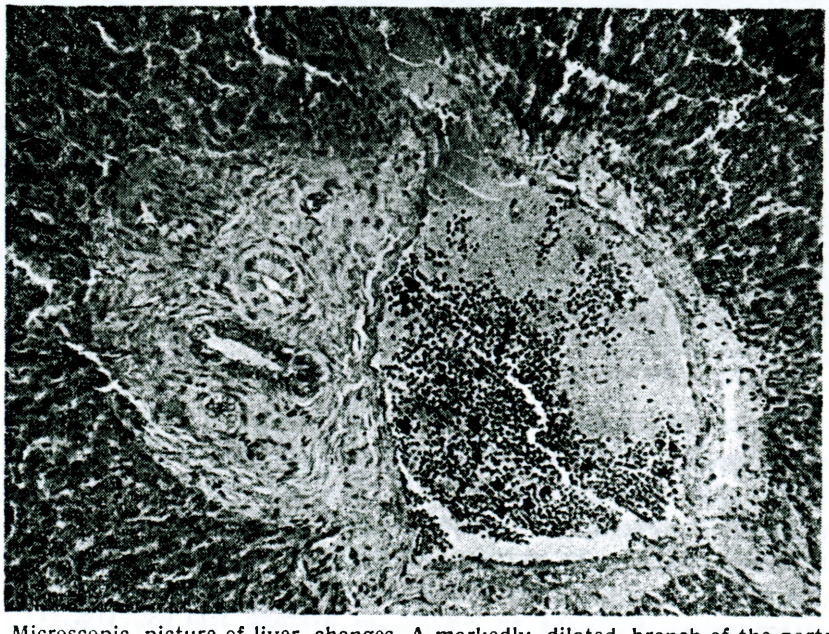

Fig. 5. Microscopic picture of liver changes. A markedly dilated branch of the portal vein can be seen in the portal area. H. E., × 150.

by the partial narrowing of the inferior vena cava above the diaphragm. The level of protein in this ascitic fluid is about 3·5 g% (9, 18, 23). The average protein content in the intestinal lymph in our dogs was 0·89 g% and differed slightly from the protein level in the ascitic fluid. The hepatic lymph contained an average of 4·37 g% of protein and the lymph from the thoracic duct 3·22 g%, which is less than in the hepatic lymph and more than in the intestinal lymph. In the immunoelectrophoretic studies of the protein of blood, ascites and lymph a considerable decrease of the albumin level and the increase of the β and γ globulin level was found. The enlarged level of transaminase in the serum indicated a damage of the hepatic cells.

The mechanism of the development of portal hypertension and ascites following partial obstruction of the common bile duct is not completely clear. Perhaps the small ramifications of the portal vein get compressed, as a result of the stasis of bile and of the distension of the biliary canaliculi in the portal areas and this fact results in stasis and secondary hypertension. The assumption, that the connection between the veins and the lymphatic vessels in the liver, or communications between the biliary ducts and veins play an important role in the development of ascites, may be rejected (14). In histological sections of the liver only fibrotic proliferation in the portal areas and growth of the biliary canaliculi was found, but it was not yet the biliary cirrhosis of liver.

On the basis of our results it seems appropriate to consider whether the partial narrowing of the common bile duct could be applied to develop experimental portal hypertension and ascites, since none of the methods used at present were satisfactory. The narrowing or obstruction of the portal vein (15, 17, 26) leads only to a transitional rise of pressure lasting from one to two weeks. Later on this pressure comes down to normal. The production of arterioportal shunts (13, 26) does not cause permanent hypertension.

In experimental liver cirrhosis produced by using carbon tetrachloride (25) or other substances the portal pressure remains usually normal, although the anatomopathological sections resemble cirrhosis observed in humans. An injection of silicone dioxide in the portal vein (24) produces a focal necrosis of liver, fibrosis and sometimes a slight increase of pressure, however the percentage of failures is considerable. The irritation of the adventitia of the portal vein using barium, strontium and quartz cristals gave sometimes a rise in pressure to 23 cm of H_2O, but the ascites did not develop.

The obstruction of the hepatic veins (8, 16) and the narrowing of the inferior cava above the diaphragm (21, 23) cause the formation of ascites and a slight, transitory rise of portal pressure. However, the conditions of this type of experiment, do not fully correspond to those which exist in an intrahepatic block in human.

On the basis of our observations it seems that the method used by us can have certain value in the experimental studies on portal hypertension and ascites.

By the partial obstruction of the common bile duct histological changes can be obtained in the liver indicating the tendency to cirrhosis. Moreover, permanent portal hypertension with the well developed collateral circulation, disturbances in lymph circulation, ascites, damage of the liver and icterus develop.

CONCLUSIONS

1. The characteristic picture of cholangiostasis and of portal hypertension develop following the partial obstruction of the common bile duct.

2. This method can be applied in experimental work to obtain the model for studies on portal hypertension and ascites.

Translated by W. Wajszczuk, M. D.

REFERENCES

1. *Aiello, R. et al.*: An experimental study of the role of hepatic lymph in the production of ascites. Surg. Gyn. Obst., 1960, 111, 77.
2. *Aronsen, K.*: Liver function studies during and after complete extra-hepatic biliary obstruction in the dog. Acta Chir. Scand., 1961, supl. 275.
3. *Baker, J., Jones, H., Hazelrigg, H.*: Surgical stricture of the common duct followed by biliary cirrhosis and portal hypertension. Gastroenter., 1950, 15, 359.
4. *Boba, A., Hostnik, W., Carter, J.*: The production of portal pressure increases in the dog. Surg. Forum, 1959, 10, 267.
5. *Bono, R. et al.*: Studies on portal hypertension. Surgery, 1960, 48, 119.
6. *Camishion, R., Ballinger, W.*: Portal hypertension and biliary cirrhosis. Surg. Gyn. Obstr., 1960, 111, 91.
7. *Craig, J., Gellis, S., Yi-Yung Hsia, D.*: Cirrhosis of the liver in infants and children. Am. J. Dis. Child, 1955, 90, 299.
8. *Cross, F. et al.*: Effect of complete hepatic vein ligation on portal pressure and ascites formation in dogs with portocaval shunts. Proc. Soc. Exper. Biol. Med., 1953, 82, 505.
9. *Drapanas, Th. et al.*: Hepatic hemodynamics in experimental ascites. Ann. Surg., 1960, 152, 705.
10. *Ellis, E., Holman, E.*: Portal hypertension accompanying cholangitis due to stricture of the common bile duct: correction by splenorenal shunt. Surgery, 1955, 37, 463.
11. *Ekman, O., Sandblom, Ph.*: Bilio-intestinal anastomosis as a cause of liver cirrhosis with portal hypertension. Acta Chir. Scand., 1962, 123, 383.
12. *Ekman, C.*: Portal hypertension. Acta Chir. Scand., 1957, supl. 222.
13. *Fisher, B. et al.*: Further experimental observation in animals with arterialized liver. Surgery, 1955, 38, 181.
14. *Hultborn, A., Jacobson, B., Rosenbren, R.*: Cholangiovenous reflux during cholangiography. Acta Chir. Scand., 1962, 123, 111.
15. *Morris, A., Miller, H.*: Chronic portal vein occlusion and portal hypertension in the dog. Surgery, 1954, 36, 1138.
16. *Orloff, M., Snyder, G.*: Experimental ascites. I. Production of ascites by gradual occlusion of the hepatic veins with an internal vena caval cannula. Surgery, 1961, 50, 789.
17. *Remillard, G., Conen, P., Walker, G.*: Production of portal hypertension in dogs by a new method. Surg. Gyn. Obst., 1961, 112, 543.
18. *Rusznyak, I., Földim, M., Szabo, G.*: Lymphatics and lymph circulation. Oxford, London, New York, Paris, 1960.