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METABOLIC AND HEMODYNAMIC DISTURBANCES IN THE LIVER SUBDUED TO EXTRACORPOREAL PERFUSION

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During extracorporeal liver perfusion the peripheral parts of this organ are turgid and ischemic. This ischemia is associated with metabolic acidosis of blood flowing out of the liver.

In previous experimental studies (3) carried out in 30 pigs we observed that pig which perfuses extracorporeal liver develops considerable arterial hypotension and metabolic acidosis already in the first few hours of perfusion. The decrease of blood pressure and metabolic acidosis are preceded by changes in the liver appearance which gradually becomes livid starting from the periphery. This seems to indicate the development of peripheral ischemia of the liver. We observed that the greater were macroscopic lesions of this type, the higher hypotension and the more intense acidosis. This is true in spite of intense arterial and portal blood flow, high liver oxygen consumption and normal ammonium and BSP clearance.

Often this phenomenon may be the cause of a sudden deterioration of the condition or even death of the patient subjected to perfusion. This is a very important problem deciding to a considerable extent on the practical importance of extracorporeal liver perfusion. The purpose of present paper was to study:

1) acid-base balance of the liver-leaving blood under circumstances of various blood flow through the liver,

2) the distribution of blood flowing through central and peripheral portions of the liver.

MATERIAL AND METHOD

The studies were performed on 20 pig livers, divided into three groups, using artificial perfusing system comprising a pump ISL 2, oxygenator Polystan and heat exhanger (Fig. 1). The perfusion lasted 3 hours. The liver was taken in aseptic conditions after previous 3-day treatment of the donor with antibiotics. Blood was rinsed out from the liver using 6 l of Ringer solution of 4°C, buffered to pH 7·8.

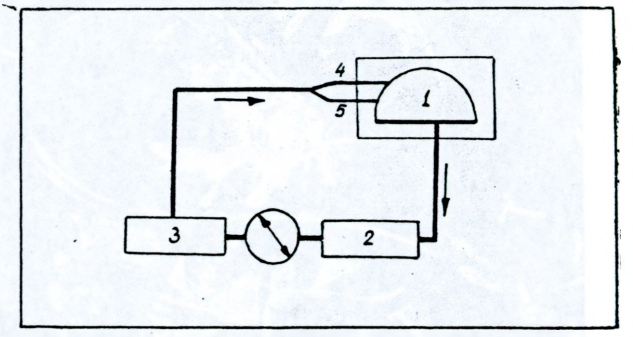

Fig. 1. Scheme of perfusion system: 1 — liver, 2 — oxygenator, 3 — heat exchanger, 4 — hepatic artery, 5 — portal vein.

Group I comprised ten animals in which the blood flow was kept below normal values (hepatic ischemia). In consecutive experiments blood pressure in hepatic artery ranged from 40 to 100 mm Hg and blood flow was lower than 1 ml/g of liver/min.

Group II comprised five animals in which the blood flow was high (over 1·5 ml/g/min) and the blood pressure ranged from 140 to 160 mm Hg.

In both groups total hepatic blood flow was estimated every half an hour by measuring the volume of blood flowing out from hepatic veins during 1 minute. Liver oxygen consumption, pH, pCO_2 and alkali reserve were determined in the blood flowing from the liver.

Group III comprised five animals. In this group the distribution of blood flowing through the liver was checked with ^{133}Xe and the function of liver cells with ^{131}I-tagged rose bengal under the circumstances of normal blood pressure and blood flow.

RESULTS

Group I. Total blood flow through the liver ranged in particular experiments from 0·19 to 1·0 ml/g of liver/min. Liver oxygen consumption was from 0·01 to 0·04 ml/g/min, being thus lower than the values accepted as normal. In all

experiments the blood flowing out of the liver showed acid reaction despite steady buffering of the inflowing blood with sodium bicarbonate (Table I). Central portions of the liver within a radius of 5 cm from the hilum were pink, the other ones were deep-livid during the entire observation. The area of lividity steadily increased centripetally (Fig. 2A, B).

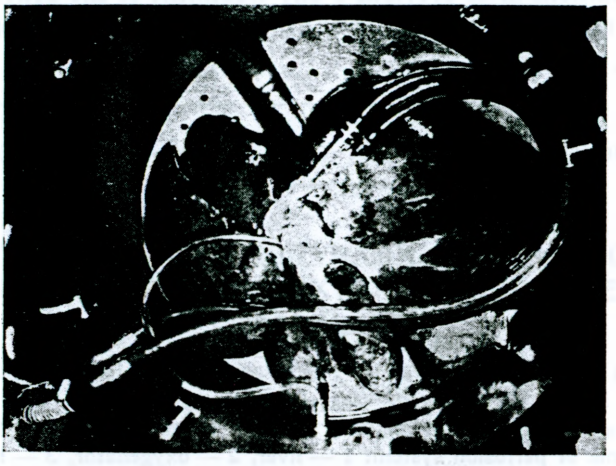

Fig. 2A.

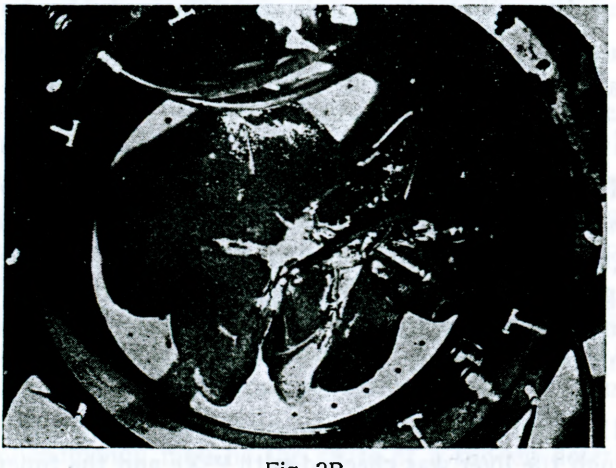

Fig. 2B.

Fig. 2. Perfused liver: A — first hour of experiment, B — third hour of experiment.

Group II. Blood flow through the liver ranged from 1·4 to 2·3 ml/g/min. Liver oxygen consumption was low and not exceeded 0·04 ml/g/min. pH of blood flowing from the liver was neutral or slightly alkaline (Table II). During the entire experiment the liver was pink only the peripheral segments 1—1·5 cm broad being livid.

Table I

pH of blood flowing out from hepatic veins at low pressures and blood flow through the liver (in the 3rd hour of experiment, steady buffering of inflowing blood with sodium bicarbonate)

No.	Pressure in mm Hg		Blood flow in ml/g of liver/min	Consumption by liver tissue (ml/g/min)	pH of blood flowing out from the liver
	in hepatic artery	in portal vein			
1	40	5	1·0	0·025	7·1 —7·26
2	40	12	1·0	0·02	6·85—7·26
3	50	6	1·0	0·04	6·91—7·3
4	50	7	0·2	0·03	6·95—7·24
5	75	7	0·19	0·025	7·04—7·39
6	75	10	0·7	0·017	7·14—7·35
7	80	10	0·74	0·035	6·92—7·13
8	100	20	1·0	0·015	7·17—7·31
9	100	5	0·3	0·01	5·04—7·4
10	100	15	0·57	0·01	7·18—7·31

Table II

pH of blood flowing out from hepatic veins at high pressures and blood flow through the liver (in the 3rd hour of experiment)

No.	Pressure in mm Hg		Blood flow in ml/g of liver/min	Consumption by liver tissue (ml/g/min)	pH of blood flowing out frov the liver
	in hepatic artery	in portal vein			
1	140	20	2·5	0·01	7·4 —7·54
2	140	10	2·3	0·04	7·37—7·54
3	140	25	1·4	0·02	7·36—7·38
4	140	15	1·5	0·01	7·33—7·4
5	160	20	1·4	0·01	7·4 —7·45

Group III. The investigation of the blood flow in various liver portions using ^{133}Xe showed it to be very high in the perihilar regions, sometimes higher than the total one. In contrast, in peripheral areas the blood flow amounted to 9—50% of the total (Table III). Scintigrams performed 45 min after intravenous administration of ^{131}I-labeled rose bengal revealed entire lack of the uptake of dye in peripheral liver portions (Fig. 3, Table IV).

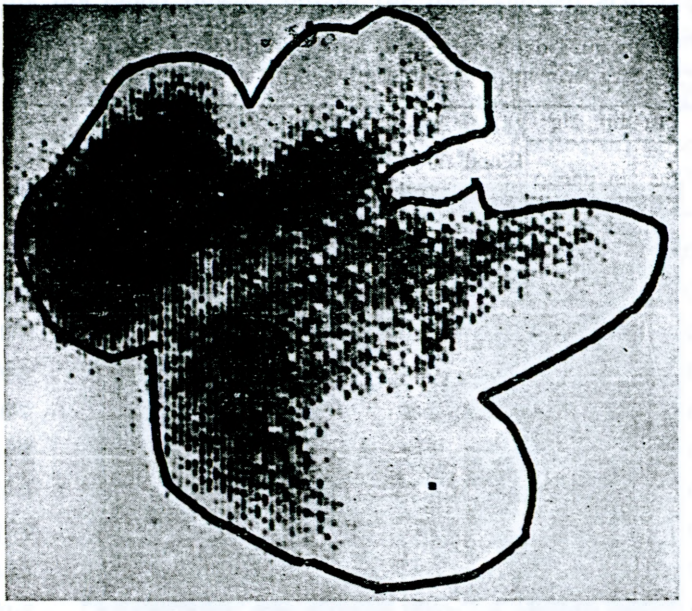

Fig. 3. Scintigram of the perfused liver in the 3rd hour of experiment made using rose bengal labeled with ^{131}I. Very low uptake of the dye in peripheral liver portions.

Table III

Distribution of blood flowing through the liver and total flow studied with ^{133}Xe (in ml/g of liver/min)

No.		Total flow	Flow in the field			
			pink, central	pink, paracentral	slightly livid, peripheral	deep livid, peripheral
1	ml	0·72	1·02	0·63	0·47	0·35
	%	100	143	90	67	50
2	ml	1·02	0·95	0·66	0·16	0·07
	%	100	94	65	16	75
3	ml	1·4	1·5	1·04	0·51	0·13
	%	100	107	74	36	9
4	ml	1·4	0·54	0·66	0·25	0·12
	%	100	40	48	18	9
5	ml	0·5	0·43	—	—	0·18
	%	100	86	—	—	36

Table IV

Uptake of ^{131}I-labeled rose bengal in particular portions of perfused liver (in % of the number of impulses/min/g of the tissue)

No. of experiment	Perihilar portion	Central portion of lobes	2 cm from external border
1	100	89	5
2	100	—	48
3	100	13	1·6
4	100	40	4·6

DISCUSSION

Reduced blood pressure and gradually developing metabolic acidosis represent essential complications of extracorporeal perfusion of isolated liver (5). These complications are more striking the longer lasted liver ischemia, it means the period from the moment of taking the liver from the donor to that of the restoration of blood flow in the recipient. This particularly concerns the so called warm ischemia. The possible causes of hypotension can be listed as follows: a) hiperpotassemia resulting from the destruction of liver cells, b) effect of substances deriving from hepatic bacteria, c) loss of blood to the liver vascular bed at the moment of the beginning of perfusion, d) accumulation of acid products of carbohydrate metabolism in the liver during ischemia, e) secretion of a hypothetic hypotensive substance by ischemic liver (1, 2).

It appears, however, that the drop of blood pressure is the fact even when the level of potassium in the blood flowing from the liver is normal (1). Hypotension is also present in the course of perfusion of livers the tissue and blood of which are sterile (1). Hypotension due to the loss of blood to hepatic vascular bed can be prevented by previous blood transfusion. The problem of acidosis remains open. It is unknown whether acidosis is the cause or result of hypotension. The results of the majority of studies indicate that it is very frequent, particularly when the blood flow is less than 0·5 ml/g/min. Under such circumstances the blood flowing out from the liver shows an acid reaction as a rule (4). The same conclusion can be drawn from our investigations: with the low blood flow pH of hepatic venous blood was decreased in spite of steady buffering of blood with sodium bicarbonate.

Observations concerning the determination of the distribution of the blood flowing through the liver using ^{133}Xe are worth attention. Even when the total blood flow is normal the peripheral portions of the liver can be steadily ischemic. The central liver portion which is normally supplied with blood is able to keep

normal clearance reflected by normal period of the removal from the blood of ammonium, BSP and rose bengal. In contrast, the peripheral, ischemic, liver portions can constitute the site of formation and release into the blood of acid products of carbohydrate metabolism and hypotensive substances. Steady, high liver blood flow and its uniform distribution in the organ seems to be indispensable for effective, prolonged perfusion of isolated liver.

CONCLUSIONS

1. Blood which flows out from the liver perfused for 3 hours under low pressure and at low flow shows acid reaction.

2. The distribution of liver flowing through isolated liver is not uniform. Peripheral liver portions are steadily ischemic. They can constitute a source of acid products of carbohydrate metabolism and substances of hypotensive action.

Translated by A. Korczak-Kruś, M. D.

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