UPTAKE OF A COLLOID IN RAT LIVER FOLLOWING INTRAVENOUS INTRASPLENIC AND INTRAMESENTERIC INJECTION

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Intramesenteric and intrasplenic injections of ^{99m}Tc-sulfur colloid in the rat resulted in significant differences between the mean uptakes in only some of the liver lobes. More important were the wider interlobular variations seen in the intrasplenic and intramesenteric routes of injection compared with the intravenous route. It is suggested that these differences result from laminar blood flow in the portal vein. In the light of our findings, previous evidence must be considered inconclusive. Laminar flow appears to vary between individual animals and may also vary from time to time in the same animal. Caution is therefore advised when other than systemic routes of injection are used.

The selective distribution of blood to the lobes of the human liver has been the subject of much investigation (*1–4*). Preferential localization of abscesses and metastases within the right lobe of the liver (*5,6*) has been assumed to result from such selective distribution. Evidence of laminar flow has also been sought in other species (*7–10*) but these investigations reported only limited data. For this reason and because of the development of techniques for direct portal injection in the rat (*11*) the present study was undertaken. Investigation of the intrahepatic distribution of ^{99m}Tc sulfur colloid was made following injection into the jugular vein, the inferior mesenteric vein, and into the spleen pulp.

MATERIALS AND METHODS

Twenty-six adult Sprague-Dawley rats were used in the study. The animals were bred in the animal unit of the Welsh National School of Medicine, weaned at 3 weeks, and subsequently maintained on Spillsbury's Breeding Diet. All experiments were carried out under general anesthesia induced with ether and continued with intraperitoneal Nembutal (60 mg/ml, 0.07 ml/100 gm body weight). The animals were immobilized in a supine position and a midline abdominal incision was made. The viscera were disturbed as little as possible and the radioactivity was injected slowly.

Technetium-99m sulfur colloid was prepared by the method of Larson and Nelp (*12*) and 20 μCi were administered in all cases in a volume which was usually much less than 1 ml.

The animals were divided into three groups. In the first group (eight animals) the ^{99m}Tc-sulfur colloid was injected through the jugular vein. Injection in the second group (nine animals) was made into the pulp of the spleen. In the third group (eight animals) injection was made into a tributary of the inferior mesenteric vein close to the gut wall. In each case injection was made fairly slowly to avoid leakage around the needle.

The animals were sacrificed 5 min after injection in the first group to allow adequate clearance from the blood. In the latter two groups sacrifice was performed 1 min after injection to minimize the effects of recirculation. The liver was removed and divided into lobes, washed, and excess moisture removed. Each lobe was placed in a preweighed counting tube, shaken to the bottom, weighed, and counted in an automatic gamma counter.

In order to avoid the necessity of homogenizing the tissue, the lobes were counted whole and a correction made for variation in counting efficiency due to the different masses of liver. The efficiency curve obtained for different weights of a solution of technetium in the same tubes is given in Fig. 1. A small error of 1–2% was thus introduced because of the irregular shape of the liver. Correction was made for

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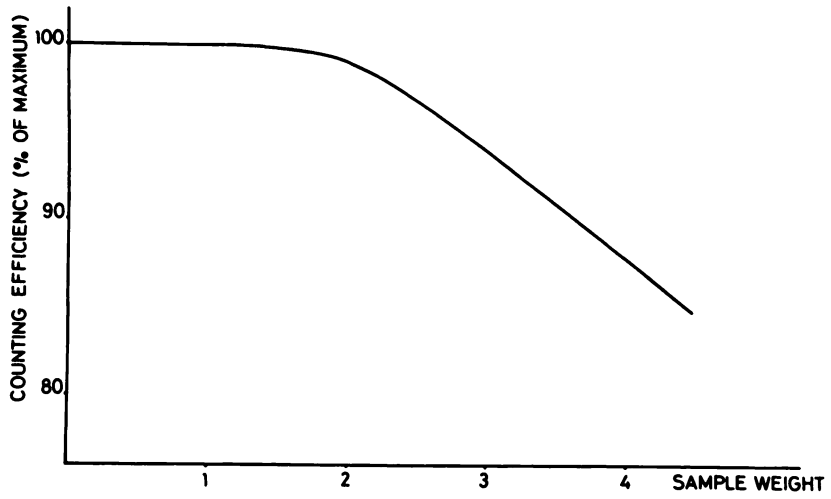

FIG. 1. Efficiency of counting of ^{99m}Tc-sulfur colloid with change in sample volume.

radioactive decay during the counting of a series of tubes.

RESULTS

The counting rate per gram in each lobe was calculated and expressed as a percentage of the mean counting rate per gram for all lobes in a particular animal. The average value for each lobe from all the animals injected by a particular route was then calculated together with the standard deviation (Fig. 2). The significance of the differences between corresponding lobes of the three groups was evaluated. In only two cases were there significant differences between the average uptake in a particular lobe when the three methods of injection were compared. For the anterior lateral lobe the intrasplenic value differed from the intravenous one ($p = 0.005$) and for the posterior right lobe the mesenteric value differed from the intravenous one ($p = 0.01$). In addition, the variability of the uptakes following intrasplenic and intramesenteric injections was considerably greater than that for intravenous injection.

DISCUSSION

The results obtained are strong evidence that laminar flow does occur in the portal system of the rat. The wide variability in the differences between the lobes from one animal to another indicates that such streamlining varies from animal to animal although a small preference for particular lobes is

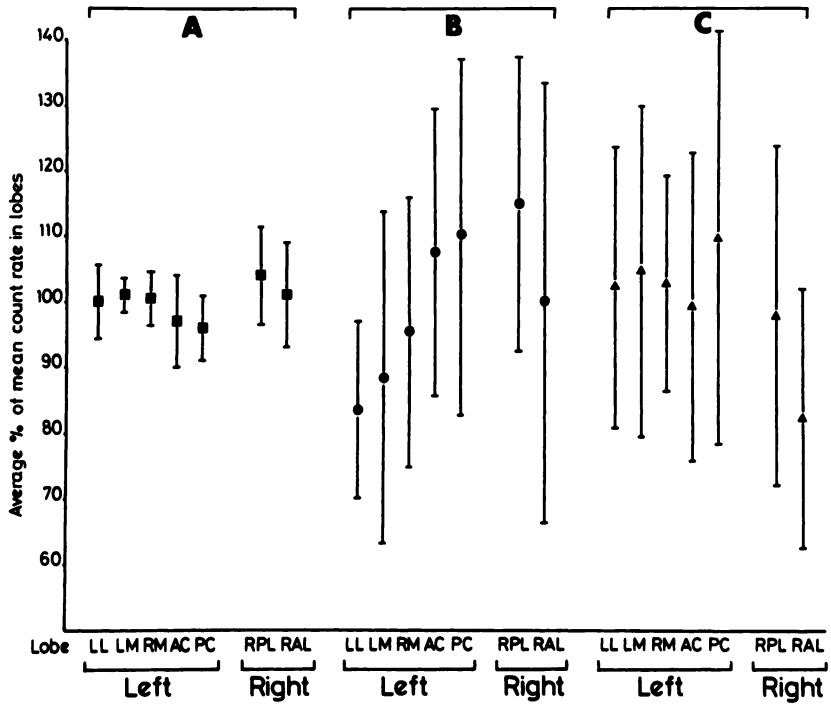

FIG. 2. Average uptake of ^{99m}Tc-sulfur colloid in the lobes of rat liver (percent of mean). (A) Jugular, (B) splenic, and (C) mesenteric injections. Lines show plus and minus 1 s.d. Nomenclature and grouping are as used by LeBouton and Hoffman (7). LL is left lateral, LM is left median, RM is right median, AC is anterior caudate, PC is posterior caudate, RPL is right posterior lateral, and RAL is right anterior lateral.

maintained in a limited number of instances. The fact that such variation occurs is perhaps not surprising in view of the complex nature of the blood supply to the rat liver. Indeed, variation from time to time in the same animal would not be unexpected but the present method is of course unable to demonstrate such temporal changes.

Following jugular venous injection, blood flowing through the spleen is at least partially cleared of colloid by this organ. Thus the values obtained by this route should tend towards those obtained by intramesenteric injection. Our values of mean uptake per gram show no such tendency although the effect may account for some of the variation seen with the systemic route. However, the tendency will, to some extent, be masked by the contribution of the hepatic artery to liver blood supply.

Our findings differ somewhat from those of LeBouton and Hoffman (*7*) who showed a difference in uptake when the left lobes as a whole were compared with those on the right following the injection of ^{14}C-labeled leucine intramesenterically and intrasplenically. However, they investigated only one animal by each route.

Because the ^{99m}Tc-sulfur colloid is not extracted with 100% efficiency on one passage through the liver, the sensitivity of our method is slightly less than would occur with complete extraction. Since the particle size is relatively large at around 0.5 μm (*12*), it is probably extracted with approximately 80% efficiency (*13,14*). Thus, although recirculation will reduce the sensitivity to a small extent, the difference is minimized by the early sacrifice of the animal. In the case of splenic injections the effect is reduced even further since the ^{99m}Tc-sulfur colloid is not cleared immediately from this organ. The efficiency of extraction of ^{99m}Tc-sulfur colloid is certainly better than that for leucine as used by LeBouton and Hoffman (*7*). These authors waited 15 min before sacrifice. An investigation similar to ours by Gates and Dore (*4*) makes no mention of extraction efficiency and no measurements were made until at least 24 hr after mesenteric injection.

Although it seems probable that the variation in uptake found in this study is due to laminar flow, it is apparent that caution must be observed in the interpretation of results obtained by techniques employing injection into any part of the portal system.

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