In Vivo Assessment of Hepatic-Arterial and Portal-Venous Components of Liver Perfusion: Concise Communication

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An in vivo technique for assessment of the relative contributions of hepatic artery and portal vein to liver perfusion has been developed in the rat. Dynamic scintigrams have been obtained following i.v. bolus injection of Tc-99m sulfur colloid. Temporal separation of the arterial and venous phases has been verified by hepatic-arterial ligation and portacaval diversion. The former procedure abolishes the early arterial phase of normal uptake. Portacaval diversion similarly eliminates the delayed venous phase. Assessment of the individual components of liver perfusion is of promise in the investigation of hepatic dysfunction.

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Dynamic studies of the clearance of radioactively labeled colloid following intravenous injection have been used extensively to obtain information on total liver perfusion (*1–3*). Temporal separation has been suggested as a means of distinguishing between arterial and portal components of liver blood flow during first passage of a tracer in such dynamic gamma-camera studies (*4,5*).

The present study was undertaken in the rat to investigate the use of colloid in first pass to determine the ratio of hepatic-arterial to portal-venous flow by temporal separation. Such a technique is of potential value in studies of hepatic dysfunction.

THEORY

The dynamics of a colloid on first passage through the circulation following intravenous bolus injection are illustrated in Fig. 1. The bolus gradually becomes diffused as it passes first through the heart and lungs and then through the arterial circulation to the rest of the body. The amount of colloid arriving at each organ on first passage is proportional to the perfusion of that organ. Colloid passing along the hepatic and splenic arteries is removed efficiently by these organs. Colloid passing through the mesenteric vessels to the gut reaches the liver through the portal vein a few seconds later. Colloid carried to other organs, except bone marrow, passes back to the heart and some reaches the liver by recirculation.

Separation of the two components of hepatic perfusion, and the quantification of their relative proportions, depends on the following conditions:

1. Nearly all colloid passing along the hepatic artery should reach the liver before the initial appearance of that delivered by the portal vein (time t_a).
2. Nearly all colloid arriving through the portal vein should appear in the liver before significant recirculation through the hepatic artery occurs (time t_p).
3. Extraction efficiency of colloid in the liver should approximate 100%.
4. Splenic contribution to portal flow should be low. Colloid reaching the spleen is removed, so this part of portal supply will not be included in the measurement of colloid removed by the liver.

Conditions (3) and (4) are fulfilled in the rat. Extraction efficiency for Tc-99m sulfur colloid in normal liver is 85% and the relative perfusions of liver and spleen are 35:1 (*6*). In the present study the validity of Conditions (1) and (2) are examined.

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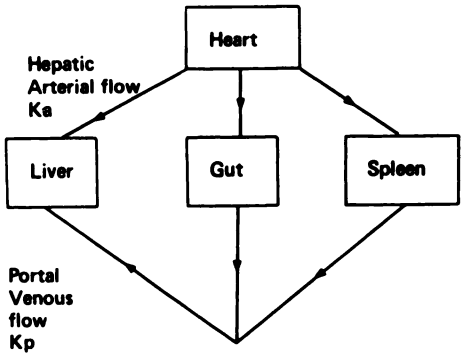

FIG. 1. Diagram illustrating first-pass dynamics of intravenously injected colloid.

The amount of colloid arriving by each route is proportional to the perfusion through that vessel. Provided the above conditions are met, therefore, the ratio of hepatic-arterial to portal-venous perfusion is given by the formula

$$\frac{K_a}{K_p} = \frac{L(t_a)}{L(t_p) - L(t_a)} \qquad (1)$$

where K_a is the arterial contribution, K_p the portal contribution, and L(t) the amount of colloid in the liver.

METHOD

Male Wistar rats weighing 200–350 g were used in this study. They were anesthetized with intraperitoneal pentobarbital, 50 mg/kg, and then placed under a gamma camera fitted with pinhole collimator (*7*) so that heart, liver, and spleen were included in the field of view. Approximately 5 mCi of Tc-99m sulfur colloid, in a maximum volume of 0.4 ml, were injected as rapidly as possible into the tail vein. Digital images recorded as 64 × 64 matrices were stored on magnetic tape at 0.5-sec intervals for 50 sec following injection, using an on-line computer system. Playback of the integrated digital image enabled cardiac, hepatic, and splenic regions to be chosen by light pen. The area of liver examined (Fig. 2) was carefully selected to avoid overlap by lungs, kidneys, or major vessels. Inclusion of any of these produced an overestimate of the hepatic-arterial component of perfusion. Time-activity histograms were constructed for each region and smoothed to reduce random errors.

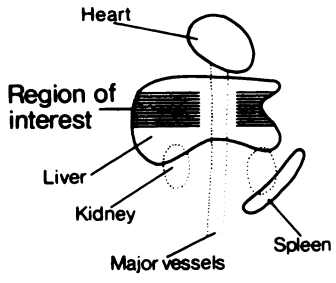

FIG. 2. Schematic anterior view of relative positions of organs in the rat. Hepatic region of interest is shaded area.

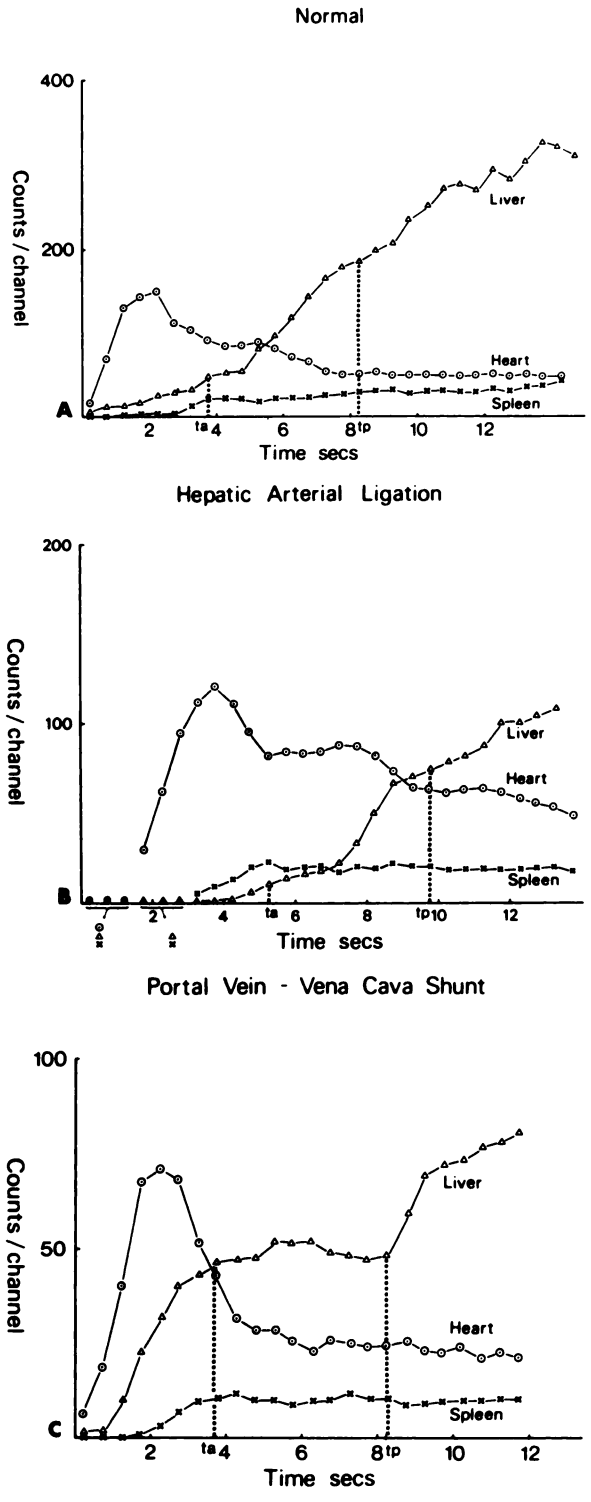

FIG. 3. Typical histograms obtained in cardiac, hepatic, and splenic regions of interest in different groups of animals: (A) normal, (B) hepatic-artery ligation, and (C) portacaval diversion. Time of end of arterial phase, t_a, and time of end of portal phase, t_p, are shown on each graph. Times t_a and t_p are, respectively, 1.5 and 6.0 sec after the heart peak.

Three groups of animals were studied using the above procedure:

1. Normal rats (n = 10).
2. Animals following ligation of the hepatic artery. Care was taken to ensure complete ligation of all arterial inflow (n = 10).
3. Animals following end-to-side porta-caval anastomosis. In this group, perfusion occurred through the hepatic artery alone (n = 10).

RESULTS AND ANALYSIS

Typical histograms for the three groups of animals are shown in Fig. 3. In all animals a rapid peak of activity was observed in the heart. The sharpness of this peak gave an indication of the true bolus nature of the injection. If time to reach peak value exceeded 2.5 sec, the study was rejected, since slower boluses were considered likely to result in undue overlap between the two components of uptake. Zero time was defined as the time of this peak. The splenic histogram rose to a plateau value within 2 sec of the cardiac peak; it remained at that level for 5–6 sec and then began to rise again. The count rates in the splenic histogram, however, were generally too low to allow accurate timing of arterial supply and recirculation. Hepatic histograms in the different groups varied in the following manner.

Normal animals. Here the rise in hepatic uptake started during the cardiac peak and rose monotonically thereafter (Fig. 3A). Although the rate of rise in the first 7 sec was not uniform in all animals, in most a section of relatively low gradient was observed ~1.5 sec after the heart peak (t_a) followed by a second low-gradient section at ~6 sec after the heart peak (t_p). The contribution of the portal vein (P), expressed as a percentage of total hepatic perfusion, was calculated for each animal from Eq. 1 using different values of t_a and t_p after the heart peak. These results are shown in Table 1.

Hepatic arterial ligation. Hepatic uptake in these animals began approximately 1 sec after the heart peak (Fig. 3B). A region of relatively low gradient was observed at about 6 sec after the heart peak (t_p). Timing of the portal-vein phase was obtained in this group of animals. It was assumed that the level of the liver curve at 6.0 sec after the heart peak ($L_{6.0}$) represented total portal-venous first pass of colloid. The variation with time of portal-venous colloid uptake was then evaluated as a percentage of $L_{6.0}$. In this group of animals, background radiation from activity in other organs was likely to affect measured count rates significantly. This was particularly important in the early part of the uptake curve, where there was relatively low hepatic activity. Subtraction was therefore performed in an attempt to allow for this radiation. It was assumed that the level of background was constant and equal to that measured in the liver region of interest at the time of the heart peak, since at that time there should be minimal hepatic activity following arterial ligation. Hepatic activities before and after background subtraction are shown in Fig. 4.

Porta-caval diversion. In these animals the hepatic uptake curve was similar in shape to the splenic uptake curve, but with a higher count rate (Fig. 3C). The former was produced by hepatic-arterial inflow alone. The plateau value, which was reached between 3–5 sec after the heart peak, was assumed to be proportional to total hepatic-arterial first pass of colloid. The temporal course of hepatic-arterial colloid uptake was then expressed as a percentage of this plateau value (Fig. 4). Information on hepatic-arterial recirculation was also obtained from this group of animals. Using the calculated plateau value, the time course, after the heart peak, for percentage of colloid recirculated through the hepatic artery could be estimated. This is also illustrated in Fig. 4.

DISCUSSION

The temporal separation between the completion of

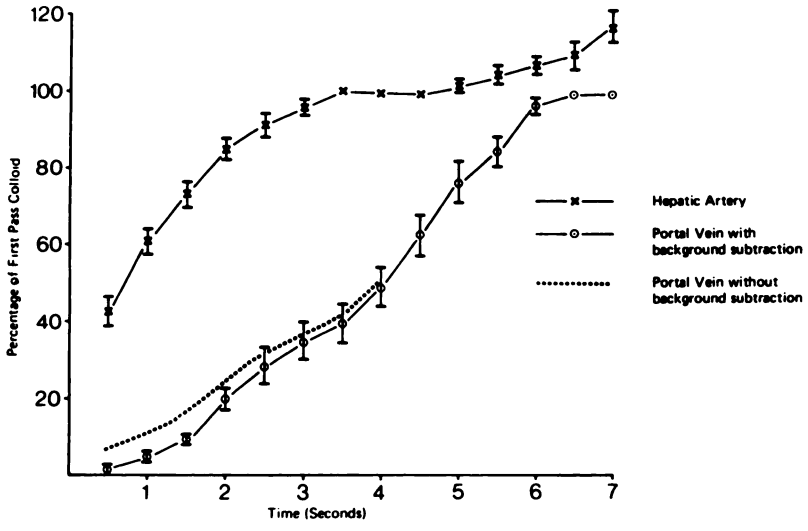

FIG. 4. Mean variation, with time after heart peak, of amount of colloid in liver for first-pass arrival via hepatic artery and portal vein, and recirculation via hepatic artery. Amount of colloid is expressed as percentage of total first-pass colloid arriving via that vessel.

TABLE 1. VARIATION OF CALCULATED PERCENTAGE FOR PORTAL-VEIN CONTRIBUTION WITH CHOICE OF TIMES t_a AND t_p AFTER THE HEART PEAK

	Time t_p (sec)				
Time t_a (sec)	5.0	5.5	6.0	6.5	7.0
1.0	74.0	74.4	74.8	75.2	75.5
1.5	70.9	71.4	71.8	72.2	72.6
2.0	69.3	69.7	70.2	70.6	71.1

the hepatic-arterial phase and the commencement of the portal-vein phase is shown in Fig. 4. This suggests that the optimum time for t_a is ~1.5 sec after the heart peak, by which time (73 ± 3)% (s.e.m.) of the arterial-phase colloid has reached the liver, compared with only (10 ± 1)% of the portal-phase colloid. The estimation of the latter figure is complicated by a relatively high background contribution in the early part of the liver histograms in the hepatic-arterial group (Fig. 4). Despite this difficulty, however, it can be seen that the two phases are well separated.

Figure 4 also illustrates the separation between the end of the portal-vein phase and the commencement of hepatic-arterial recirculation. Clear separation between these two phases was observed, and an optimum mean time for t_p of 6.0 sec after the heart peak is suggested from our results. The main difficulty in the determination of t_p arises from the assumption that the portal-vein phase is completed in 6.0 sec. This assumption was made from the observation that, following hepatic-arterial ligation, there was a period of relatively low gradient in the liver histogram between approximately 5.5 and 7 sec after the heart peak in all animals studied.

Table 1 shows the way in which errors in the choice of t_a and t_p affect measurement of the percentage for portal-vein contribution in normal animals. Taking optimum mean values of t_a and t_p after the heart peak, the mean portal-venous contribution (P), expressed as a percentage of total hepatic perfusion, is (71.8 ± 5.3)% (s.d.). Variations of the optimum t_a and t_p values in individual animals contributed to the error in this result. If typical errors for t_a and t_p are estimated as ± 0.25 and ± 0.5 sec, respectively, the error in P is ± 3%. Additional errors of the order of ± 3% in the evaluation of P result from counting statistics.

The validity of this method for total hepatic values depends upon uniform perfusion within the liver, since information can be obtained only from the shaded areas shown in Fig. 2. The method also depends on the assumption that the extraction efficiency of technetium sulfur colloid is close to 100%. In diseased livers the extraction efficiency is probably decreased. This will lead to errors in accurately quantitating the ratio of arterial to portal-venous flow, although a gross assessment of the relative flows should still be possible.

It was possible to make an alternative evaluation of P from measurements of total liver perfusion (*6*) in animals following either hepatic-arterial ligation or porta-caval diversion. This previously described method gave P a value of (69.2 ± 2.8)% (s.d.) in the present study. Close agreement between the results of the two methods supports the validity of this new technique. Alterations of hepatic perfusion occur in many diseases, e.g., portal hypertension and following hepatic resection (*6*). Assessment of the relative contributions of arterial and portal-venous components of perfusion by dynamic scintigraphy is of promise in patients undergoing porta-caval diversion and in studies of the regenerative response.

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