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INTRAHEPATIC DISTRIBUTION OF PORTAL AND HEPATIC ARTERIAL BLOOD FLOWS IN ANAESTHETIZED CATS AND DOGS AND THE EFFECTS OF PORTAL OCCLUSION, RAISED VENOUS PRESSURE AND HISTAMINE

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SUMMARY

1. Radioactive microspheres were used to determine the distribution of arterial and portal flows within the liver. ^{141}Ce-microspheres and ^{51}Cr-spheres were given to allow two determinations of flow distribution in each animal and experiments are described to establish the accuracy and validity of the method.

2. Mean flow/g to any lobe or segment of a lobe in a group of animals was not markedly different from the mean flow/g to the whole liver, and in general the liver was homogeneously perfused with both portal and arterial blood. However, in any one liver, some areas received a relatively greater flow (up to 300 %) and some a relatively smaller flow (down to 50 %) at the time the microspheres were given. The gall bladder received a much smaller portal flow/g than the parenchyma but its arterial flow/g varied widely in different animals.

3. If portal flow to an area of parenchyma was reduced by occlusion of a branch of the portal vein, this area received a significantly increased arterial flow.

4. An increase in hepatic venous pressure did not cause a significant change in the intrahepatic distribution of either arterial or portal flows in cats.

5. In dogs, infusions of histamine into the portal vein caused a redistribution of portal flow away from the free ends of the lobes towards the hilar ends but the distribution between lobes did not change and there was no redistribution of arterial flow.

INTRODUCTION

Greenway & Stark (1971) recently reviewed the available data on a variety of hepatic vascular parameters and their control. A great deal of information was available on the range of total hepatic arterial and portal flows and on factors which varied these flows, but few studies have been made on their intrahepatic distribution. Although work has been done on transilluminated liver edges and by preparation of corrosion casts, these methods do not give quantitative data. A recent study using a diffusible indicator is discussed later. A new technique with radioactive microspheres has become available for studying the distribution of the cardiac output or the gross distribution of flow within regional vascular beds (Grim & Lindseth, 1958) and it was carefully evaluated by Rudolph & Heymann (1967) who used it to study distribution of flow in the foetus. Other workers have studied distribution in the heart (Domenech, Hoffman, Noble, Saunders, Henson & Subijanto, 1969) and kidney (McNay & Abe, 1970; Slotkoff, Logan, Jose, D'Avella & Eisner, 1971). This paper describes experiments to establish the validity and accuracy of the technique for studying the intrahepatic distribution of portal and arterial flows in anaesthetized cats and dogs. The microsphere technique now allows us to measure the relative amounts of arterial or portal blood flow to each lobe or to any area of the liver.

Since a decrease in total portal flow causes a reciprocal increase in total arterial flow (Greenway & Stark, 1971), we have examined whether this relationship occurs within a single lobe of liver when a branch of the portal vein is occluded. Our previous studies on raised hepatic venous pressure in cats suggested that although this procedure caused a myogenic vasoconstriction of the hepatic arterial bed, it did not alter sinusoidal surface area (Greenway & Lautt, 1970). This suggests that no intrahepatic redistribution of flow occurs and we have tested this prediction. In dogs, large doses of histamine cause outflow block and a marked congestion of the liver (Oshiro & Greenway, 1971) and it was of interest to examine whether histamine caused a redistribution of intrahepatic flows.

METHODS

Cats were anaesthetized by I.P. injections and dogs by I.V. injections of sodium pentobarbitone (Nembutal, Abbott Laboratories, 30 mg/kg). When reflex limb, ear and swallowing movements returned, supplementary doses of pentobarbitone (2 mg/kg) were given through a cannula in a forelimb cutaneous vein. The trachea was intubated (dogs) or cannulated (cats) and arterial pressure was recorded from a cannula in a femoral artery with a Statham P23AC pressure transducer. The abdomen was opened by a mid-line incision and the following procedures were carried out when required.

For injection of microspheres into the portal vein, a small cannula with side holes for 3 mm from the sealed tip was introduced into the portal vein through a small vein from the appendix or spleen. For injection of microspheres into the hepatic artery, the spleen was removed and a small cannula was inserted through the splenic artery into the coeliac artery. The gastric and gastroduodenal arteries were tied so that the coeliac artery supplied blood only to the liver. Two types of microspheres, one tagged with ^{141}Ce, the other with ^{51}Cr, were used to allow two determinations of flow distribution in each animal. These spheres were 15 ± 5 μm diameter and they were suspended in 10% dextran (3M Nuclear Products, Minnesota). Microscopic examination showed that after vigorous shaking there were very few clumps of spheres in the solution used for injection. We did not use Tween 80 to aid the suspension of the spheres since it can release histamine and in dogs this might cause some degree of outflow block in the liver (Greenway & Stark, 1971). A dose was chosen to produce convenient levels of radioactivity in the tissue slices (5000–25,000 counts per minute (cpm)). This dose contained approximately 10^5 microspheres and this is sufficient for maximum precision (Buckberg, Luck, Payne, Hoffman, Archie & Fixler, 1971). It was injected in a volume of 0·5 ml. and washed in with 1·0 ml. 0·9% (w/v) NaCl solution.

Infusions of histamine acid phosphate (British Drug Houses) were prepared in 0·9% (w/v) NaCl solution and infused into the portal vein through a cannula in a small branch of the splenic vein. Doses are expressed as free base.

In some cats, a long-circuit technique was set up to allow measurement and control of hepatic venous pressure (Greenway & Lautt, 1970). Briefly, the inferior vena cava was ligated below the liver and the hepatic outflow was drained from a cannula in the thoracic inferior vena cava. Blood entering the inferior vena cava below the occlusion drained from cannulae in the femoral veins. Blood was returned from a reservoir through cannulae in the external jugular veins. Hepatic venous pressure was controlled by raising or lowering the outlet of the hepatic venous cannula. In other cats, inferior vena cava pressure was increased by partial occlusion of the thoracic inferior vena cava by a ligature. The pressure was recorded at the level of the hepatic veins by a cannula inserted through a femoral vein.

At the end of each experiment, the animal was killed and the portal vein and hepatic artery were tied to prevent backflow of blood during removal of the liver. The liver was weighed and separated into its seven lobes. The gall bladder was separated and emptied. Each lobe was cut into transverse slices (2 mm thick, 1–4 g weight) beginning at the end furthest from the hilum, and each slice was placed in a plastic tube, weighed and counted in a two-channel auto-gamma spectrometer (Packard Instrument Co.). The settings of the counter to cover the two peaks of radioactivity were determined from measurements of the energy spectra of the radioactive microspheres and in each experiment samples of each type of spheres were counted to determine the overlap of radioactivity between the channels. The overlap of ^{141}Ce into the ^{51}Cr-channel was $0{\cdot}29 \pm 0{\cdot}12$% (mean $\pm$ S.E.) and no correction was made for this. The overlap of the ^{51}Cr into the ^{141}Ce-channel was $23 \pm 1{\cdot}1$% and this overlap was subtracted to obtain the true ^{141}Ce count. The total radioactivity due to each type of microsphere was obtained by summing the radioactivity in all the samples. The lung was also weighed and the radioactivity in two samples was measured to estimate the extent to which the microspheres passed through the liver and were trapped in the lungs.

The cpm/g for each type of microspheres for each tissue slice, for each lobe and for the whole liver were calculated and the cpm/g for each slice and each lobe were expressed as a ratio of the cpm/g for the whole liver. These values were designated as 'relative flows' throughout the paper. A value of 0·5 or 2·0, for example, indicates that the area of liver received half or double respectively the mean flow through the

whole liver. Using these relative flow data and the known position of each tissue slice in the liver, maps of the gross distribution of flow were constructed.

To obtain qualitative data on the distribution of the spheres within each slice, radioautography was carried out on Type NTB 3 Nuclear Track Plates (Kodak Ltd). Representative slices from different parts of the liver after injection of ^{141}Ce-spheres were wrapped in thin plastic sheets and placed on photographic plates. The exposure time was 24 hr and the plates were kept at $-20°$ C for this period to minimize shrinkage of the tissue slices.

RESULTS

The mean arterial pressure was 123 ± 4 mm Hg (mean $\pm$ S.E.) in cats and 125 ± 5 mm Hg in dogs at the time of injection of the microspheres. The mean data on body weight, liver weight and the weights of the individual liver lobes are given in Table 1. There was considerable variation in the relative sizes of the different lobes in different animals.

Intrahepatic flow distribution in control experiments

The radioactivity in the lungs did not exceed 0·3 % of the total injected in any experiment and the mean value was $0{\cdot}14 \pm 0{\cdot}03$ %. Thus the proportion of microspheres which passed through the liver and were trapped in the lungs was negligible. Blood samples contained no detectable radioactivity 10 min after injection of the microspheres (four experiments) and the loss of radioactivity on to the tissue paper during slicing of the liver was negligible (four experiments).

In eleven experiments, including controls and histamine treatments, autoradiography was carried out on 86 slices of liver. The microspheres were uniformly distributed within each slice and no concentration of spheres in the centre or near the surface of the slice was observed. The measurement of distribution by counting radioactivity of transverse slices is therefore reasonable.

The mixing of microspheres in the inflowing blood was studied by simultaneous injection of the two types of microspheres through separate cannulae into the portal vein (four experiments) or hepatic artery (two experiments). The variation between the relative flows determined from the two isotopes in each slice of liver is a measure of the error due to incomplete mixing in the inflowing blood. The coefficient of variation (Steel & Torrie, 1960) in these experiments was 15 %. A representative experiment is shown in Fig. 1. The relative flows for the slices of liver determined from each isotope are shown. The 99 % confidence interval was 0·82–1·18 and the areas marked with an asterisk received a significantly higher or lower flow/g than the liver as a whole. The data in these experiments were also analysed by Tukay's procedure to determine the honestly significant difference (Steel & Torrie, 1960). The areas with relative flows above or below the 99 % confidence limits were also significantly different ($P < 0{\cdot}01$)

by this procedure. Thus in any one liver from either a cat or a dog, some areas received significantly high or low relative flows. The highest relative flow was 3·8 and the lowest 0·4 but such values were exceptional. Large differences in the relative flows of adjacent slices were not seen.

The mean values of the relative flows for each area and each lobe were calculated for the control injections in all the experiments in cats (arterial flow $n = 11$; portal flow $n = 12$) and dogs (arterial flow $n = 15$; portal

TABLE 1. The means (± S.E.) for body weight, liver weight, weights of individual liver lobes (as % total liver weight) and relative portal and hepatic arterial flows in each lobe in twenty-two cats and twenty-three dogs

	Cat			Dog		
Body weight ...	2·3 ± 0·09 kg			7·1 ± 0·3 kg		
Liver weight ...	62 ± 2·6 g			200 ± 11 g		
	Lobe weight as % total liver weight	Relative flows		Lobe weight as % total liver weight	Relative flows	
		Portal	Arterial		Portal	Arterial
Left lateral	30 ± 0·7	0·86 ± 0·08	0·90 ± 0·05	29 ± 0·7	0·91 ± 0·04	1·01 ± 0·05
Left medial	12 ± 0·7	1·14 ± 0·07	0·98 ± 0·06	14 ± 0·4	0·94 ± 0·04	0·90 ± 0·05
Quadrate	12 ± 0·5	0·97 ± 0·09	1·07 ± 0·08	7 ± 0·4	0·87 ± 0·06	1·21 ± 0·09
Right medial	21 ± 0·9	0·96 ± 0·13	0·98 ± 0·04	17 ± 0·5	0·91 ± 0·06	0·92 ± 0·06
Right lateral	11 ± 0·6	1·20 ± 0·16	1·12 ± 0·12	16 ± 0·6	1·24 ± 0·09	0·89 ± 0·09
Caudate	9 ± 0·4	1·38 ± 0·24	1·23 ± 0·13	10 ± 0·5	1·34 ± 0·07*	0·97 ± 0·08
Papillary process	3 ± 0·1	1·20 ± 0·14	1·27 ± 0·17	6 ± 0·1	0·94 ± 0·09	1·68 ± 0·10*
Gall bladder (empty)	2 ± 0·1	0·04 ± 0·01*	3·14 ± 0·70	1 ± 0·1	0·06 ± 0·01*	1·87 ± 0·58

* Indicates significantly different from 1·0 (t test, $P < 0·01$).

flow $n = 15$). In cats, these mean values were not significantly different from the mean flow through the whole liver (1·0) in any area or lobe (t test, $P > 0·05$). In dogs, the portal flow to the caudate lobe and the arterial flow to the papillary process were significantly higher than the mean flow to the whole liver. The mean values for the lobes are shown in Table 1. The gall bladder received a much lower portal flow than the hepatic parenchyma in both cats and dogs but its relative arterial flow was very variable in different animals and ranged from 0·5 to 6·0 in both cats and dogs. The causes of this variability were not clear and it was still present after acute hepatic denervation in six cats.

Relative distribution of portal and arterial flows in each area of liver

In eight experiments, ^{141}Ce-microspheres were administered into the portal vein at the same time that ^{51}Cr-spheres were given into the hepatic

artery. The arterial flow in any area was not inversely related to the portal flow in the same area (correlation coefficient 0·06, $P > 0·3$). In these experiments, there were eighty-one slices of liver where the relative portal flow was significantly less than the mean portal flow through the whole liver ($P < 0·01$). The mean relative arterial flow in these areas was 1·07 ± 0·07. Thus areas which received a spontaneously low portal flow did not receive a significantly high arterial flow.

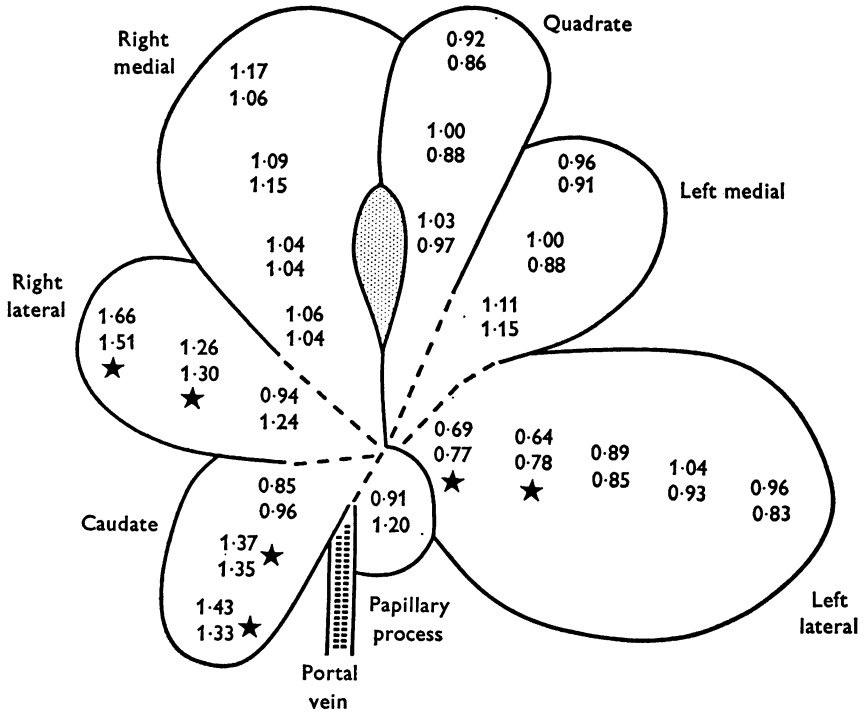

Fig. 1. Map of gross intrahepatic distribution of portal flow during the control period in one cat. Each pair of data represent the relative flows in a tissue slice determined from the two types of microspheres given simultaneously through different cannulae in the portal vein. The values for alternate slices have been omitted for clarity. The relative flows in the areas marked with an asterisk are significantly different ($P < 0·01$) from the mean flow for the whole liver (1·0).

Since it is well established that reduction in total portal flow causes hepatic arterial vasodilatation, this problem was investigated further in five experiments in which a large branch of the portal vein to the left lateral lobe was ligated. ^{141}Ce-microspheres were given into the portal vein at the same time that ^{51}Cr-spheres were given into the hepatic artery. The mean results for four of the five experiments are shown in Fig. 2. The

relative portal flow was markedly reduced in the free end of the left lateral lobe while that in the hilar end was not significantly altered. Clearly the ligated portal vein branch supplied blood to the free end of the lobe. In the areas with a reduced portal flow, the relative arterial flow was significantly increased (unpaired t test, $P < 0{\cdot}01$). The relative distribution of portal and arterial flows in the other lobes of the liver were not significantly different from the control animals. In the fifth dog, arterial flow was not increased in the free end of the left lateral lobe even though portal flow was reduced.

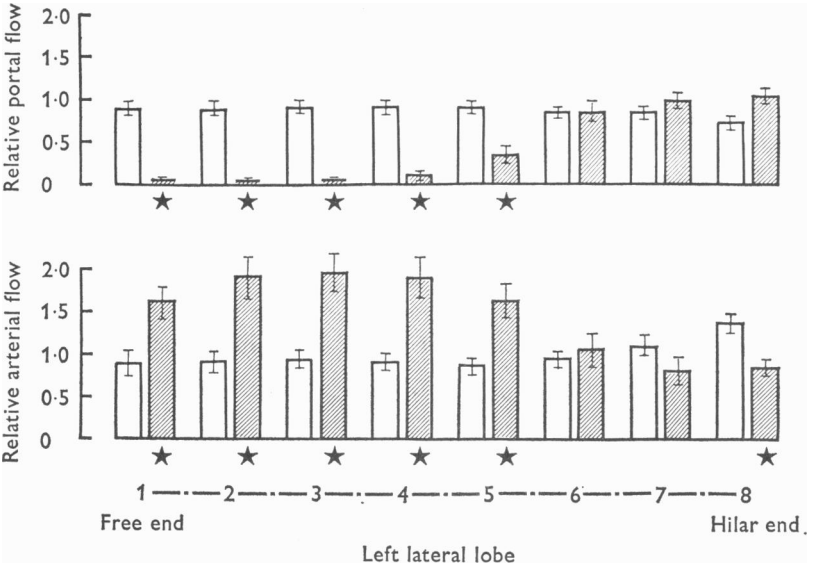

Fig. 2. The means (± S.E.) of relative portal and arterial flows in eight transverse slices of the left lateral lobe determined by simultaneous injection of microspheres into the portal vein (^{141}Ce-spheres) and hepatic artery (^{51}Cr-spheres) in eight control dogs (open bars) and in four dogs after occlusion of a branch of the portal vein to the left lateral lobe (shaded bars). The asterisks indicate $P < 0{\cdot}01$, t test for unpaired data.

The relative arterial flows in all the areas of the left lateral lobes in the four successful experiments were plotted against the relative portal flows in the same areas and the regression line was calculated (Steel & Torrie, 1960). The regression intercept was 1·93, the slope was 1·05 and the correlation coefficient was 0·71 ($P < 0{\cdot}001$). Thus at zero portal flow, the mean relative arterial flow was 1·93.

These experiments suggest that areas of liver which receive a spontaneously low portal flow do not receive an increased arterial flow but in areas where portal flow is reduced by occlusion of a portal branch, arterial flow is significantly increased.

Increased hepatic venous pressure

In four cats, the caval long-circuit was set up to allow hepatic venous pressure to be increased by 7 mm Hg (Greenway & Lautt, 1970). In two of these cats, ^{141}Ce-microspheres were injected into the portal vein before and ^{51}Cr-spheres were injected 10 minutes after hepatic venous pressure was increased. In the other two cats, the spheres were given at the same times but into the hepatic artery. Another four experiments were done in which hepatic venous pressure was raised to the same level by partial occlusion of the thoracic inferior vena cava with a ligature. In these cats, venous pressure increased not only in the liver but in all beds drained by the inferior vena cava and arterial pressure decreased from $122 \pm 8{\cdot}3$ mm Hg (mean $\pm$ S.E.) to $80 \pm 3{\cdot}5$ mm Hg. The microspheres were given at the same times into the portal vein in two cats and into the hepatic artery in two cats.

In these eight experiments, there were no significant changes in the relative portal or arterial flows to any areas or lobes of the liver during the periods of raised hepatic venous pressure (paired t test, $P > 0{\cdot}1$). It is concluded that increased hepatic venous pressure does not alter gross intrahepatic distribution of arterial or portal flows in the cat.

Histamine infusions

In four dogs, histamine (4 μg min^{-1} kg^{-1}) was infused into the portal vein. ^{141}Ce-microspheres were injected into the portal vein before and ^{51}Cr-spheres were injected 5 min after the infusion of histamine was begun. The mean relative portal flow in each area and each lobe for the four experiments before and during histamine infusion were compared (paired t test). Since this involves nearly 100 sets of data, the results are presented in the following way. Fig. 3 shows a diagrammatic map of the liver. In the striped areas, relative portal flow decreased during histamine infusions, in the stippled areas it increased while in the blank areas it showed no change. It can be seen that there was a redistribution of portal flow towards the hilum of the liver. The data from the slices of liver in each lobe were pooled into three groups, viz. the outer third (free end), middle third and inner third (hilar end). The mean data for the free and hilar ends of each lobe are shown in Table 2. The papillary process was considered as a whole since it is small and lies close to the hilum. The relative portal flow in the free ends showed a significant decrease except in the caudate lobe. The flow in the hilar ends and papillary process showed a relative increase and these increases were significant in five of the seven lobes. The centres of the lobes showed no significant changes and there were no changes in the distribution between lobes (except for the papillary process).

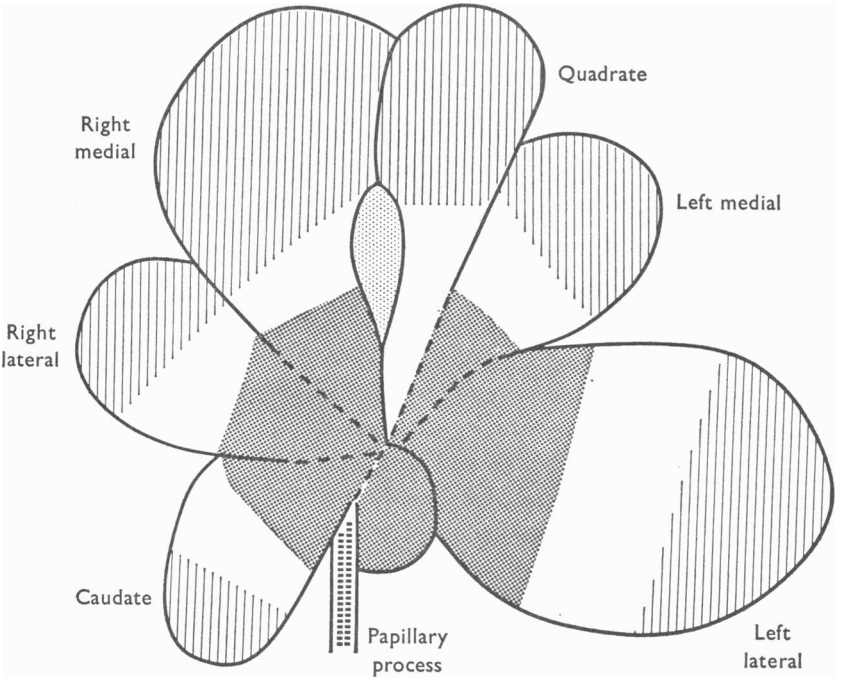

Fig. 3. The changes in the intrahepatic distribution of portal flow in dogs during infusion of histamine (4 μg min^{-1} kg^{-1}) into the portal vein. The relative flow decreased in the areas shaded by diagonal lines and increased in the stippled areas.

TABLE 2. The means ($\pm$ paired S.E.) of the relative portal flows in the free and hilar ends of each lobe of the liver before and during infusion of histamine (4 μg min^{-1} kg^{-1}) in four dogs

	Relative portal flow					
	Free end			Hilar end		
Lobe	Control	Histamine	(S.E.)	Control	Histamine	(S.E.)
Left lateral	0·93	0·55*	(0·03)	0·79	1·28*	(0·08)
Left medial	0·84	0·40*	(0·02)	0·90	1·37*	(0·19)
Quadrate	0·77	0·49*	(0·04)	0·87	0·75	(0·12)
Right medial	0·89	0·71*	(0·04)	0·95	1·49*	(0·09)
Right lateral	1·43	0·97*	(0·07)	1·18	1·47*	(0·09)
Caudate	1·56	1·39	(0·11)	1·18	1·46	(0·18)
Papillary process				1·22	2·53*	(0·16)

* Indicates $P < 0{\cdot}01$, t test for paired data.

Although this redistribution towards the hilum was significant, it represents small changes in the relative flows. The largest changes were to half or double the mean flow through the whole liver and in many areas the redistribution was smaller than this.

In four dogs, the same procedures were carried out except that the microspheres were given into the hepatic artery. There were no significant changes in the distribution of hepatic arterial flow during histamine infusions.

DISCUSSION

Several problems were encountered in this attempt to use the microsphere technique as a measure of the distribution of flow within the liver. The first problem was measurement of distribution in an organ as large as the liver. The most accurate localization of the spheres is obtained by autoradiography and this was attempted first. The autoradiographs indicated that the distribution of microspheres within each transverse slice was uniform. We looked particularly for redistribution between the surface relative to the deep parts of each slice but no evidence for such changes was seen. Quantitative comparison between different slices was not possible by autoradiography and it was decided to count the slices in a gamma-spectrometer. This also allowed the use of two isotopes so that comparisons of distribution could be made within each liver.

The second problem was to obtain uniform mixing of the injected microspheres in the inflowing stream of blood (Wagner, Rhodes, Sasaki & Ryan, 1969). We tested this by simultaneous injection of microspheres labelled with two different isotopes through different cannulae into the same inflow vessel. The variation between the simultaneous duplicate measurements was thus a measure of mixing errors. In these experiments, the coefficient of variation was 15% and the 99% confidence interval represented flows of 80–120% of the mean. Thus the method appeared to be sufficiently precise to show redistributions which were likely to be of physiological significance. The total portal and arterial flows during the control periods in anaesthetized animals are well established and the changes produced by the experimental procedures used here are well known (Greenway & Stark, 1971). Therefore we did not measure the flows in these experiments in order to minimize the surgical interference with the animal.

In the experiments where simultaneous injections of the two types of microspheres were made into the same vessel, it was shown that certain areas of liver received a high or a low portal or arterial flow at the particular moment the microspheres were given. There was no evidence of any reciprocal relationship between arterial and portal flows in these areas and the mechanisms and causes of this spontaneous inhomogeneous perfusion are

not known. These areas were randomly distributed in different animals and the mean flow in any area of liver for a group of animals was not significantly different from the mean flow for the whole liver with two exceptions. These exceptions were the portal flow to the caudate lobe and the arterial flow to the papillary process in dogs. The greater flows in these areas were not dramatic from the physiological point of view but might indicate a hydrostatic gravitational effect on the distribution of portal flow. Thus in general, the liver appears to be homogeneously perfused with both portal and arterial blood. These findings are similar to those in a recent study on the distribution of labelled water in the liver (Griffen, Levitt, Ellis & Lifson, 1970; Lifson, Levitt, Griffen & Ellis, 1970). This similarity between data obtained with microspheres and that obtained with a diffusible indicator is further support for the validity of the techniques.

The gall bladder received a very small portal flow but its relative arterial flow was very variable and in different animals it ranged from 50 to 600 % of that to the hepatic parenchyma. The mechanism and causes of this variability were not obvious but since it occurred in experiments where the hepatic nerves were sectioned, sympathetic vasoconstriction of the vessels to the gall bladder appears to be excluded.

It is well established that a decrease in portal flow causes hepatic arterial vasodilatation, probably by a myogenic response of the hepatic arteriolar smooth muscle to a reduction in sinusoidal pressure (Hanson & Johnson, 1966; Greenway & Stark, 1971). Our experiments demonstrate that this compensatory arteriolar vasodilatation can occur in relatively small areas of liver when portal flow to that area is selectively reduced. The relative arterial flow could increase to 3·0 but the average increase was to 1·9. This agrees with our previous data that maximal hepatic arteriolar vasodilatation in the splenectomized cat increased arterial flow up to 300 % (mean 200 %) of control. It seems likely that in the one animal which did not show this response, the hepatic arterial bed was already maximally dilated due to the reduction in portal flow after splenectomy. As we discussed previously (Greenway & Lawson, 1969), hepatic arteriolar vasodilator responses in splenectomized animals represent underestimates of the responses likely to occur in the intact animal.

The radioactivity in the lungs was negligible in all the experiments reported here. Thus there was no arterio-venous or porto-venous anastomoses large enough to allow microspheres (15 ± 5 μm diameter) to pass through them. This confirms other evidence that there are no shunt vessels in the normal liver (Gordon, Flasher & Drury, 1953; Ohlsson, Rutherford, Boitnott, Haalebos & Zuidema, 1970).

We have previously shown that an increase in hepatic venous pressure

causes a continuous transsinusoidal fluid filtration (Greenway & Lautt, 1970). No protective mechanisms, involving, for example, reduction in sinusoidal surface area, appeared to exist in the liver although they have been demonstrated in the vascular bed of skeletal muscle (Mellander, Oberg & Odelram, 1964). In addition, vasodilator drugs such as isoprenaline and histamine do not change sinusoidal surface area and they do not modify transsinusoidal filtration induced by an increased hepatic venous pressure in cats (Greenway & Lautt, 1972). From this data, we predicted that an increased hepatic venous pressure would not change intrahepatic distribution of either portal or arterial flow and the results in this paper confirm this prediction.

We have recently been studying the mechanism of outflow block caused by histamine in the dog liver (Oshiro & Greenway, 1971). During this response, the liver becomes congested and its volume increases due to contraction of the hepatic and sublobular veins. We were interested in whether there was a gross redistribution of flow within the liver. The results suggest that a redistribution of portal flow occurs from the free ends towards the hilar ends of the lobes. This redistribution is consistent with observations on hepatic venous and portal pressures during histamine infusions. Pressure was recorded from several sites in a major hepatic vein which runs down the centre of each lobe. The increase in this pressure during histamine infusion was greater near the free end of the lobe than at the hilar end. Thus the pressure gradient for flow (portal minus hepatic venous pressure) was smaller at the free end of the lobe than at the hilar end during histamine infusion (G. Oshiro & C. V. Greenway, unpublished observations). Since arterial pressure is much greater than portal pressure, this increase in venous pressure is not sufficient to alter the distribution of arterial flow. It seems unnecessary to postulate any pre-sinusoidal actions of histamine to explain its effects on intrahepatic flow distribution.

In general, this work confirms our previous conclusions from studies on transsinusoidal filtration that presinusoidal sphincters do not occur in the liver (Greenway & Lautt, 1970; Greenway & Stark, 1971; Greenway & Lautt, 1972). Stimuli which change portal or hepatic arterial resistances appear to act uniformly in the liver and they change total flows and pressures without causing a marked intrahepatic redistribution of these flows. However, this conclusion cannot be regarded as established until a wider variety of stimuli is examined. Areas of parenchyma with spontaneously high or low flows can occur and the mechanisms responsible for this remain to be elucidated.

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