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Significance of increased 'splenic uptake' on liver scintiscanning

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SUMMARY Peak activity over the spleen as a percentage of peak activity over the liver was measured in 265 ^{99m}Technetium sulphur colloid liver scintiscans. The value exceeded 70% in 50 cases. In 32 of these cirrhosis was present; the other 18 scans were from patients with a wide variety of conditions, including secondary deposits, hepatitis, and diseases involving the reticuloendothelial system. A measure of the total activity in the spleen was derived from the peak activity and the length of the spleen. In cirrhosis this was closely related to the finding of oesophageal varices thus showing the importance of a collateral circulation (which allows colloid to bypass the liver) in the increased uptake of colloid by the spleen.

In eight patients with hepatosplenomegaly due to blood dyscrasia or disease involving the reticuloendothelial system, total activities in the liver and spleen were estimated from the anteroposterior colour dot scan, and both liver and spleen blood flow were measured by methods independent of reticuloendothelial cell function. The results showed that the main factor causing increased uptake of colloid by the spleen in these diseases was an increased blood flow in the spleen relative to that in the liver.

The features of cirrhosis on liver scintiscans performed with colloidal materials have been described in detail (Christie, MacIntyre, Gomez Crespo, and Koch-Weser, 1963). The colloid tends to be concentrated in the perihilar region and in the left lobe and activity over the spleen is often increased. The count rate over the liver is often reduced and statistical fluctuations in the count rate produce a patchy appearance on the scan. The mechanisms underlying the increase in activity over the spleen have not been clearly elucidated. In addition to cirrhosis, increased activity over the spleen has been shown in liver scintiscans from patients with bilharzial hepatic fibrosis (Mustafa, Razzak, Mahfouz, and Guirgis, 1966) and sarcoidosis (McAfee, Ause, and Wagner, 1965). A number of other conditions in which colloid is taken up by the spleen have been described by Méchaly, Desgrez, and Kellershorn (1965), but it would appear from their descriptions that in many of these cases uptake was slight and probably within the normal range.

We have been using ^{99m}Technetium sulphur colloid for liver scintiscanning for 18 months and have now scanned 265 patients. It has become apparent that increased uptake of colloid by the spleen may be a feature in many different diseases. In this paper we report an analysis of patients whose scans showed markedly increased activity in the spleen and also describe haemodynamic studies in certain patients with diseases involving the reticuloendothelial system which were carried out to elucidate the mechanisms involved.

MATERIAL AND METHODS

The majority of patients referred for liver scintiscanning were suspected of having intrahepatic, space-occupying lesions, obstructive jaundice, various forms of hepatitis, or cirrhosis. In most patients the diagnosis was confirmed by liver biopsy or at operation.

In eight patients with hepatosplenomegaly due to blood dyscrasia or disease involving the reticuloendothelial system, both liver and spleen blood flows were estimated. Spleen blood flow was measured (ml per 100 g of tissue per min) using the radioxenon method of Williams, Condon, Williams, Blendis, and Kreel (1968). The weight of the spleen was estimated from its area on an anteroposterior radiograph of the sinusoidal filling phase of a splenic arteriogram (Blendis, Banks, Ramboer, and Williams, 1969). Total spleen blood flow could then be calculated. Total hepatic blood flow was estimated using a constant infusion of indocyanine green and measuring hepatic extraction (Caesar, Shaldon, Chiandussi, Guevara, and Sherlock, 1961).

SCANNING TECHNIQUE According to the method of Patton, Garcia, and Webber (1966) 1 mCi of ^{99m}Technetium sulphur colloid was prepared, injected intravenously, and starting 20 minutes later the liver and spleen areas were scanned, with the patient supine, using a Picker Magnascanner V with a 5 in. coarse focus collimator. The peak count rate over the liver in most cases was in the range 30,000 to 80,000 counts per minute. The scans were performed at a speed of 70 cm per min with a time constant of 0·1 second. If the peak count rate was less than 30,000 counts per min the speed was reduced to 40 cm per min and the time constant increased to 0·4 sec to eliminate the patchy appearance which would otherwise be present. A dot factor was chosen to produce a density of 20 dots per centimetre over the region of maximum activity.

RESULTS

Count rates over the spleen and liver were measured and the peak activity over the spleen was expressed as a percentage of the peak activity over the liver. The range of this value in patients finally found to have no evidence of disease involving the liver or spleen was 0 to 35%. Activity over the spleen was moderately increased (35 to 70%) in a large number of scans and this group will not be discussed further. Peak activity over the spleen of more than 70% of peak activity over the liver was present in 50 of the 265 scans. These included 32 of 54 cases with cirrhosis, but marked activity over the spleen was also found in a wide variety of other conditions (Table I). Noteworthy among these were cases of Hodgkin's disease, Gaucher's disease, Felty's syndrome, hepatitis due to *Toxoplasma gondii* (Fig. 1a), and polycythaemia rubra vera (Fig. 1b).

TABLE I

FIFTY CASES WITH PEAK COUNT RATE OVER THE SPLEEN MORE THAN 70% OF THAT OVER THE LIVER

Diagnosis	*Total No. Scanned*	*No. with Increased Activity over the Spleen*
Liver disease		
Cirrhosis	54	32
Budd-Chiari syndrome	1	1
Portal vein block	1	1
Infective hepatitis	11	2
Toxoplasma hepatitis	1	1
Secondary deposits	66	3
Hepatic abscess	2	1
Blood and reticuloendothelial disease		
Polycythaemia rubra vera	2	2
Felty's syndrome	2	1
Myelomatosis	2	1
Gaucher's disease	1	1
Hodgkin's disease	1	1
Unknown	12	3
Total	156	50

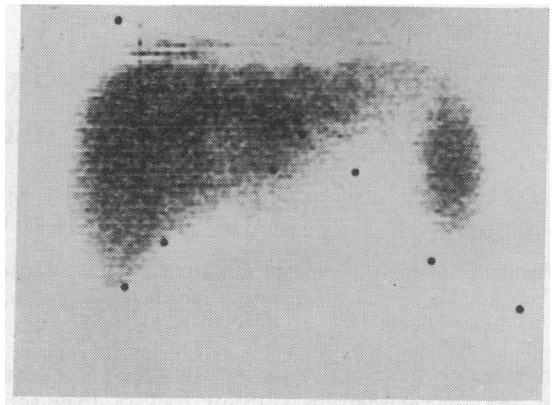

FIG. 1a

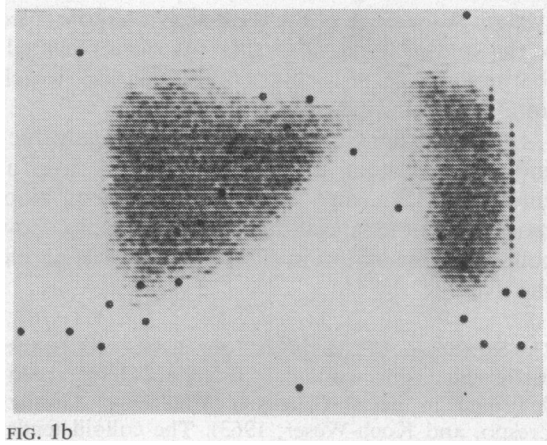

FIG. 1b

FIG. 1. *Two examples of scintiscans in which the peak activity over the spleen was more than 70% of that over the liver. Fig. 1a, hepatitis due to* Toxoplasma gondii; *Fig. 1b, polycythaemia rubra vera.*

These marks (●●) outline the costal margin, xiphisternum, umbilicus, and nipples, and also the palpated edge of the liver and spleen.

The frequency with which uptake of colloid by the spleen was markedly increased in the different types of cirrhosis was also analysed. The term 'active chronic hepatitis' was used to include cases in which there was histological evidence of inflammation and piecemeal necrosis, whether or not cirrhosis was present. There was no significant difference between the frequency with which markedly increased activity over the spleen occurred in cryptogenic cirrhosis (Fig. 2) but the frequency was significantly less in cases with alcoholic cirrhosis or haemochromatosis ($t = 3{\cdot}68$, $P < 0{\cdot}005$ and $t = 3{\cdot}20$, $P < 0{\cdot}005$).

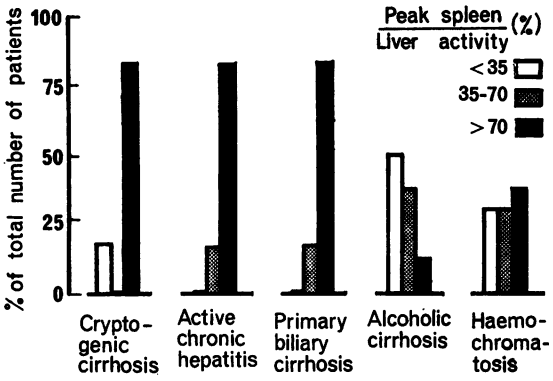

FIG. 2. *The frequency with which markedly increased activity over the spleen occurred in different types of cirrhosis. The patients with each type of cirrhosis were divided into three groups according to the degree of activity over the spleen.*

Peak activity over the spleen is a reflection of both the total uptake of colloid and the size of the organ. Of the linear dimensions of the spleen, length shows the closest correlation with weight (Whitley, Maynard, and Rhyne, 1966). Spleen length was measured from the anteroposterior colour dot scan. A measure of total activity in the spleen was then obtained by multiplying the length by the ratio already mentioned of the peak activity over the spleen to that over the liver. The mean spleen length in active chronic hepatitis was significantly less than that in cryptogenic cirrhosis ($t = 2{\cdot}99$, $P < 0{\cdot}01$), and, although the peak activity over the spleen expressed as a percentage of that over the liver was similar in these two conditions, the total activity in the spleen as estimated by this measure in active chronic hepatitis was much less than that in cryptogenic cirrhosis (Table II). This measure of total activity in the spleen was also low in alcoholic cirrhosis and haemochromatosis.

TABLE II

SPLEEN LENGTH AND MEASURE OF TOTAL ACTIVITY IN THE SPLEEN IN DIFFERENT TYPES OF CIRRHOSIS

Diagnosis	*Mean Spleen Length (cm)*	*Measure of Total Activity in the Spleen*
Cryptogenic cirrhosis	16·7	19·6
Primary biliary cirrhosis	16·5	22·9
Alcoholic cirrhosis	13·8	8·1
Haemochromatosis	12·5	7·8
Active chronic hepatitis	12·4	12·8

Total activity in the spleen as estimated above was closely related to the presence of oesophageal varices on barium swallow. The patients were divided into three groups: those with obvious varices, those with doubtful or possible varices, and those with no evidence of varices. Extensive oesophageal varices were seen on barium swallow in 66% of the cases with cryptogenic cirrhosis, in 10% of cases with active chronic hepatitis, and in none of those with alcoholic cirrhosis or haemochromatosis.

RELATION BETWEEN BLOOD FLOW AND COLLOID UPTAKE BY THE SPLEEN Of the eight patients who had haemodynamic studies, spleen blood flow was increased in six and liver blood flow increased in two (Table III). A quantitative measurement of total spleen and liver activities was obtained from the anteroposterior colour dot scan. The area of each colour zone was measured and multiplied by the average dot density in that zone. The sum of these activities over the liver or spleen areas was taken as a measure of the total activity of the organ.

The distribution of colloid between the spleen and liver, if extraction efficiency is equal, will be proportional to the ratio of their blood flows. If splenic vein blood is colloid-free the amount of blood containing colloid flowing through the liver will be equal to the total liver blood flow minus the spleen blood flow. Hence the ratio of the total activity in the spleen to the total activity in the liver

TABLE III

HAEMODYNAMIC STUDIES AND PREDICTED SPLEEN BLOOD FLOW

Patient	*Diagnosis*	*Total Activity (Spleen) / Total Activity (Liver)*	*Liver Blood Flow (ml/min)*	*Spleen Blood Flow (ml/min)*	*Predicted Spleen Blood Flow (ml/min)*
J.I	Tropical splenomegaly	0·116	1,460	170	152
K.W	Gaucher's disease	0·405	2,030	820	585
E.B	Lymphoma	0·373	1,280	488	348
R.C	Felty's syndrome	0·851	1,210	710	556
E.J	Chronic lymphatic leukaemia	0·170	1,515	342	220
G.M	Myelosclerosis	1·012	2,900	1,520	1,459
C.T	Follicular lymphoma	0·295	1,030	300	235
P.A	Congenital spherocytosis	0·465	1,350	420	428
	Normal values	< 0·1	1,200 to 1,800	100 to 300	

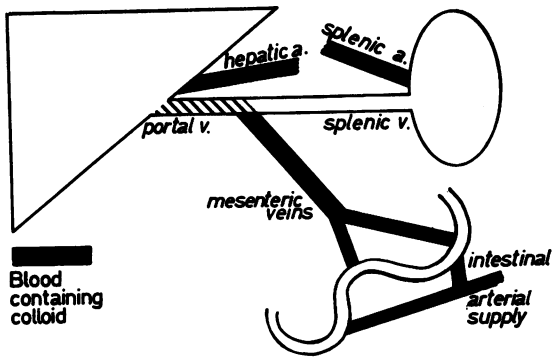

FIG. 3. *Derivation of the formula for predicting blood flows (ml/min) in spleen (x) from that measured in liver (y) and ratio of total activities in the spleen* (S) *and liver* (L).

$$\frac{S}{L} = \frac{x}{y - x} \text{ or } x = \frac{\frac{S}{L}, y}{1 + \frac{S}{L}}$$

will be equal to the spleen blood flow divided by the liver minus spleen blood flow. By rearrangement, a formula can be obtained for predicting spleen blood flow from the measured liver blood flow and the ratio of the total activities in the spleen and liver (Fig. 3).

This formula was used to predict spleen blood flow in the eight patients studied and the result was compared with the spleen blood flow estimated by the radioxen method (Fig. 4.) A highly significant relationship was found over a wide range of values for blood flow. Spleen sizes and total activity varied considerably in this small group of patients. Thus in patient J.I., with tropical splenomegaly, the measured spleen and liver blood flows were within the normal range and total activity in the spleen was only 12% of that in the liver (Fig. 5a). Patient R.C., with Felty's syndrome, had a normal liver blood flow but a markedly increased spleen blood

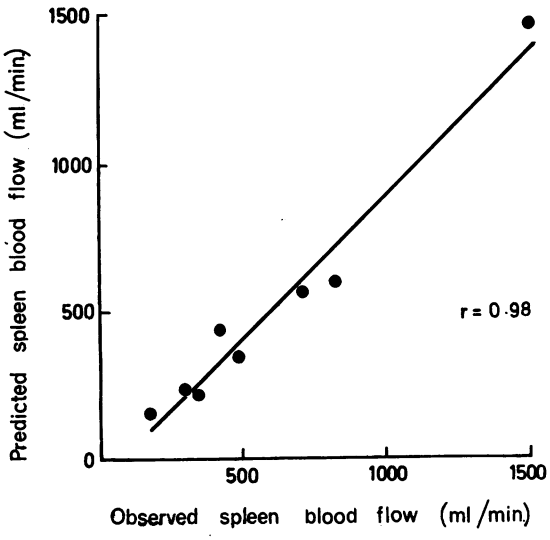

FIG. 4. *The predicted blood flow in spleen is plotted against the observed blood flow using a radioxenon method.*

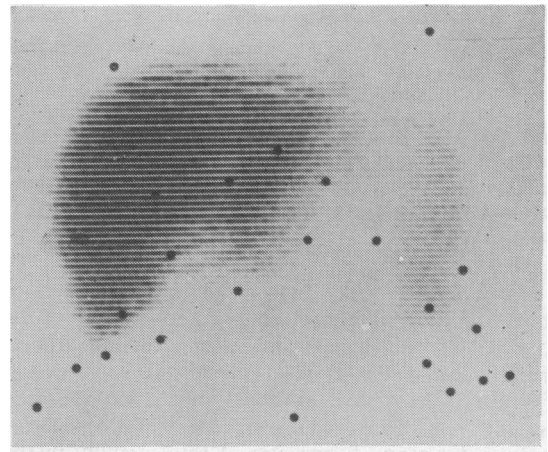

FIG. 5a

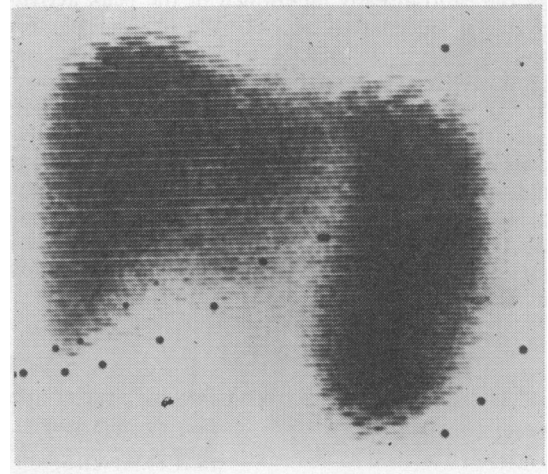

FIG. 5b

FIG. 5. *Scans from two of the patients who had haemodynamic studies.*

FIG. 5a. *Patient J. I., liver blood flow 1,460 ml/min, spleen blood flow 170 ml/min, total activity in the spleen was 12% of that in the liver.*

FIG. 5b. *Patient R. C., liver blood flow 1,210 ml/min, spleen blood flow 710 ml/min, total activity in the spleen was 85% of that in the liver.*

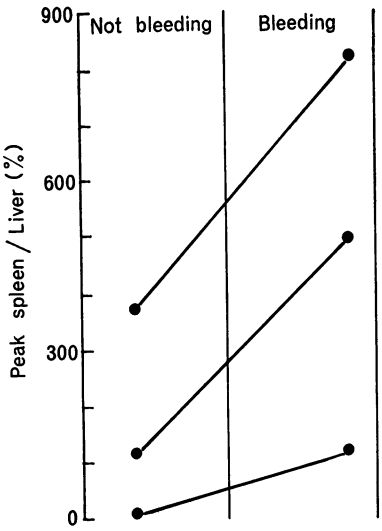

FIG. 6. *The increase in peak activity over the spleen as a percentage of that over the liver in three patients with cirrhosis during an episode of gastrointestinal haemorrhage.*

flow, and total activity in the spleen was 85% of that in the liver (Fig. 5b).

The dependence of uptake on blood flow was further shown in three patients with cirrhosis who were scanned during an episode of gastrointestinal bleeding. Peak activity over the spleen as a percentage of peak activity over the liver was much higher than the corresponding value obtained in each of these patients after recovery (Fig. 6), which would suggest that the reduction in liver blood flow expected at this time was disproportionately greater than that in the spleen.

DISCUSSION

Increased activity over the spleen on liver scans performed with colloidal materials is a characteristic finding in cirrhosis and was present in 32 (59%) of the 54 cases. It was also present, however, in other conditions, and in the absence of more specific features of cirrhosis, namely, perihilar concentration of isotope, dominant activity over the left lobe, and atrophy of the right lobe, it is not diagnostic.

This increased uptake of colloid by the spleen implies an alteration in the distribution of colloid between the liver and spleen. This could theoretically arise in several ways. It has been shown that the normal liver clears over 90% of colloid from the blood flowing through it (Shaldon, Chiandussi, Guevara, Caesar, and Sherlock, 1961). We have been able to demonstrate in the patient P.A., with spherocytosis, during splenectomy, that the spleen cleared 94% of colloid. With hepatic disease it is possible that clearance of colloid by the liver is reduced, thus increasing the amount of colloid available for uptake by the spleen. A reduced clearance of colloid by the liver is unlikely to be due to reduction in the number of Kupffer cells since the amount of colloid used in scanning is less than 2% of that required to saturate the reticuloendothelial system (Chiandussi, Greco, Cesano, Muratori, Vaccarino, and Corradi, 1963). Reduction in the phagocytic ability of the Kupffer cells is another theoretical possibility but in cirrhosis Chiandussi *et al* (1963) found evidence that the phagocytic ability of the reticuloendothelial system, as a whole, was increased rather than decreased.

However, clearance of colloid by the liver would be decreased by the presence of intrahepatic shunts which bypass the sinusoids. Such shunts are commonly present in cirrhosis, and Shaldon *et al* (1961) showed that this was the explanation for the reduced hepatic clearance of colloidal albumin in this condition. Extrahepatic portosystemic collaterals further reduce the amount of colloid reaching the liver, and Castell and Johnson (1966) have shown a close relationship between the extent of the increased activity in the spleen on liver scans from patients with cirrhosis and the degree of abnormality of the ammonia tolerance test, a known index of intra- and extrahepatic collateral circulation. In the present studies we have shown a similar relationship between a measure of total activity in the spleen in patients with cirrhosis and the presence of obvious oesophageal varices on barium swallow.

The distribution of colloid between the liver and spleen must also be dependent upon the ratio of their blood flows (Dobson and Jones, 1952). Williams *et al* (1968) have shown increased splenic blood flow in cirrhosis which will further increase the uptake of colloid by the spleen in this condition. Hepatic blood flow may be reduced in patients with cirrhosis during an episode of gastrointestinal bleeding but why this appears to be reduced disproportionately to splenic blood flow requires further study.

Significant portosystemic collateral circulation is rarely seen in patients with blood dyscrasia or disease involving the reticuloendothelial system, and no collaterals were seen on venography in the cases we studied. Recent studies by Blendis *et al* (1969) have shown that splenic blood flow is often increased in these patients, and, if clearance of colloid were normal, the increased activity in the spleen could be related simply to the increased blood flow. The formula for predicting spleen blood flow from liver blood flow and the ratio of the total activities in the spleen and liver was developed from this hypothesis. The close correlation between the predicted values and the measured splenic blood

flow implies that this hypothesis was correct and that the increased activity in the spleen in these patients was due to the increase in splenic blood flow.

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