SPLENOPORTOSCINTIGRAPHY TO DEMONSTRATE PORTOSYSTEMIC SHUNTS

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Heat-denatured, radioiodine-labeled human serum albumin was first introduced in 1957 by Benacerraf *et al* as a new radiocolloid for studying the phagocytic activity of the RES (*1*). An essential advantage of this new material was its ability to be metabolized because the albumin aggregates were broken down by proteolytic enzymes immediately after being phagocytized by the RES cells; this was in contrast to other radiocolloids such as ^{198}Au and labeled carbon particles. The disadvantage of this method, on the other hand, was that the preparation of heat-denatured albumin was not only a complicated and time-consuming procedure, but the material was also extremely difficult to prepare with a uniform and definite particle size. It was Taplin who succeeded in simplifying and standardizing the preparation of human serum albumin so that albumin particles of any desired particle size could be produced without great difficulty.

After careful animal studies Wagner *et al* (*2*) and Taplin *et al* (*3,4*) were the first to advocate the use in man of albumin particles larger than 1 micron. Because particles of this size do not pass a capillary filter, it was possible to visualize by scintiscanning the first capillary bed upstream to the site of the injection. After injecting macroaggregates of radioiodine-labeled human serum albumin (MAA) intravenously, these authors were able to visualize the lung by scintiscanning (*2*). In principle any capillary filter upstream to the site of injection can be visualized with MAA; for example, the capillary bed of the extremities after injection into the femoral or brachial artery (*5,6*) or the capillaries of the brain after intracarotid injection (*7,8*) can be seen. A further possible application of this principle is the detection of abnormal connections between the pre- and postcapillary blood stream.

If MAA is injected into the spleen, it should be completely trapped in the splenic and hepatic capillary network, and these organs can thus be visualized by scintiscanning. MAA can appear in the pulmonary artery only in the presence of abnormal portosystemic shunts. In this case some of the MAA will reach the pulmonary artery and will therefore be trapped in the capillaries of the lung (*9*).

METHOD

MAA labeled with ^{131}I obtained from Hoechst was used in our examinations. The average particle size of the preparation was 5–50 microns.

Percutaneous puncture of the spleen was performed in the usual way with the patient lying on his right side. The injected volume was kept constant at approximately 10 ml because a larger part of the tracer might remain at the site of injection if smaller quantities were used. On the other hand, there is considerable risk in using large volumes for intrasplenic injections.

Scintiscanning of the liver, spleen and lung moving in the caudocranial direction was started immediately after injection of the tracer. The scanner was a Nuclear-Chicago Phodot Model 1738 with a 3 × 3-in. NaI(Tl) crystal and a 37-hole standard collimator. Recently the Pho/Gamma III scintillation camera with the pinhole collimator was used.

RESULTS

Figure 1 shows normal splenoportoscintigram. After intrasplenic injection, the radioactive material is detected exclusively over the spleen and liver. No accumulation of the tracer in the lungs can be seen. This means that no shunts occur between the portal and the systemic circulation. In Figs. 2, 3 and 4 splenoscintigrams of three patients with portosystemic shunts are shown. In addition to the accumulation of the tracer in the spleen and liver, pulmonary uptake of varying degrees is seen. These findings indicate the presence of portosystemic communications.

In contrast to Fig. 2 where only a moderate ac-

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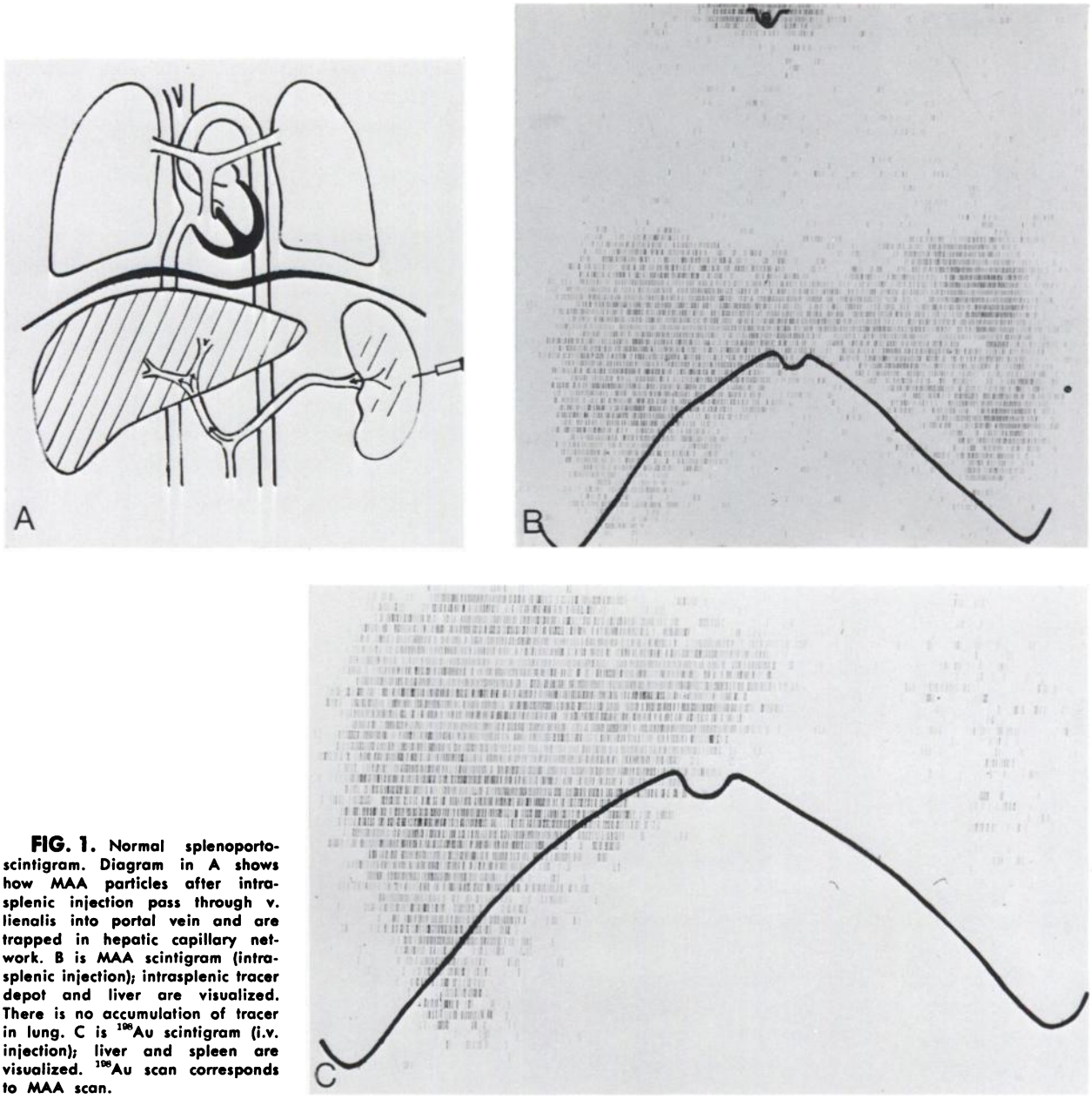

FIG. 1. Normal splenoportoscintigram. Diagram in A shows how MAA particles after intrasplenic injection pass through v. lienalis into portal vein and are trapped in hepatic capillary network. B is MAA scintigram (intrasplenic injection); intrasplenic tracer depot and liver are visualized. There is no accumulation of tracer in lung. C is ^{198}Au scintigram (i.v. injection); liver and spleen are visualized. ^{198}Au scan corresponds to MAA scan.

cumulation of the MAA particles can be seen, an almost exclusive uptake occurs in the lungs of a patient with portosystemic shunts due to thrombosis of the v. lienalis (Fig. 3). Figure 4 shows another case with portosystemic shunts due to partial thrombosis of the v. lienalis.

The clinical data of all our patients are summarized in Table 1. This table shows that in eight of the 12 cases examined by splenoportoscintigraphy portosystemic shunts could be detected, while only two were positive by x-ray examination of the esophagus. In Patient 2, where the x-ray of the esophagus was negative and splenoportoscintigraphy was positive, autopsy confirmed the scintigraphic diagnosis of portocaval anastomoses. In Patient 4 where neither the x-ray nor splenoportography gave any signs of portosystemic shunts, this finding was also confirmed by autopsy.

DISCUSSION

The clinical value of this method can be demonstrated with some typical results. If MAA is injected into the spleen of a patient with normal portal circulation, the liver and parts of the spleen showing the intrasplenic depot of the tracer are visualized. There is no accumulation of the radioactive material in the lung. This fact is thought to be evidence of the absence of functioning portosystemic shunts. To

confirm that after intrasplenic injection the scintigram visualizes parts of the liver in addition to the splenic depot, a liver scan with ^{198}Au radiocolloid was performed immediately after with pulse-height analysis.

It is obvious that the tracer can reach the systemic circulation and therefore the lungs only if the diameter of the shunting vessels is larger than the average particle size (ranging from 5 to 50 microns). Shunts smaller in diameter than this will not be detected by this method. Another principle for the detection of portosystemic shunts is based on the early appearance of a soluble rare gas in the expired air after intrasplenic injection compared with the appearance time after i.v. injection in the antecubital vein. This technique is not subject to the limitations mentioned above, and it is therefore possible to demonstrate shunts even smaller in diameter than those detected by the MAA method (*10–12*). A disadvantage of the rare-gas method, however, is the wide range of scattering of normal values. With the limited experience available it is not possible for us to discuss the relative value of one method against the other. This must be reserved for further studies on larger series.

In this study our results by splenoportoscintigraphy have been evaluated in comparison with x-ray examinations of the esophagus. It is well known that the demonstration of esophageal varices by x-ray is negative in a considerable number of cases with portal hypertension and esophageal varices confirmed by esophagoscopy (*13*). In such cases hypersplenism —even when isolated—is the most important criterion suggesting portal hypertension. If, on the other hand, esophageal varices are demonstrable by x-ray,

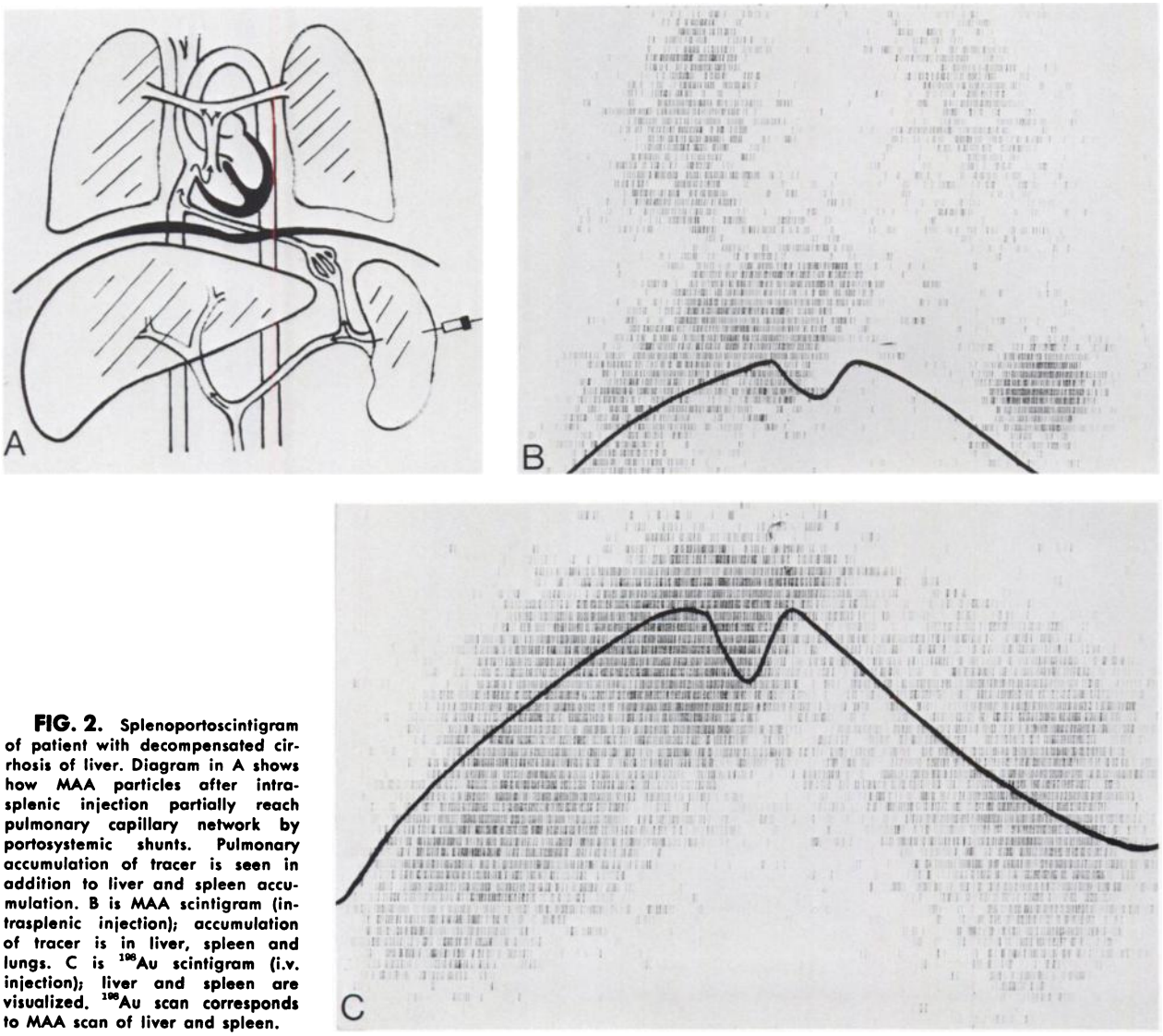

FIG. 2. Splenoportoscintigram of patient with decompensated cirrhosis of liver. Diagram in A shows how MAA particles after intrasplenic injection partially reach pulmonary capillary network by portosystemic shunts. Pulmonary accumulation of tracer is seen in addition to liver and spleen accumulation. B is MAA scintigram (intrasplenic injection); accumulation of tracer is in liver, spleen and lungs. C is ^{198}Au scintigram (i.v. injection); liver and spleen are visualized. ^{198}Au scan corresponds to MAA scan of liver and spleen.

their presence is thought to be evidence for the existence of portosystemic bypasses caused by hypertension of the portal system.

The impossibility of demonstrating esophageal varices by x-ray may also be due to the fact that portosystemic shunts can develop on different places of the splanchnic vascular system. There may be other functioning portosystemic communications like those leading from the retroperitoneal or lumbar veins to the v. azygos and v. hemiazygos or over the pancreatic sieve diaphragmatic veins to the left renal vein (*14*).

The higher sensitivity of splenoportoscintigraphy in comparison to x-ray examination was clearly demonstrated in this study. Evidence for portosystemic shunts was found in six cases by splenoportoscintigraphy, and only two of these cases had varices of the esophagus demonstrable by x-ray. Four cases were negative with both methods. These findings were partly confirmed by autopsy.

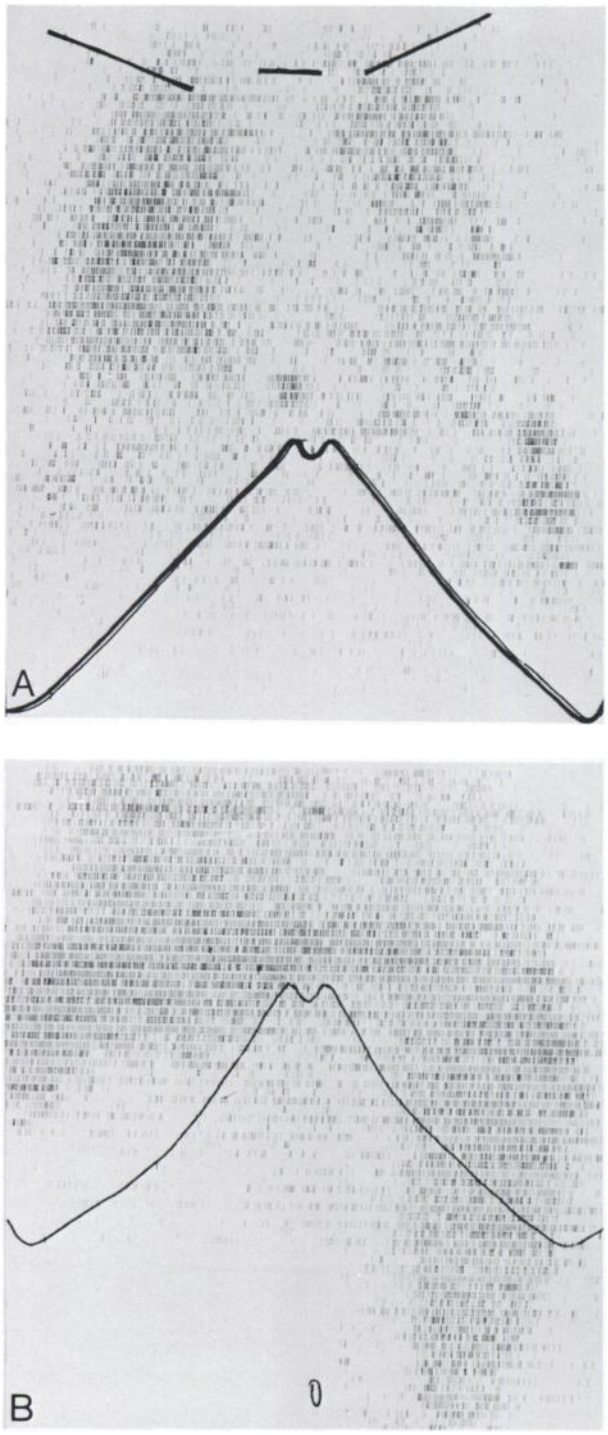

FIG. 3. Splenoportoscintigram in case of thrombosis of v. lienalis. A is MAA scintigram (intrasplenic injection); in addition to intrasplenic tracer depot accumulation of tracer is demonstrated almost exclusively in lungs. No MAA particles can reach hepatic capillary network of portal vein since v. lienalis is completely occluded. B is ^{198}Au scintigram (i.v. injection); in contrast to A, it shows normal-shaped liver and grossly-enlarged spleen.

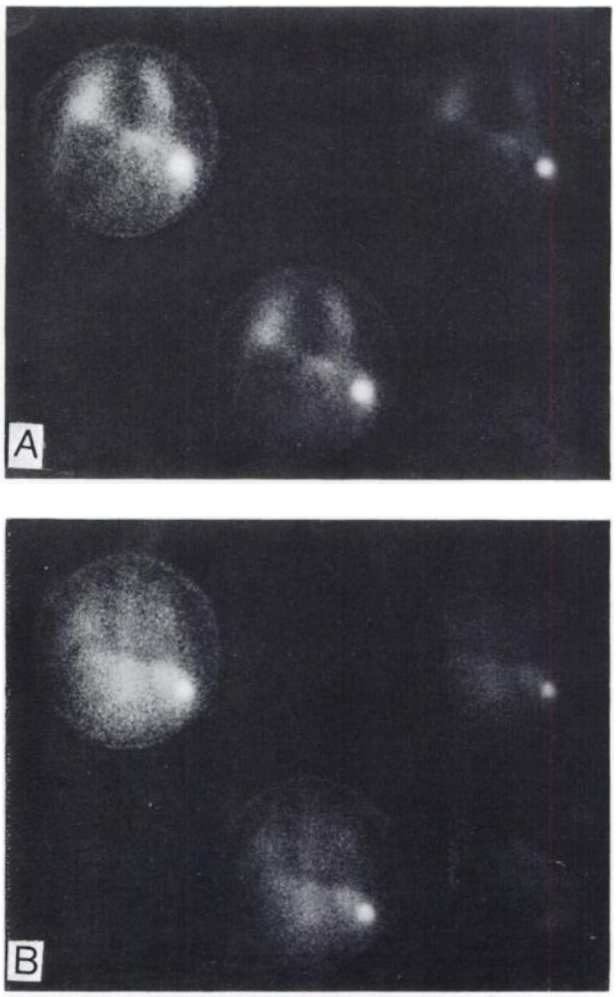

FIG. 4. Camera splenoportoscintigram of patient with post-necrotic cirrhosis of liver. A is MAA scintigram (intrasplenic injection); accumulation of tracer is in liver, spleen and lungs. B is ^{198}Au scintigram (i.v. injection) performed immediately after MAA scintigram using pulse-height discrimination. Two scintigrams can be superimposed, and radioactivity of MAA scan pertaining to liver can be recognized easily.

TABLE 1. CLINICAL DATA OF PATIENTS

Patient No.	Age (yr)	Sex	Final diagnosis	Bilirubin (mg%)	Thymol turbidity	Zinc sulfate turbidity	SGOT	BSP	Total protein (gm%)	Electrophoresis (% total) Alb	α_1	α_2	β	γ	X-ray of esophagus	Splenoportoscintigraphy
1	70	F	Postnecrotic cirrhosis of liver	3.4	4.4	6.5	36		5.1	58.1	4.5	8.4	7.7	21.3	+	+
2	37	M	Postnecrotic cirrhosis of liver	6.2	10.7	23.3	51		5.4	27.9	2.8	4.2	4.2	60.9	—	+
3	70	F	Chronic lymphog., leukemia	0.5	6.5	8.2	11	32	5.5	55.2	3.3	11.4	12.9	17.2	—	—
4	27	M	Reticulum cell sarcoma	0.5	1.1	5.4	18		7.1	45.2	8.9	16.2	10.4	19.3	—	—
5	66	F	Myelofibrosis with myeloid metaplasia	0.5	0.4	1.5	18	12	6.5						—	+
6	18	M	Posthepatitic hyperbilirubinemia	1.5	1.1	8.2	7	4	8.3	59.3	2.9	8.3	9.5	19.9	—	—
7	25	M	Splenomegaly of unknown origin	1.1	2.1	6.8	14	14	7.1	60.2	4.0	9.0	11.6	15.2	—	—
8	70	F	Hepatosplenomegaly of unknown origin, hypernephroma of left kidney	0.6	2.2	7.5	32	29	6.3	37.6	5.9	17.0	10.0	29.5	—	++
9	38	M	Cirrhosis of liver, obstruction of v. lienalis	1.2	9.8	11.8	20	26	7.1	44.6	2.7	5.8	10.7	36.2	— (+ 6 later)	++ months
10	62	M	Obstruction of v. lienalis	0.9	5.7	10.0	11			61.0	2.5	8.8	10.7	17.0	—	++
11	46	F	Cirrhosis of liver, portocaval anastom. by operation 3 mos before	1.9	7.0	14.3	10		7.0	49.0	3.5	7.9	11.4	28.2	—	++
12	47	M	Cirrhosis of liver	3.2	5.5	3.3	37	42	6.7	53.0	4.5	6.8	9.7	26.0	—	++

Patient 1. Liver puncture showed severe cirrhosis of the liver.

Patient 2. Autopsy, gross examination: 6 liters ascitic fluid. Liver is characterized by relatively large nodules up to 1 cm in diameter, irregularly distributed in the liver with small areas of preserved architecture lying between the nodules. Septa of fibrous tissue of varying width separate these nodules. There are esophageal varices in the lower third of the esophagus. Microscopy: nodules composed of groups of hepatic cells are separated by broad bands of scar tissue with lymphocellular infiltration.

Patient 3. Splenic puncture showed lymphatic cells in excess and neutrophils. Normal intrasplenic pressure.

Patient 4. Autopsy, gross examination: liver is of normal shape and size, but infiltrated with multiple tumor nodes measuring about 1 cm in diameter consisting of polymorphonuclear tumor cells of the undifferentiated type. No sign of esophageal varices.

Patient 5. Autopsy: fatty infiltration of the enlarged liver. Areas of myeloid metaplasia occur in the liver and grossly enlarged spleen. There were also areas of fibrosis and infarction in the spleen. Esophagus showed postmortem autolysis of the lower parts.

Patient 6. Liver puncture showed normal liver tissue with lipofuscin pigment in the central zone of the lobules.

Patient 7. Splenic puncture revealed normal blood elements with predominantly mature lymphocytes. Normal intrasplenic pressure.

Patient 8. Autopsy: hypernephroma of the left kidney penetrating the lower parts of the spleen and the v. lienalis. No thrombosis of the portal vein occurs. Liver puncture *intra vitam* showed fatty infiltration and hemosiderosis.

Patient 9. Hepatic vein catheterization and measurement of WHVP (wedged hepatic venous pressure) showed elevated values. Comparison with values of portal venous pressure obtained by splenic puncture showed combined intra and predominantly prehepatic block.

Patient 10. Hepatic vein catheterization and portal venous pressure obtained by splenic puncture showed prehepatic block due to obstruction of v. portae or v. lienalis.

Patient 11. Patient 3 months after end-to-side portocaval anastomosis operation. Gross examination and microscopic finding of the material obtained by liver puncture at surgery showed severe cirrhosis of the liver.

Patient 12. Liver puncture confirmed the diagnosis cirrhosis of the liver.

A further fact to be considered is that splenoportoscintigraphy can only demonstrate shunts between the portal system and the systemic vessels afferent to the lungs (i.e., portocaval anastomoses leading to the pulmonary arteries by way of the right heart). On the other hand, venous anastomoses connecting the portal and the pulmonary veins have also been shown in cirrhotic patients by postmortem injection (*15*). Here again the use of rare-gas examination is of value. The ^{85}Kr used for this examination is completely removed from the circulation in the expired air. Its appearance in arterial blood in a higher concentration after intrasplenic injection compared with the level after peripheral intravenous injection indi-

cates a connection between the portal circulation and the left side of the heart (portopulmonary anastomosis) (*12*).

In addition to the higher sensitivity compared with results of x-ray examination of the esophagus, splenoportoscintigraphy offers some possibility of a rough estimation of the volume shunted from the portal to the systemic circulation within the limitation mentioned above. The relative distribution between liver and lung of the tracer that has reached the portal vein by intrasplenic injection will depend on the relative amount of the portosystemic bypass flow which is shunted to the afferent vessels of the lung. However, in those cases with complete thrombosis of the v. lienalis, the relative distribution of radioactivity between liver and lung must be considered from a different point of view. In this case the tracer cannot reach the liver by way of portal circulation at all, and almost all of the radioactivity is found in the lungs (see Patient 9).

Recently we used an Anger camera instead of the conventional scanner for splenoportoscintigraphy, considerably improving the technique. With the gamma camera the whole procedure, including splenic puncture, is carried out within about ½ hr while it takes about 2½ hr including the radiogold scan if the ordinary scanner is used.

SUMMARY

After intrasplenic injection of MAA in a patient with normal portal circulation, the liver and parts of the spleen can be visualized by scintiscanning. Accumulation of the tracer in the lung indicates the presence of portosystemic shunts. The degree of accumulation of MAA in the lungs depends on the volume shunted. The result may therefore be quantitated to some extent. In our experience splenoportoscintigraphy is more sensitive for detecting portosystemic shunts than x-ray examination of the esophagus.

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