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Effect of a Liver Bypass and Overtransfusion on "Trapping" of Red Cells.* (29826)

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When a dog whose red cell volume is known is overtransfused with blood containing a known volume of red cells, the final measured cell volume is less than expected(1,2). The term "trapped" has been applied to these missing cells on the assumption that they are still in the circulation, but as a consequence of the overtransfusion have been sequestered and are not in the active circulation. An attempt was made to locate the red cells after an overtransfusion, and it was found that there was a marked increase in the volume of red cells in the liver, representing 46% of the trapped cells(3). In the present experiment, trapping of cells by the liver was prevented, and the effect of this procedure on trapping in the rest of the circulation was measured.

Methods. The dogs were anesthetized with 10 mg/kg morphine sulfate subcutaneously followed in 20 minutes with 15 mg/kg pentobarbital. Cell and plasma volumes were determined by the Cr^{51}-tagged red cell and T-1824 dye dilution methods, respectively(4). Plasma protein concentration was calculated from the specific gravity measured by the falling drop method(5). Mean arterial blood pressure in the left common carotid artery was measured by a mercury manometer. Blood samples were taken from the right atrium through an indwelling #8 or #9 cardiac catheter. The left and right femoral veins were isolated for injection of the tagging materials and for infusion of blood.

Two groups of dogs were used. A group of 6 dogs was operated on to create a portal vein to femoral vein shunt. Blood volume and protein determinations were done immediately before and after the bypass and samples obtained over the following 2½- to 3-hour period. In the 12 dogs of the second

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group, the shunt was made before determinations were made of cell, plasma volumes and protein concentration, following which they were given a transfusion of a mean volume of 45.4 ml/kg of whole blood at a mean rate of 0.85 ml/kg/min. Twenty minutes after the transfusion the determinations were repeated with samples taken up to 2 hours after injection of the tagging materials.

Procedure for liver bypass. A midline incision was made, the viscera exposed, and a 2 to 3 cm section of the portal vein was isolated as close to the liver as possible. Three ligatures were placed on the vein: one was tied as close to the liver as possible, the more distal one was used for occluding the blood flow during insertion of the cannula, and the third one to tie the U-shaped cannula into the portal vein. This cannula was connected with polyethylene tubing to a straight glass cannula which was inserted and tied securely into the right femoral vein. Cannulae and tubing used were approximately the size of the portal and femoral veins, respectively. The hepatic artery was tied off just before the cannulae were inserted, the total procedure requiring approximately 20 minutes. Blood loss during the operation was negligible. While the mean arterial pressure fell during the occlusion of the portal vein, a period of about 5 minutes, as soon as the blood flow was reestablished blood pressure returned close to the initial level.

In a few dogs, portal venous pressure was measured using a Statham pressure transducer before and after the bypass and during transfusion following the bypass. Before the bypass was inserted, venous pressure was measured with a size 18 needle connected to a transducer by teflon tubing. After insertion of the bypass, the pressure was measured through a teflon tube which had been placed in the polyethylene tubing with the tip of the teflon tubing extending slightly beyond the tip of the U-shaped glass cannula. The other end of the teflon tubing was exteriorized through a T-connection in the bypass and connected to the transducer.

Results. A. Liver bypass without a transfusion. Table IA. Insertion of the bypass had no statistically significant influence on

TABLE I

	Venous hematocrit, %	Cell vol, ml/kg	Plasma vol, ml/kg	Blood vol, ml/kg	Circulatory hematocrit, %	BVR_{cells}‡	Protein concentration, g/100 ml	Total protein, g/kg	Mean arterial blood pressure, mm Hg
A. Liver bypass without transfusion*									
Measured before the bypass	44.1 ± 1.23	30.7 ± 1.44	46.2 ± 2.72	76.9 ± 2.57	40.1 ± 2.13	.92 ± .04	5.82 ± .31	2.66 ± .26	106 ±11
Measured after the bypass	47.3 ± 1.94	30.1 ± 1.91	43.1 ± 2.47	73.3 ± 3.40	41.1 ± 1.79	.87 ± .02	5.88 ± .16	2.50 ± .21	83 ± 7
B. Liver bypass followed by transfusion†									
Control (after bypass)	45.4 ± 1.71	30.2 ± 1.53	42.8 ± 1.91	73.0 ± 2.32	41.3 ± 1.81	.91 ± .02	5.99 ± .16	2.56 ± .12	101 ± 3
Blood transfused	39.6 ± 1.61	18.0 ± 2.28	27.4 ± 2.96	45.4 ± 5.31			6.47 ± .35	1.77 ± .23	
Expected after transfusion	43.1 ± 2.0	48.2 ± 2.63	70.2 ± 3.92	118.4 ± 5.58	40.7 ± 1.56		6.16 ± .21	4.33 ± .23	
Measured after transfusion	49.1 ± 1.65	42.2 ± 2.15	44.5 ± 3.33	86.7 ± 4.08	49.0 ± 2.04	1.00 ± .06	6.61 ± .13	2.94 ± .21	90 ± 3

* Values are means and S.E. for 6 dogs with an avg wt of 11.4 ± .37 kg. † Values are means and S.E. for 12 dogs with an avg wt of 12.8 ± .56 kg.
‡ Circulatory hematocrit/venous hematocrit.

the measured cell and plasma volumes, total protein, venous hematocrit and BVR_{cells}.

The initial mean arterial pressure for the group of 6 dogs averaged 106 ± 11 mm Hg, while the pressure after insertion of the bypass was 83 ± 7 mm Hg. The latter mean includes one dog whose mean pressure fell from 150 to 80 mm Hg during the operative procedure. In the other 5 dogs the fall in pressure ranged from 5 to 20 mm Hg.

B. Liver bypass followed by a transfusion. Table IB. In the group of 12 dogs given an overtransfusion of 45 ml/kg, significant discrepancies occurred between the measured and expected cell and plasma volumes and total circulating plasma proteins. The measured cell volume after the transfusion was 6.0 ml/kg less than the expected when calculated from the volume of cells the dogs had before the transfusion and those added with the blood. Thus, a significant volume of red cells was trapped (6.0 ml/kg, $p<0.01$) as a result of the transfusion after the bypass. There was also a significant difference between the measured and expected plasma volume of 25.7 ml/kg ($p<0.0001$); 93% of the plasma given during the transfusion escaped from the circulation. Concurrent with the plasma loss was a significant loss of 1.39 g/kg of protein; $p<0.0001$. This amounted to 78% of the protein transfused. Consequently plasma volume and total protein were only slightly higher after than before the transfusion, while protein concentration was significantly higher than both the initial and the expected ($p<0.05$).

The circulatory hematocrit after the transfusion increased significantly ($p<0.001$) from 41.3 to 49.0% while the venous hematocrit increased from 45.4 to 49.1%. As a result the BVR_{cells} ratio increased significantly ($p<0.02$) from the initial 0.91 after the bypass to 1.00 after the transfusion.

In this group, after insertion of the bypass, mean arterial pressure was 101 ± 3 mm Hg decreasing to 90 ± 3 mm Hg after the transfusion. In 3 dogs there was no blood pressure change while in nine dogs there was a reduction of from 10 to 30 mm Hg.

Insertion of the bypass resulted in an increase of 6 cm H_2O in portal venous pressure in 3 dogs from the control level, and with the overtransfusion the pressure in the portal vein increased further by approximately 9 cm H_2O. One hour after the transfusion, portal venous pressure had returned to the level found prior to the transfusion.

Discussion. Although, in previous experiments(3) when an overtransfusion of blood was given, the liver was the primary organ in which red cells were trapped, the present experiments indicate that in the absence of the liver from the circulation other organs or areas of the circulation are able to trap red cells in significant volume. In fact, in the present experiment with the liver removed from the circulation and an overtransfusion, the percentage of red cells trapped was distinctly greater than with an overtransfusion alone. Also, the volume of cells trapped was greater in proportion to the amount of blood transfused. In the present experiment the bypass and a transfusion of 45 ml/kg of blood resulted in 6 ml/kg of trapped cells while, with a transfusion of 50 ml/kg in intact dogs, red cells were not trapped (unpublished data). Previously, in order to obtain a comparable degree of red cell trapping in intact dogs, a transfusion of 114 ml/kg of blood was required(3).

A difference between the expected and measured plasma volume was also found: 25.7 ml/kg or 93% of the plasma infused was unaccounted for in contrast to earlier experiments with the liver in the circulation and a transfusion of 114 ml/kg of whole blood where 26.3 ml/kg, or only 40% of the infused plasma, was not accounted for(3).

After the liver bypass was inserted, there was a mean increase of 6 cm H_2O in portal venous pressure over the control level, and a slight decrease in mean blood pressure and in red cell and plasma volume which was not significant. The mean circulatory and venous hematocrits increased slightly giving a ratio of 0.87 which is not significantly different from the control value of 0.92. That there was no significant shift in this ratio when the liver was bypassed was not surprising in view of Chien's findings where he demonstrated that the ratio of small to large vessel hematocrits in the splanchnic area was the

same as for the total circulation(6). Further, the BVR_{cells} for control and eviscerated dogs are the same(7).

Previously, after an overtransfusion, the ratio of the two hematocrits remained the same. In the present experiments when the liver was bypassed and then an overtransfusion was given, the circulatory hematocrit increased more than the venous hematocrit resulting in a BVR_{cells} ratio of 1.0. Under these circumstances the involvement of the spleen in the BVR_{cells} ratio was probably negligible because of the anesthetics used(8). Also, observation of the size of the spleen at the end of the experiment indicated that it was contracted. This suggests that at this time the circulating red cells were evenly distributed throughout the vascular system. There are two possible explanations for this phenomenon. Either a portion of the capillary bed in which cells and plasma were differentially distributed has been eliminated from the circulation, or, while a small area of the circulation was shut down containing the red cells trapped, the majority of the capillaries had the same concentration of red cells as the large vessels. In view of the increased portal venous pressure after the transfusion and the fact that on gross inspection the vessels of the splanchnic area were found to be dilated and well-filled, the latter alternative seems to be the likely one. Whether the rise in portal venous pressure plays a role in the trapping of red cells and loss of plasma cannot be decided on the basis of these experiments.

Summary. In anesthetized dogs, the measured cell and plasma volumes, protein concentration, venous hematocrit and BVR_{cells} were the same before and after bypassing the liver with a portal vein to femoral vein shunt. An overtransfusion of blood after the bypass produced significant changes in all measured circulatory parameters. At the end of the experiment the volume of trapped cells was 33% of the cells infused, and the escaped plasma was 93% of the infused. Protein lost represented 78% of the infused. Circulatory and venous hematocrits were the same after the bypass and transfusion, suggesting that under these circumstances cells and plasma were evenly distributed throughout the circulation. Mean arterial pressure was reduced slightly after insertion of the bypass and also after the overtransfusion. Portal venous pressure increased when the liver was bypassed and further increased after the transfusion following the bypass.

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Quantitative Determination of the Group Specific Protein in Normal Human Serum.* (29827)

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Three phenotypes of the group specific α globulin (Gc) can be recognized in human serum by starch gel and immunoelectrophoresis; a fast component Gc 1-1, a slow component Gc 2-2 and an intermediate com-

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