8-1982

Blood Reservoir Function of the Fetal Guinea Pig Liver

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Abstract

BLOOD RESERVOIR FUNCTION OF THE FETAL GUINEA PIG LIVER

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To determine of the fetal liver functions as a blood reservoir, we measured liver blood volume under normal conditions and after hemorrhage and volume loading. Nineteen pregnant guinea pig sows and 54 near-term fetuses were injected intravenously with ^{51}Cr-labeled red cells while the fetuses remained in utero. Ninety seconds later a 0.5-1.0 g sample of liver was garroted with a sharp wire into a tared tube with minimal blood loss. A blood sample was taken to measure counts per ml of blood, the fetus killed and the remainder of the liver weighed. Blood volume of the liver and body were calculated. Groups of fetuses were studied with normal volume, after 14% hemorrhage and 12% volume loading. Adult sows weighed 1235 $\pm$ 29 (SEM) g with a blood volume of 60.4 $\pm$ 2.3 ml, of which the liver contained 11.2 $\pm$ 0.5 ml. Fetuses weighed 58.2 $\pm$ 1.8 g. Under normal conditions fetal blood volume was 5.1 $\pm$ 0.2 ml and the liver contained 22.7 $\pm$ 1.8% of total blood volume. This fell to 16.9 $\pm$ 1.6% after hemorrhage,

but did not change significantly from normal during volume loading. These results indicate the fetal liver is relatively larger than the adult and contains more blood per gram of tissue. Following decreases in blood volume the fetal liver acts as a blood reservoir by releasing blood into the circulation. It releases a volume equal to about 60% of the shed blood after a moderate hemorrhage.

LOMA LINDA UNIVERSITY

Graduate School

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A Manuscript Submitted by Gregory A. Roda

in Partial Fulfillment of the Requirements for the Degree

Master of Science in Physiology

August 1982

Each person whose signature appears below certifies that this manuscript in his opinion is adequate, in scope and quality, in lieu of a thesis for the degree Master of Science.

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The blood volume of many organs changes in times of stress. Due to its high compliance, the adult liver has been cast as a major blood reservoir that would buffer changes in blood volume during times of stress. Greenway & Lister (1974), for example, studied the pressure-blood volume relationship in the liver of adult cats. They found that following infusion of 10-34% of the total blood volume the liver pooled about 20% of the added volume. Carneiro and Donald (1977) using plethysmographic techniques on dogs showed that during both moderate and severe hemorrhage the liver was able to release a volume equal to 14% of the blood loss. Bennett and Rothe (1981) studied hepatic flow-volume relationships in perfused canine livers. While keeping hepatic venous outflow constant they varied hepatic arterial inflow; stopping the flow of the hepatic artery resulted in a decrease in hepatic blood volume, while increasing hepatic arterial inflow resulted in an increase in hepatic arterial blood volume. They calculatated a hepatic compliance of 19.8 ml/mmHg/kg tissue in the adult dog. This value is comparable to the adult cat whose compliance has been found to range from 13-34 ml/mmHg/kg liver (Lautt & Greenway,1976). Koo and

Liang (1977) using fiber optics have visually observed a constriction of the hepatic sinusoids during hemorrhage in the rat.

To date, only one study of fetal liver compliance has been reported. Gilbert et al. (1981) found that hepatic compliance for the fetal lamb in utero averaged about 2-fold more than that found in the adult. This raises the possibility that the fetal liver may be a more important blood reservoir than in the adult. The purpose of this study was to compare the fetal liver to the adult liver in the guinea pig and to further test the hypothesis that the fetal liver acts as a significant blood volume reservoir for the fetus in utero.

METHODS:

A total of 19 pregnant guinea pig sows (Camm Hartley) weighing between 1000 and 1400 g with 54 near-term (term = 65 days) fetuses were studied. Nonpregnant sows were used as donors for erythrocytes to be labeled with ^{51}Cr. We withdrew 10 ml of blood from the inferior vena cava of the anesthetized sow into a syringe containing 2 mls of ACD solution. We added 5 uCi of ^{51}Cr to the blood, incubated it for 30 minutes at 25 ^{o}C, and then added 30 mg of ascorbic acid to prevent further tagging. This mixture

was then centrifuged, the plasma and buffy coats removed and the volume reconstituted with isotonic saline.

The pregnant sow was anesthetized (0.5 mg/kg body weight ketamine) and a catheter placed in the jugular vein. She was allowed to recover for 3 hours, then 0.3 ml of ^{51}Cr-labeled was injected intravenously, and the animal reanesthetized (ketamine). With the sow in a supine position, 1% Xylocaine was infiltrated subcutaneously along the abdominal midline. The abdomen was opened, the distal end of one uterine horn was exposed, and the fetal hindquarters was delivered taking care to preserve the umbilical circulation. From 0.1 to 0.3 ml of labeled blood was injected into the umbilical vein and allowed to mix for 90 s, then a sample of circulating blood was taken from the umbilical vein. Next the fetal liver was exposed very quickly (within 15 seconds) and a sample of the liver (0.5-1.0 g) was garroted with a loop of dental wire into a tared tube with minimal blood loss; the procedure was designed to minimize shifts of blood between the biopsied sample and remainder of the liver. The fetus was killed and the remaining liver weighed. The procedure was repeated using two other fetuses from widely separated locations in the uterus. Then a maternal

blood sample was withdrawn from the inferior vena cava and a section of maternal liver obtained by the same method as in the fetus. Blood and liver samples were weighed, placed in counting tubes and counted for five minutes in a well-counter (Packard).

By varying the amount of blood injected into and withdrawn from the fetus before liver biopsy, three different conditions of volume were studied. Normal blood volume was studied by injecting and withdrawing approximately the same amount of blood from the umbilical vein; the procedure resulted in control volumes averaging 96% of normal. Hypovolemia was induced by withdrawing about 0.7 ml more blood than was injected, which resulted in a volume depletion that averaged 14%. Hypervolemia was studied by withdrawing less than the injected volume, a procedure that increased blood volume an average of 12%. Except for anesthesia no attempt was made to suppress neural or humoral responses to volume changes.

We also studied liver blood volume in five non-pregnant guinea pigs for comparison with the pregnant sows.

Calculations. Background counts were subtracted from the blood and tissue samples and the corrected counts ex-

pressed per ml of blood or gram of liver. The amount of blood per gram of liver was determined by dividing the corrected counts in each gram of liver tissue by the corrected counts per ml of blood. The total liver blood volume was determined by multiplying the amount of blood per gram of liver by total liver weight. Finally the total blood volume of the fetus was calculated by dividing the counts per ml of blood into the total counts injected.

RESULTS

Pregnant sows weighed 1235 ± 29 (SEM) g and had a total blood volume of 60.4 ± 2.3 ml. The liver contained 11.2 ± 0.5% of the total blood volume although it constituted only 2.73% of the total body weight. These results are listed in Table 1. Twenty percent of liver mass could be attributed to the blood contained therein, assuming the hematocrit of blood within the liver and general circulation to be the same.

Nonpregnant adult sows weighed 974 ± 65 g and had a blood volume of 49.1 ± 3.6 mls. The liver constituted 3.82% of total body weight and contained 17.2 ± 1.2% of the total blood volume. Blood constituted 23% of liver mass.

Fetuses weighed 58.2 ± 1.8 g and under normal conditions had a blood volume of 5.1 ± 0.2 ml. Under normal

conditions the liver contained 22.7 ± 1.8% of the total blood volume, whereas the liver averaged 5.62 ± 1.5% of total body weight. Blood made up 34% of fetal liver mass.

After a 12% increase in total blood volume, hepatic volume increased only slightly and insignificantly. The liver then contained 21.6% of total blood volume. Thirty percent of the liver mass was attributable to blood.

After a hemorrhage during which an average of 14% of total blood volume was removed, liver blood volume diminished markedly. The liver then contained 16.9% of total blood volume. The blood content of the liver itself fell to 24% of liver mass from its control value of 34%.

DISCUSSION

The liver is a relatively large and vascular organ that has been shown to change its blood volume with changes in vascular pressure in adult rats, cats, and dogs (Baker & Tomlinson, 1969; Bennett et al. 1981; Greenway et al. 1974). Because of these compliance characteristics the liver has the potential to participate in the control of cardiac output by buffering changes in blood volume and therefore maintaining adequate venous return to the heart. For example, during hemorrhage with a loss in central venous pressure, the liver would be expected to release a volume

of blood into the general circulation to help maintain an adequate venous return. During volume loading with an increase in central venous pressure passive engorgement of the liver would be expected. Whether these changes are significant in overall cardiovascular regulation would depend on the relative compliance of the liver compared to the total body.

Vascular compliance has been measured for several organs including the liver, spleen, and gut (Bennett, 1981; Carneiro & Donald, 1977; Gilbert et al.,1981; Greenway et al.,1974; Guneroth & Mullins, 1963; Laine, Hall & Granger, 1979; Lautt & Greenway, 1976). Futhermore, the distribution of added blood among these organs has been studied (Carneiro et al., 1977), and in general, the increase in volume parallels the compliance of the individual organs. This would be expected, of course, if the pressure rise in the different organs were similar to the pressure rise in the major veins of the body when volume was added. In the case of the liver this is likely since evidence in the adult cat liver (Greenway et al., 1974) shows that the pressure rise in the hepatic sinusoids parallels the pressure change in the inferior vena cava. The rational for our study was that the percentage change in hepatic blood volume to total blood volume would be a ratio of hepatic compliance to

whole body compliance. That is:

$$\frac{V \text{ (liver)}}{V \text{ (body)}} = \frac{\text{Compliance of the liver}}{\text{Compliance of the body}}$$

In these experiments we induced changes in total blood volume to determine the effect this had on the liver blood volume, and in so doing quantitated a ratio of liver compliance to whole body compliance. This was done for both volume loading and depletion since liver compliance has been found to vary with blood volume (Gilbert et al., 1981). We also compared the mass of the fetal liver to that of the adult and the resting blood volume of the fetal liver with that of the adult.

The results of the present study suggest the fetal guinea pig liver is relatively more important as a blood reservoir than in the adult for reasons relating to its size, vascularity, and compliance characteristics. The fetal liver constituted 5.62% to the total body weight, whereas the pregnant adult liver constituted only 2.73% of total body weight. The fetal liver was also relatively larger when compared with the nonpregnant adult liver which contributed 3.82% of body weight. A second factor relates to blood volume per gram of liver tissue. The fetal liver contained 0.347 ml blood/g, whereas the pregnant adult liver contained 0.201 ml/g, and non-pregnant adult

0.227 ml/g. The blood volume per gram of tissue, taken together with the liver weight, indicate the fetal liver normally contains about 23% of the total blood volume, compared to 11% for the pregnant adult and 17% for the nonpregnant adult.

Other studies have shown newborn hepatic blood volume is also greater than adults and suggest a fetal-newborn-adult progression. Linderkamp et al. (1980) using newborn piglets, found liver blood volume at 24 hours of age to be 0.670 ± 0.089 ml/g. By fourteen days the blood volume decreased significantly to 0.408 ± 0.093 ml/g, but was still higher than in adult livers. Smith et al. (1972), working with beagles, showed that at birth the liver contained 8.13% of the total blood volume and at 46 days contained only 4.38% of the total blood volume. These findings suggest that the importance of the liver as a blood volume reservoir diminishes with age after birth.

In the present study the response of the fetal liver to various perturbations in blood volume is shown in Fig. 1. Figure 1 shows the percentage of total blood volume contained in the liver as a function of total blood volume in the three groups of fetuses. At control blood volume (96% of normal) the fetal liver contained 22.7% of the

total blood volume. When the total blood volume was reduced to 86% of normal the liver contained only 16.9% of the total blood volume. Thus during hemorrhage the liver released into the general circulation a volume of blood equal to about 60% of the hemorrhaged volume. On the other hand, when blood volume was increased to 112% of normal, the liver blood volume increased only slightly and insignificantly (Table 1). The liver pooled only about 3.5% of the added volume and the percentage of total blood volume contained in the liver did not change significantly from normal. As noted above, changes in the fraction of total blood volume contained in the liver is an index of the relative compliance of the liver to the whole body. Thus hepatic compliance is estimated to change from a relatively high value during hemorrhage to a lower value, comparable to whole body compliance, during volume loading.

These data may be compared with results from other species. In fetal sheep, Gilbert et al. (1981) report the fetal liver comprises 28% of the total vascular compliance. This is in contrast to adults where values range from 14-26% in the dog (Bennett et al., 1981; Carneiro et al., 1977) and 8-16% in the cat (Lautt et al., 1976).

In contrast to adult animals which have the ability to

increase their cardiac output during times of stress, Gilbert (1980) has shown the fetus to normally function near the top of its Starling function curve. Therefore compensations in cardiac output, which ultimately depend on venous return, must be made by other components of the vascular system, including alterations in circulating blood volume. In the case of the guinea pig, the evidence shows that the fetal liver is relatively larger than the adult and contains 1.5-1.7 times more blood per gram of tissue. Following blood loss the fetal liver acts as a major blood reservoir by releasing up to 60% of the volume change, thereby tending to maintain an adequate venous return. Following volume loading the liver sequesters only a very small part of added volume. We conclude that hepatic compliance is such that it stabilizes cardiac output when volume is lost, but is far less effective in protecting the body against volume overloading.

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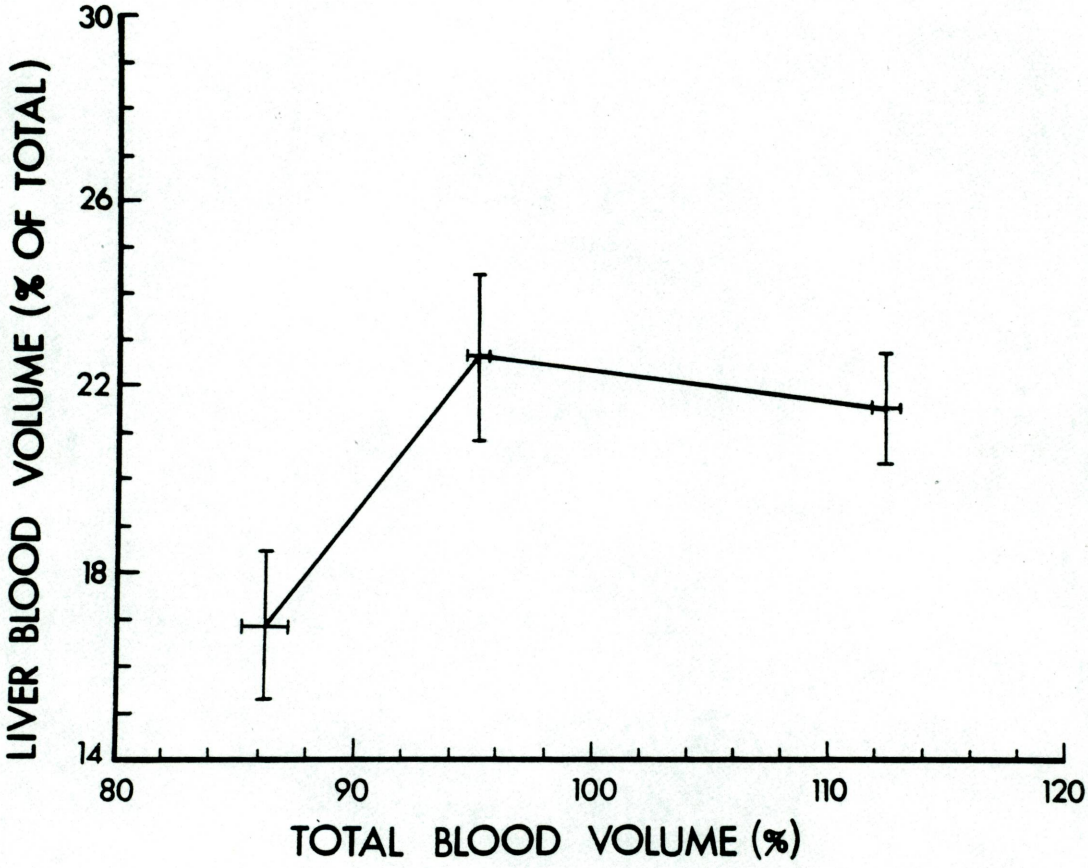
Table 1. Average body and liver weights, and body and liver blood volumes for nonpregnant and pregnant guinea pig sows and fetuses.*

	No.	Body Weight (g)	Liver Weight (g)	Total blood volume initial (ml)	Total blood volume final (ml)	Liver blood volume (ml)	Blood vol liver / Total blood vol
Nonpregnant Adult	6	975 ±65	37.3 ±1.6	49.1 ±3.7		8.45 ±0.75	0.172 ±0.013
Pregnant Adult	19	1235 ±29	33.7 ±1.2	60.8 ±0.2		6.81 ±0.41	0.112 ±0.005
Fetus							
Hypovolemic	15	55.1 ±2.2	3.33 ±0.14	5.17 ±0.22	4.48 ±0.23	0.789 ±0.103	0.169 ±0.016
Normovolemic	13	59.2 ±1.5	3.34 ±0.14	5.36 ±0.19	5.11 ±0.09	1.14 ±0.09	0.227 ±0.018
Hypervolemic	25	59.0 ±3.8	3.93 ±0.20	4.91 ±0.26	5.48 ±0.27	1.16 ±0.07	0.216 ±0.012

* Values listed are averages (± SEM) of individual experiments.

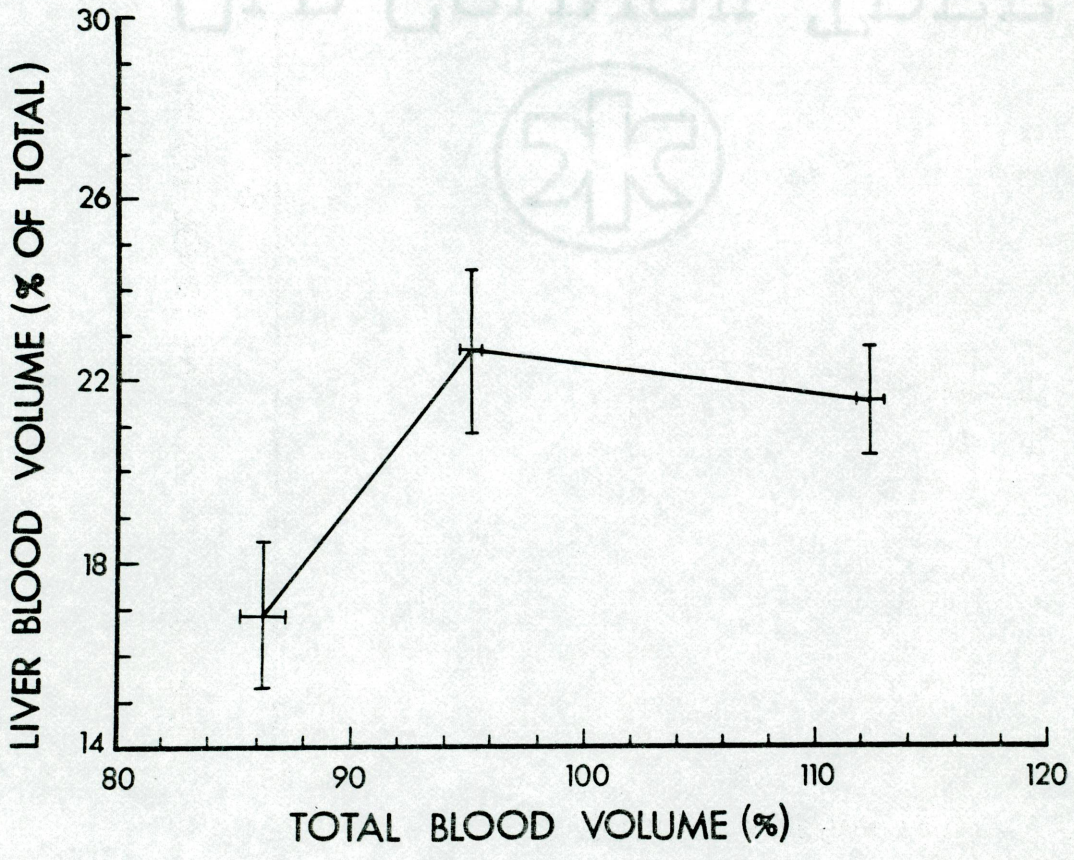
LEGEND FOR FIGURE

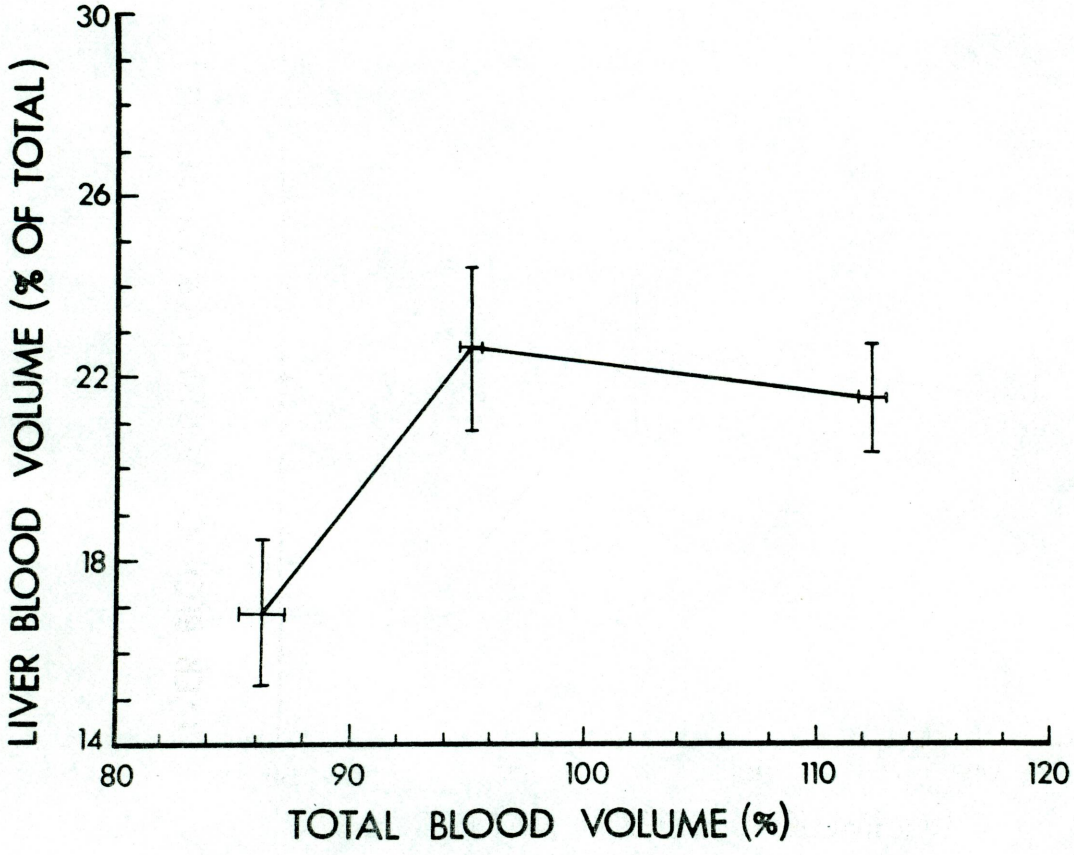
Fig. 1. Average results from 54 near-term guinea pig fetuses in which liver blood volume, expressed as percent of total, is plotted against total blood volume.


LIVER BLOOD VOLUME (% OF TOTAL)
30
26
22
18
14
80
90
100
110
120
TOTAL BLOOD VOLUME (%)

LEGEND FOR FIGURE

Fig. 1. Average results from 54 near-term guinea pig fetuses in which liver blood volume, expressed as a percent of total, is plotted against total blood volume.





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