JOURNAL OF NUCLEAR MEDICINE 7:868-877, 1966

The Hepatic Scan in Cirrhosis: Biochemical and Histologic Correlations[1,3]

Paul Rozental, M.B., B.S.[2], Edwin B. Miller, M.D., and Ervin Kaplan, M.D.

Hines, Illinois

Visualization of the liver by scintiscanning technique has become a useful clinical procedure. Apart from delineating the anatomic configuration of the liver, its principal usefulness has been the localization of areas not capable of concentrating the radioactive materials employed.

In previous reports on the liver scan in patients with cirrhosis, the possibility of "diffuse or focal" patterns has been discussed. However, no attempt has been made to correlate the scan pattern with liver function tests or a specific histologic diagnosis (1, 2, 3).

We have observed that many patients with cirrhosis who were suspected of having hepatic neoplasms because of enlarged, hard, irregular livers and abnormal liver scans were later proved to be free of carcinoma.

This study was planned to correlate the pattern of the hepatic scan of patients with cirrhosis with the clinical, laboratory and histopathologic findings.

MATERIALS AND METHODS

Forty male patients in the Gastrointestinal Section of this hospital with the diagnosis of cirrhosis were studied. The diagnosis was confirmed in 33 patients by liver biopsy or autopsy. In the remaining seven patients in whom biopsy could not be obtained because of poor cooperation or coagulation defects, the presumptive diagnosis was made on the basis of typical physical findings and the presence of splenomegaly and/or esophageal varices.

---

[1]Address requests for reprints to: Radioisotope Service, Veterans Administration Hospital, Hines, Illinois.

[2]Present address: 59 King George Avenue, Jerusalem, Israel

[3]From the Medical Service and Radioisotope Service, Veterans Administration Hospital, Hines, Illinois, and the Departments of Medicine, University of Illinois College of Medicine and Stritch School of Medicine, Loyola University.

In all instances, the liver scan and biopsy were obtained after prolonged hospitalization. At this stage, liver function tests had become stable with minimal or no elevation of the serum bilirubin or transaminases, and ascites was absent or minimal. The presence of hepatic malignancy was excluded by liver biopsy and an adequate period of clinical observation with no evidence of the progressive changes that occur in hepatic malignancy.

Liver function tests were carried out serially and at the time of the liver scan. The tests and their normal values can be seen in Table I.

Biopsy specimens were obtained with the Vim-Silverman needle or occasionally with the Menghini needle, using the intercostal approach. Hematoxylin and eosin and a reticulum or Masson stains were used. The slides were reviewed and classified into one of the following classifications:

1) Typical Laennec's cirrhosis (L)
2) Typical post-necrotic cirrhosis (PNC)
3) Mixed cirrhosis showing features of both Laennec's and post-necrotic cirrhosis.

These cases of mixed cirrhosis were included under the term "Laennec's" cirrhosis in the final classification. Laennec's cirrhosis is defined as the presence of diffuse, fine fibrosis with resulting generalized architectural distortion and with few or no central veins. Fatty infiltration may be present in variable amounts.

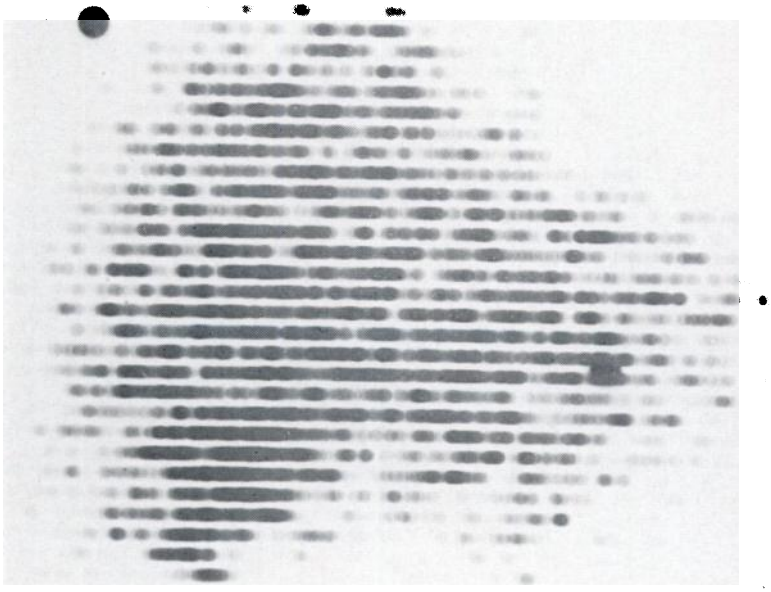

Fig. 1. A normal appearing scan of the liver using I^{131} Rose Bengal in a patient with Laennec's cirrhosis.

TABLE I

CORRELATION OF I^{131} ROSE BENGAL LIVER SCAN PATTERN WITH MEANS + STANDARD DEVIATIONS OF VARIABLES MEASURED

R.B.†Scan Appearance	*No. of Cases*	*No. days Follow-up*	*Palpated Size*		*Esoph-ageal Varices %*	*BSP%*	*Total Bilirubin*	*GOT***	*Alkaline Phosphat.*	*Thymol Turbid.*	*Ceph. Floc.*
			*Liver**	*Spleen**							
Diffuse	18	92.7±31.2	6.9±4.6	1.9±2.3	58	15.3±5.9+	1.2±0.5	45.4±23.7	7.1±3.4	5.2±2.8	2.8±1.8
Focal	13	116.5±41.1	7.8±5.3	1.2±2.4	68	9.0±4.9+	0.9±0.5	37.8±37.3	7.8±3.5	4.2±1.9	2.1±1.9
D & F	5	75.8±14.1	9.2±3.3	4.2±3.2	70	16.6±13.2	1.3±1.0	37.3±11.5	5.2±2.7	5.1±4.0	1.8±1.8
Normal	3	262.7±64.8	8.0±6.9	0	100	8.3±4.6	0.3±0.2	32.0±19.1	3.4±1.1	3.0±0.6	0
All Cases	39	110.3±61.3	7.5±4.7	1.8±2.5	78	13.7±7.5	1.0=0.59	40.0±29.2	6.7±3.4	4.9±2.8	2.3±1.8
Upper limits of normal for tests performed:						5% at 45 min.	1.0 mg/ 100 ml	40 Karmen units	4.0 Bodansky Units	4μ	2+ at 48 hrs.

*cm. below the costal margin

†I^{131} Rose Bengal

**glutamic oxalacetic transaminase

+These figures are significantly different

Post-necrotic cirrhosis is characterized by broad bands of fibrous tissue with collapse as evidenced by the aggregation of three or more portal areas. The resulting architectural distortion produces pseudolobules of variable sizes. The central veins are absent or eccentrically located within the pseudolobule. The presence and amount of necrosis and fatty infiltration were also noted in each case.

Scintiscanning was accomplished using the Picker Magna Scanner V with a 5″ NaI (Tl) crystal and an 85-hole focusing collimator. The tracer material was either colloidal gold^{198} or iodine^{131}-labeled Rose Bengal. The dosage of either material was 100 microcuries. The scanning began 60 minutes after administration of the radioactive gold or 20 minutes after radioactive Rose Bengal. When Rose Bengal was used, the scanning began with the inferior border of the liver and moved cephalad to avoid gallbladder visualization. When colloidal gold was used, the area of scanning was increased to include the area of splenic uptake. Anterior scans and a right lateral scan (only with gold) were performed in that order.

At the end of hospitalization, 25 patients were scanned with Rose Bengal alone, one patient with gold alone, and 14 patients with both materials. The scans are classified as follows:

1) Diffuse decrease in uptake (D)
2) One or more focal areas of decreased uptake (F)
3) Combination of diffuse and focal decreased uptake (D+ F)
4) Normal appearance (N)

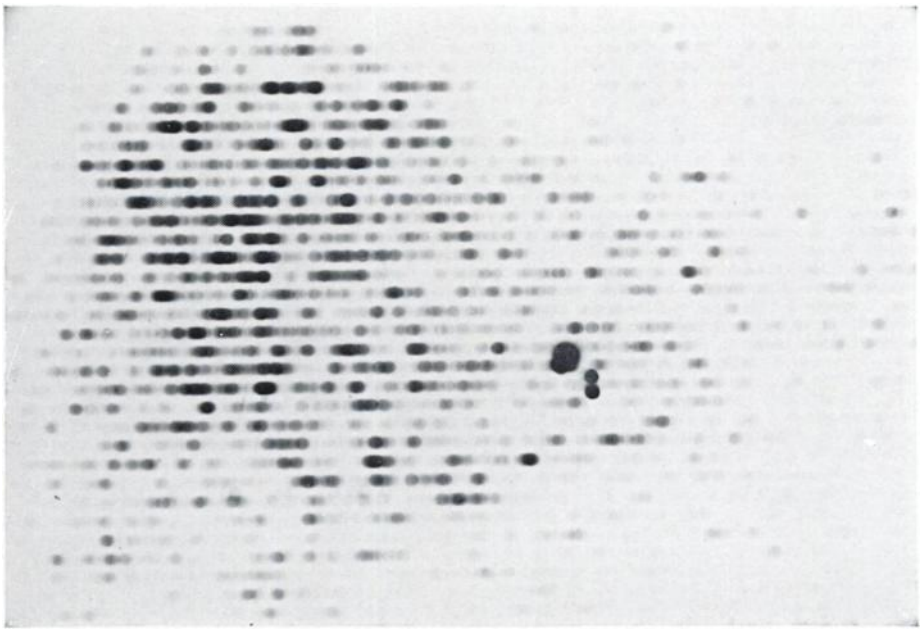

Fig. 2. A diffuse uptake of I^{131} Rose Bengal in a patient with Laennec's cirrhosis.

RESULTS

Table I correlates the clinical findings and liver function tests with the pattern of the Rose Bengal scan. Inspection of the mean biochemical data of the four groups (Table I), with the exception of the BSP clearance did not reveal any statistically significant differences between the groups. The BSP clearance values in the "diffuse" and "focal" groups are significantly different at the 5% level.

Thirty-five biopsies were obtained from 33 patients. These were classified as showing "Laennec's" cirrhosis in 21 biopsies, post-necrotic cirrhosis in 11 and biliary cirrhosis in one case. The correlation between the biopsy appearance and the interpretation of the Rose Bengal and gold scans is summarized in Table II.

With the exception of those Laennec's and post-necrotic cirrhosis cases characterized by a diffuse and focal (D+ F) scintiscan, no significant correlation was noted on comparing liver biopsy with Rose Bengal scan patterns. On using the Fisher Exact Test and given the two sample sizes, 21 (L) and 11 (PNC), the probability of obtaining 0 Laennec's and 4 post-necrotic cirrhosis in group D+ F is 0.01, under the assumption that the probability of D+ F occurring is the same for each type of cirrhosis. The difference is therefore significant at the 1% level.

Correlating the appearance of the colloidal gold liver scan with the biopsy results, the numbers were too small for meaningful statistical analysis.

Figures 1, 2, 3 and 4 demonstrate the variations in scan appearance that occurred.

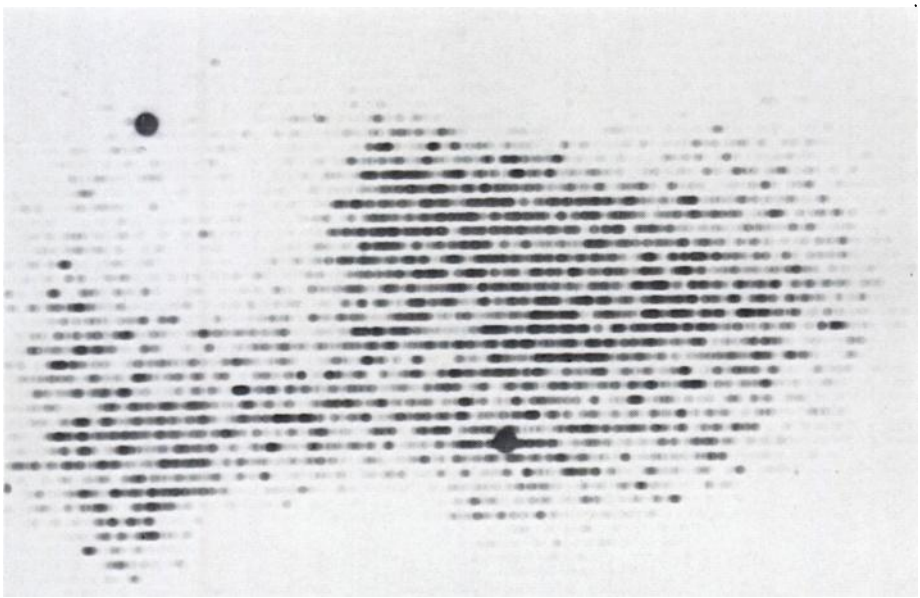

Fig. 3a. A scan of the liver using colloidal Au^{198} in a patient with post-necrotic cirrhosis demonstrating a focal lesion (anterior view).

DISCUSSION

Three factors apparently influence the liver scan of cirrhotic patients. The first factor is the reduced hepatic blood flow that occurs in cirrhosis of the liver. Normally, the colloidal gold is cleared from the blood stream within 10 minutes of administration and Rose Bengal within 25 minutes (4). In "severe" cirrhosis, it has been shown that the clearance of these agents can be prolonged for hours, and this delay has been related to reduced hepatic blood flow (4, 5, 6).

The second factor is a disturbance of hepatic parenchymal function which influences the uptake of colloidal gold and Rose Bengal. Rose Bengal is removed from the blood stream by intact parenchymal cells as shown by fluorescence studies (7). Blockage of the reticulo-endothelial system with Thorium or India ink did not influence uptake; however, reduced Rose Bengal clearance was produced in rabbits within one hour of administering carbon tetrachloride, the effect persisting up to one week (8). A study of hepatic scans in various liver conditions indicated generally an inverse relation between bilirubin serum levels and Rose Bengal clearance (9, 10).

The third factor influencing the pattern of the liver scan in cirrhosis is the replacement of liver tissue. Both the parenchymal cells that remove Rose Bengal and the reticulo-endothelial cells that clear gold may be replaced by areas of necrosis, fatty infiltration, and fibrosis detectable by scanning. Autoradiographs of the liver with radioactive gold and Rose Bengal in two patients who died with

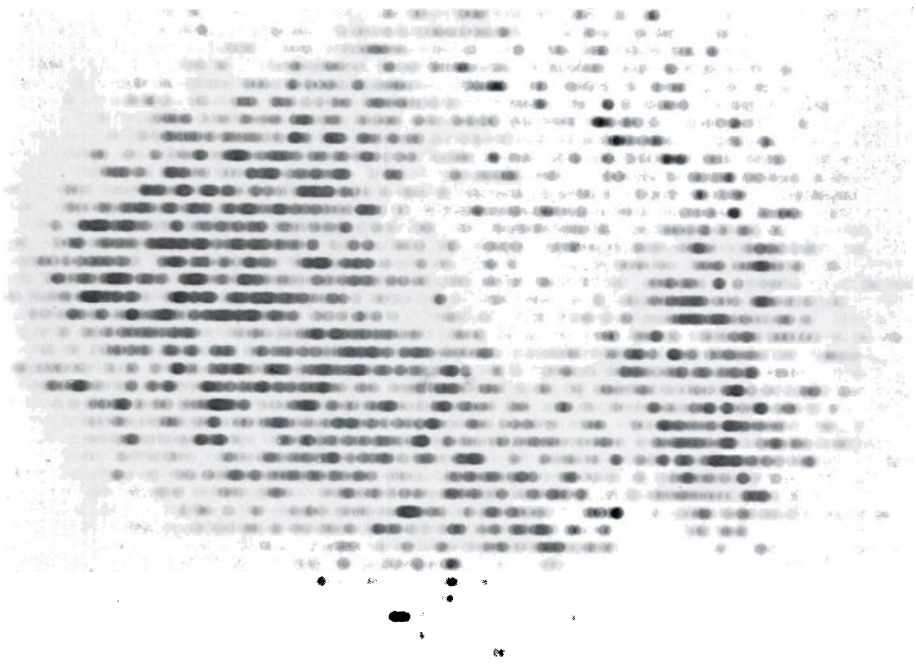

Fig. 3b. A scan of the liver using colloidal Au^{198} in a patient of post-necrotic cirrhosis demonstrating a focal lesion (lateral view).

"Laennec's" cirrhosis showed uptake defects in fibrotic areas (11). Similarly, it is well known that patients with hepatic malignancies may show a normal scan or focal areas of poor uptake, or if the malignancy is diffuse the scan may appear normal or show "reduced uptake (12)."

To minimize the effect of disturbed hepatic function on the clearance of the agents used, the scans were performed when the liver function tests were stable and elevations of the GOT and bilirubin levels were minimal. The BSP in the "diffuse" group is significantly higher than in the "focal" group; therefore focal or diffuse appearance in the Rose Bengal liver scan may be related to the liver function of these cirrhotic patients.

Post-necrotic cirrhosis showed a high correlation with "diffuse plus focal" appearance on the liver scan. This correlation is not found in Laennec's cirrhosis. The focal component of the liver scan in post-necrotic cirrhosis may be related to fibrotic replacement. These focal areas appear similar to those in neoplastic lesions in the liver.

Three of 21 patients with Laennec's cirrhosis showed normal scans, while no normal scans were seen in 11 post-necrotic cirrhosis cases. While this was not

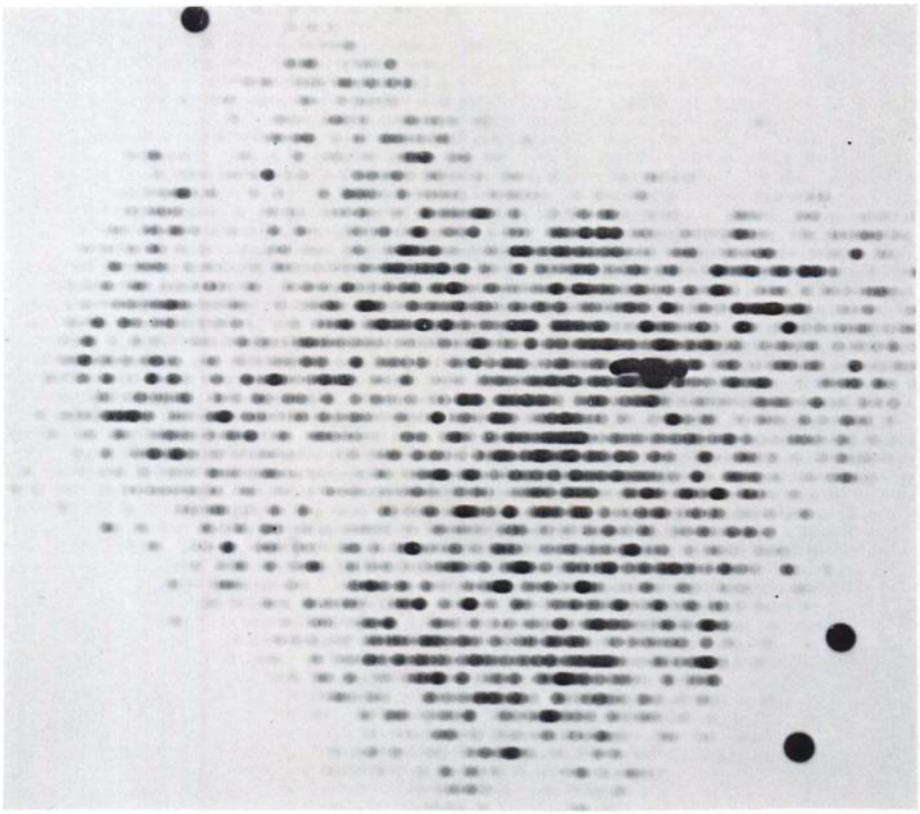

Fig. 4a. A scan of the liver using Au^{198} in a patient with post-necrotic cirrhosis showing focal lesions in the presence of diffuse decreased concentration of the radioisotope (anterior view).

a significant difference, it is reasonable to assume that a diffuse lesion, such as Laennec's cirrhosis, is more likely to have a normal appearance than would post-necrotic cirrhosis for the same reason that diffuse malignant involvement of the liver may appear normal on liver scan (11).

The Rose Bengal and gold scans in almost half of the cirrhotics examined showed focal or focal + diffuse areas of uptake which could have been interpreted as malignancy or other space-occupying lesions. The hepatic scan is therefore not diagnostic in cirrhosis, however, it can demonstrate a focal site to biopsy if this is required for diagnosis. Extreme caution should be exercised in diagnosing focal lesions by scanning since they may, as defined above, represent pathology other than malignancy. At this time, adjunct procedures are necessary to make the definitive diagnosis.

Further effort should be directed toward a quantitative evaluation of uptake of both ^{198}Au and ^{131}I Rose Bengal by the entire liver and in specific areas; however, the scintiscanner, especially when equipped with a focusing collimator, is not an adequate instrument for quantitative expression of diffuse uptake. It is conceivable that computor techniques may be developed for such application.

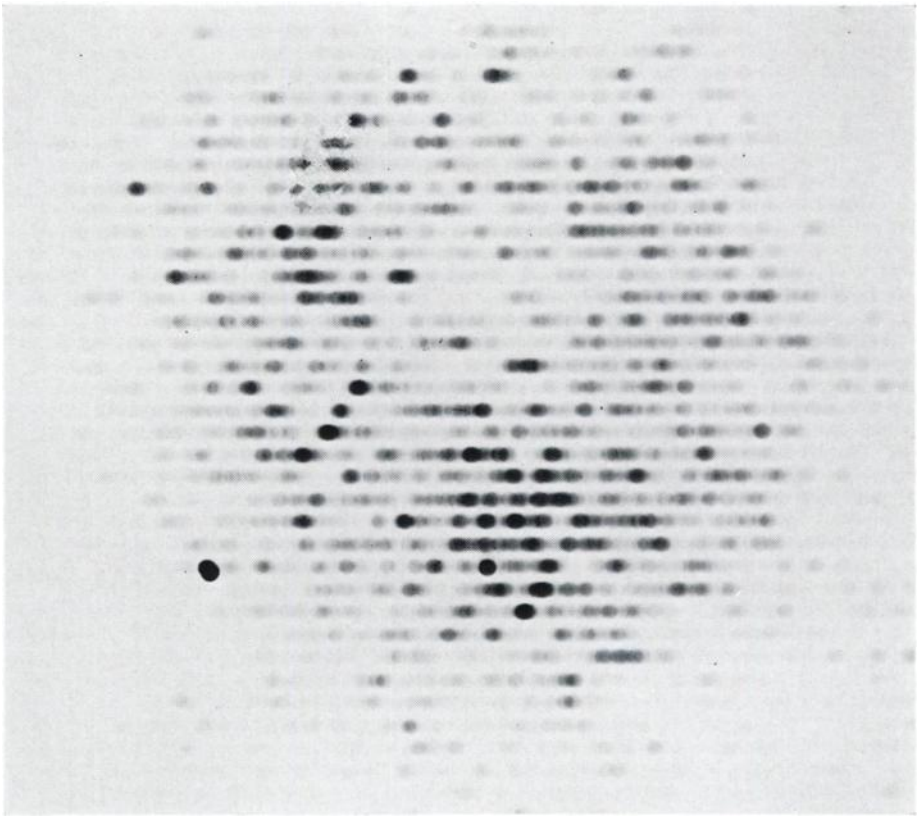

Fig. 4b. A scan of the liver using Au^{198} in a patient with post-necrotic cirrhosis showing focal lesions in the presence of diffuse decreased concentration of the radioisotope (lateral view).

TABLE II

CORRELATION OF TYPE OF CIRRHOSIS WITH SCAN PATTERN

Type of Cirrhosis	Totals		Diffuse		Focal		D & F		Normal	
	Au*	R.B.**	Au*	R.B.**	Au*	R.B.**	Au*	R.B.**	Au*	R.B.**
Laennec	7	21	2	11	4	7	1	0+	0	3
Post Necrotic	3	11	1	3	1	4	1	4+	0	0
Total	10	32†	3	14	5	11	2	4	0	3
All cases	15	39	5	18	5	13	3	5	2	3

*Au^{198} **I^{131} Rose Bengal

+These figures are significantly different.

†1 case of biliary cirrhosis was not included.

SUMMARY

The factors influencing the appearance of the Rose Bengal or colloidal gold liver scans in cirrhosis are reduced hepatic blood flow, disturbed parenchymal function and the presence of areas of parenchymal replacement by necrosis, fatty infiltration, and fibrosis. These contribute to produce the diffuse, focal or diffuse plus focal appearance of the hepatic scan. A review of 40 cirrhotic patients with stabilized liver function tests showed that half had focal changes in their liver scan. These scans were not diagnostic though they were helpful in indicating a site for biopsy. There was a correlation of "diffuse" scan appearance with the degree of BSP retention. Also, post-necrotic cirrhosis was more likely to give the diffuse plus focal appearance than was Laennec's cirrhosis.

ACKNOWLEDGMENT

We would like to thank Dr. H. J. Zimmerman, formerly of Chicago Medical School for his helpful criticism and review of the cases studied. We further wish to acknowledge the cooperation of the Biostatistical Research Support Unit under the direction of Dr. H. M. Schoolman, for assistance in evaluation of the information in this report.

REFERENCES

1. GOLLIN, S. S., SIMS, J. L., AND CAMERON, J. R.: Liver scanning and liver function tests. *J.A.M.A.* **187**:111, 1964.

2. FELDMAN, F., RUBENFELD, S., AND COLLICA, C.: The radioactive (I^{131}) Rose Bengal hepatoscan. *Radiology,* **79**:457, 1962.

3. CZERNIAK, P.: Scanning study of seven hundred livers, in *Medical Radioisotope Scanning.* II, Athens Symposium, April 1964. International Atomic Energy Agency, Vienna, 1964.

4. CHRISTE, J. A., MACINTYRE, W. J., CRESPO, G. G., AND KOCH-WESER, D.: Radioisotope Scanning in hepatic cirrhosis. *Radiology,* **81**:455, 1963.

5. LUM, C. H., MARSHALL, W. J., KOZOLL, D. D., AND MEYER, K. A.: Use of radioactive (I^{131} labeled) Rose Bengal in study of human liver disease. Its correlation with liver function tests. *Ann. Surg.*, **149**:353, 1959.

6. TAPLIN, G. V., MEREDITH, O. M., WINTER, C. C., AND JOHNSON, D.: Rose Bengal and Iodopyracet as radiodiagnostic agents in liver and kidney disease. *Ann. N. Y. Acad. Sci.*, **78**:872, 1959.

7. MENDELOFF, A. I.: Fluorescence of intravenous Rose Bengal appears only in hepatic polygonal cells. *Proc. Soc. Exp. Biol. Med.*, **70**:556, 1949.

8. TAPLIN, G. V., MEREDITH, O. M., AND KADE, H.: The radioactive (I^{131} tagged) Rose Bengal uptake–Excretion test for liver function using external gamma-ray scintillation counting techniques. *J. Lab. Clin. Med.*, **45**:665, 1955.

9. LUM, C. H., MARSHALL, W., AND KOZOLL, D. D.: Correlation of radioactive I^{131} Rose Bengal tests with liver function tests. *J. Lab. Clin. Med.*, **50**:929, 1957.

10. SANDRUCCI, G. M., AND NICOLA, P.: Research on liver function in viral hepatitis in childhood. *Minerva Pediat.*, **12**:551, 1960.

11. CRESPO, G. G., MACINTYRE, W. J., AND CHRISTIE, J. H.: A comparison of I^{131} Rose Bengal and colloidal Au^{198} in liver scanning. *Amer. J. Roentgen.*, **88**:296, 1962.

12. CHRISTIE, J. H., AND MACINTYRE, W. J.: Information limitations of radioisotope scanning. *Radiology*. **79**:472, 1962.