THE AMMONIA AND GLUTAMINE CONTENT OF THE BLOOD OF CATS WITH VARIOUS TYPES OF ANASTOMOSES DEVELOPING AFTER CONSTRICTION AND OCCLUDING LIGATION OF THE PORTAL VEINS

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A series of experiments on cats was carried out in order to study the collateral circulation which develops after the obstruction of the blood flow through the portal vein [14].

During the first laparotomy, the portal vein was ligated, narrowing its lumen. The second operation (20-25 days later) consisted of the complete ligation of the portal vein.

Autopsy of the animals which died or were killed revealed an intestinal tract which was contracted spastically and enlarged collateral circulation which was obvious to the naked eye. They were injected with ground white lead dissolved in benzene and then studied by x-rays and by preparation under a binocular lens.

After the preliminary constriction and subsequent occlusion of the portal vein of cats, two types of bypaths developed: some passed through the liver—hepato-petal, others connected the system of the portal vein with the vena cavas (by-passing the liver) —hepato-fugal, or porto-caval. The hepato-petal anastomoses were represented by enlarged veins originating from the gastroduodenal vein or the pyloric vein (running into the portal vein peripherally from the location of the ligature). Some of these enlarged veins extended along the bile duct, others beside it, still others accompanied the hepatic artery, but all of them disappeared into the hepatic tissues (Fig. 1). Such anastomoses were observed in all the experimental cats, but in some they were little developed, in others they were so strongly developed that their total diameter was greater than that of the portal vein. The described collaterals which were connected with the liver anastomosed many times along their route among themselves and with branches of the portal vein after its branches. These are true, so-called intrasystemic, anastomoses of the portal vein, which insure collateral portal circulation.

Hepato-fugal anastomoses, which connect the portal system with hollow veins develop basically:

1) between the inferior mesenteric and lienal veins and the left adrenolumbar vein, the left hepatic and the inferior vena cava;

2) between the superior mesenteric vein and the inferior vena caval system;

3) between the veins of the stomach, esophagus and diaphragm, as well as the veins of the rectum and of the ileum.

A unique bundle of anastomoses or, more accurately, a venous plexus, connecting the tributaries of the inferior mesenteric and lienal veins with the left adreno-lumbar vein, the left renal vein and, finally, with the inferior vena cava itself (Fig. 2), was observed in the majority of cats.

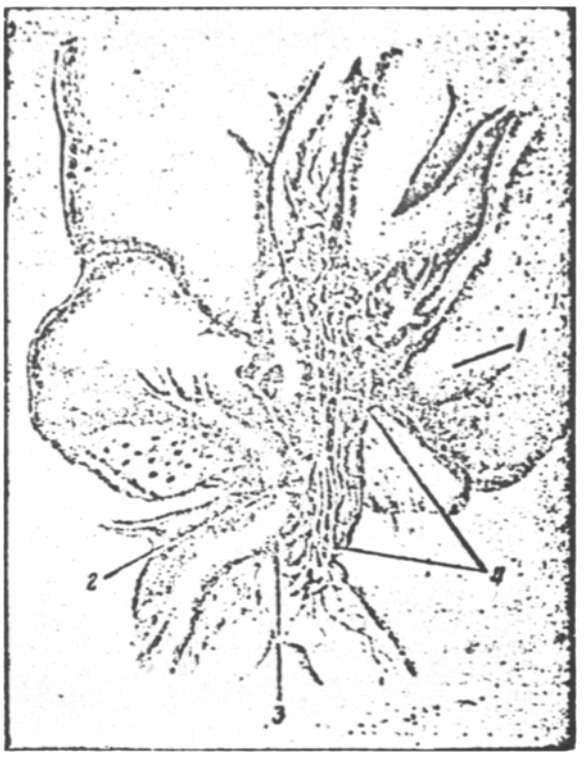

Fig. 1. Anastomoses developing after ligation of the portal vein of cats.
1) Liver; 2) location of the stenosis of the portal vein; 3), 4) anastomoses connected with the hepatic tissue.

The animals in which the development of hepato-petal anastomoses was observed to predominate throughout the experiment (over 1½ years) hardly differed at all from the control cats. In others, which developed only hepato-fugal anastomoses and insignificant hepato-petal ones, constant diarrhea, vomiting, emaciation and death 2-3 months after the operation were observed.

Some of the animals developed the hepato-petal to the same extent as the hepato-fugal collateral circulation. The duration of their life was longer.

The difference between the pathological phenomena described above, as it appeared, depended on the type of anastomoses which developed in the cats. The functional significance of these anastomoses can be established not only on the basis of their morphological determination but by physiological indicators as well [5, 6, 7].

Since the time of the work of I. P. Pavlov and M. Nentsky, their coworkers and students [8, 10, 11], it has been known that a considerable amount of ammonia, acting toxically on the central nervous system, is present in the blood and organs of dogs with an Eck-Pavlov fistula.

One of us (B. G. Gordon), with N. V. Veselkin, studied the disturbance of the metabolism and the role of ammonia in the appearance of nervous disorders among dogs with Eck-Pavlov fistulas. In addition, the ways and methods of preventing intoxication and of normalizing the metabolism of such animals were also studied [1, 2, 3, 4].

The ammonia and glutamine content of the blood was also determined in people with atrophic cirrhosis of the liver (before and after porto-caval anastomosis). It was found that the ammonia content of the blood of such patients also increased [5]. Therefore it was of especial interest to determine the ammonia and glutamine content of the blood of cats which had been subjected to constriction of the portal vein with subsequent occlusion of

Fig. 2. Plexus of porto-caval anostomoses:
1) Left kidney; 2) part of the stomach; 3) inferior vena cava; 4) lienal vein; 5) porto-caval anastomoses.

it in order biochemically to show the significance of the anastomoses which developed as a result of this.

The ammonia and glutamine content of the blood was first determined in normal cats before the operation. It proved to be (average of 19 determinations) 0.32 mg%.

After the operation, the blood was studied at various intervals: on the 3-5th day after the constricting ligation (first blood sampling), 3 weeks later, when anastomoses had already developed (second blood sampling), and, finally, on the 5-7th day after occlusive ligation of the portal vein (third blood sampling).

The blood was drawn from both experimental and normal animals under ether anesthesia usually 3-5 hours after feeding them meat, frequently from the ear, more rarely from the jugular vein or femoral arteries.

The determination of ammonia was carried out by Parnas' method [15] on the trichloracetic centrifugate of the blood, the amide nitrogen of glutamine was determined by the same method after hydrolysis of another portion of the centrifugate for 11 minutes at a temperature of 100° with an equal volume of 2 N H_2SO_4.

The preliminary experiments carried out in 1952 [14] showed an increasing amount of ammonia in the blood of cats developing porto-caval anastomoses.*

The increase of the ammonia content (106%) and glutamine content (31%) after the operation on the portal vein can be seen clearly in Fig. 3, where the data of the various series of experiments are summarized. Consequently, the ability to eliminate excess toxically active ammonia with the help of glutamic acid by forming

* Due to circumstances beyond our control, the experiments were suspended and resumed in 1954.

glutamine, which is harmless to the system, is preserved in the operated animals. Similar results with respect to ammonia were recently obtained by J. Mann, J. Bollman, T. Farrar and others in experiments on dogs [15].

A very regular relationship was established by comparison of the anatomical changes of the venous route which developed after ligation of the portal vein with data from chemical analyses. As should have been expected, the ammonia content of the blood increased following constriction of the portal vein, indicating the portal blood flowed into the inferior vena cava by collateral routes, bypassing the liver (see table).

Then, as a result of the further development of anastomoses, the ammonia level in the blood varied, depending on the type of anastomoses that developed—through the liver or bypassing it.

After complete ligation of the portal vein and development of hepato-petal anastomoses, the ammonia content increased again, especially when it was possible to direct the blood around the liver more completely by tying off the hepato-petal paths.

In cats no. 1, 4, 9, 10, 13, 14, 15 and 16, the development of porto-caval anastomoses predominated considerably in comparison with hepato-petal ones. As is apparent in the table, the amount of ammonia in their blood was high both after stenosis of the portal vein and after its complete ligation.

A considerable development of both types of anastomoses was observed in cats no. 2 and 5; in them, the considerable rise in ammonia content at the first blood sampling changed to a fall of it at the second and even at the third blood sampling (cat no. 5), since the hepato-petal anastomoses were not ligated.

The stenosis in cat no. 3 did not prove to be great, both types of anastomoses developed slightly, the increase in the ammonia content of the blood did not reach high figures. In cats no. 6 and 8 both types of anastomoses also developed insufficiently, with a slight preponderance of the porto-caval; the ammonia content did not rise sharply (no. 6); it rose noticeably only after complete ligation of the portal vein and of the hepato-petal anastomoses (no. 6, 8).

Porto-caval anastomoses were weakly developed in cat no. 7, but a greatly enlarged pancreatico-duodenal vein, running into the central end of the portal vein, was found. The ammonia content of the blood proved to be low (0,39 mg%).

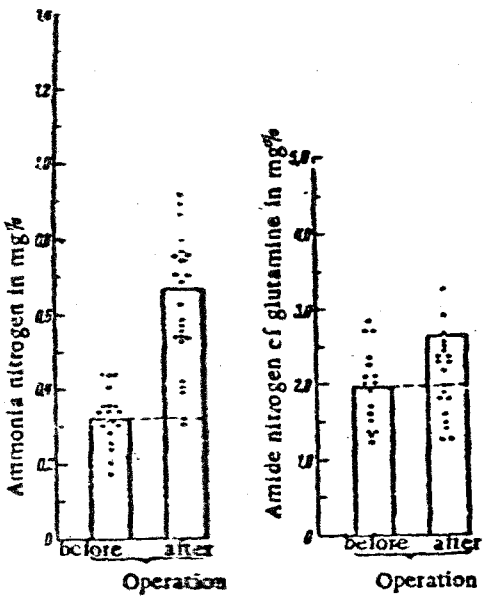

Fig. 3. Nitrogen, ammonia and amide nitrogen of glutamin content in mg% of the blood of cats when normal, after constriction and complete ligation of the portal vein.
Columns) Average data; · individual analysis

The interpretation of the data regarding the glutamine content of the blood is still difficult due to their divergence. It can be supposed that this is dependent on the brevity of the existence of excess amounts of glutamine in the blood, a hypothesis confirmed in the literature [13, 16, 17].

Attention should be called to the fact that the blood of cats after ligation of the portal vein and of the hepato-petal anastomoses seemed thinner, anemic; the trichloroacetic sediments after centrifuging were light brown with a thick leucocyte layer instead of the usual dark brown (all this frequently occurs in the blood of people with atrophic cirrhosis of the liver and of dogs with Eck-Pavlov fistula according to our data). These preliminary observations require verification.

Thus, when the portal circulation was disrupted, when a considerable amount of the portal blood entered the vena caval system, by-passing the liver, the ammonia content of the blood of the cats increased. The increase was especially sharp in cases when the portal vein was completely closed and the porto-caval anastomoses considerably developed and, on the contrary, slight when hepato-petal anastomoses were strongly developed. In other words, the changes in the ammonia content of the blood of cats following stenosis or

Ammonia Nitrogen and Amide Nitrogen of Glutamine Content of the Blood of Cats Various Periods After Stenosis and Complete Ligation of the Portal Vein in mg%.

Cat. No.	First blood sampling after stenosis of the portal vein		Second blood sampling after stenosis of the portal vein		Third blood sampling after complete ligation of the portal vein	
	nitrogen		nitrogen		nitrogen	
	NH_3	glutamine	NH_3	glutamine	NH_3	glutamine
1	—	—	0.52	1.25	—	—
2	0.89	4.81	0.31	1.43	—	—
3	0.53	2.65	0.30	1.58	—	—
4	0.86	3.88	0.53	3.71	1.34	5.03
5	1.08	1.81	0.41	3.83	0.58	3.23
6	0.51	1.95	0.55	2.45	0.75	2.36
7	—	—	—	—	0.39	2.35
8	—	—	—	—	0.79	2.31
9	—	—	—	—	0.75	2.31
12	—	—	—	—	0.68	3.66
13	0.74	1.89	0.54	1.26	0.70	2.15
14	0.70	1.47	0.76	2.54	0.62	2.92
15	0.40	1.77	0.91	2.45	—	—

occlusion of the portal vein of cats were analogous to its changes in dogs with Eck-Pavlov fistula. This can serve as the basis (for experimental purposes) for modification of the difficult operation Eck-Pavlov fistula operation by the simpler method – stenosis and subsequent complete ligation of the portal vein – leading to the development of porto-caval anastomoses. The latter, by directing the portal blood into the vena caval system, seemed to produce the Eck-Pavlov fistula.

It can be assumed that the pathological phenomena and behavioral changes of the experimental animals observed by us depend to a considerable extent on the changes in the conditions of biological neutralization and ammonia elimination.

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