RENAL EXCRETION OF RADIOIODINATED ROSE BENGAL—A PITFALL IN THE INTERPRETATION OF ROSE BENGAL ABDOMINAL SCANS

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The radioiodinated rose bengal abdominal scan has been described recently as an adjuvant to liver-function studies in the differential diagnosis of hepatocellular and extrahepatic causes of jaundice (*1–3*). Diagnosis of a patent biliary tract depends upon the rapid visualization of the dye in the small intestine. Experience has shown that in many instances of both intra- and extrahepatic disease (particularly the latter) there is a significant amount of renal excretion of the radionuclide. This urinary activity often simulates intestinal activity on the scan. The purpose of this report is to emphasize the renal excretion of radioiodinated rose bengal and to indicate how one might recognize and distinguish it from intestinal activity. Failure to do so can easily lead to an erroneous interpretation of a patent biliary tree when, in fact, complete extrahepatic obstruction might exist.

METHOD

After the intravenous administration of 3–5 μc of ^{131}I-rose bengal (tetraiodo-tetrachlorfluorescein) to a fasting patient, counts are obtained over the temporal region of the head with a scintillation probe and scaler at 5 and 20 min as advocated by Nordyke (*4–7*). This measures the efficiency with which the hepatic polygonal cells are extracting the dye from the blood stream. Diminished liver function is reflected by blood clearances of less than 40% (as determined from the 20/5-min ratio).

After the head counting is completed, a scan is started at the superior liver margin. A Picker Magnascanner with a 3 $\times$ 2-in. NaI(Tl) crystal and 19-hole focusing collimator was used in all our studies. At approximately 50–60 min, the detector is counting over the inferior liver edge and proximal small bowel. The normal 1-hr intestinal pattern is shown in Fig. 1. Serial studies show a normal progression of the activity through the gastrointestinal tract, with the colon eventually outlined at 24 hr or earlier.

Visualization of kidneys on scan. During the early phase of our rose bengal studies on jaundiced patients, we encountered a 68-year-old female with a palpable right upper quadrant mass and liver chemistries which strongly suggested extrahepatic obstruction. The 1-hr scan (Fig. 2A) showed a significant amount of extrahepatic activity in a position consistent with the usual location of small bowel. Serial supine studies were performed to further investigate what appeared to be a false indication of biliary-tract patency. Interestingly, the position of the extrahepatic activity did not change. Intensification of this activity occurred, however, and was greatest on the 24-hr study which was the last one performed (Fig. 2B). Bilaterality of the activity was also noted. A right lateral study at 24 hr confirmed the suspicion that we were dealing with renal rather than intestinal activity (Fig. 2C). At laparatomy, we found carcinoma of the head of the pancreas with extensive invasion of the common bile duct. Clearly if the study had been discontinued after the 1-hr scan, an erroneous diagnosis of a patent biliary tract would have been made.

After this initial observation, we looked for and found renal activity in the majority of cases with extrahepatic obstruction that were studied with this technique. Most often, the kidneys were first seen on the delayed scans (usually 24-hr study). However, there were many cases in which renal activity was present on the initial 1-hr study (Figs. 2 and 3) and, if it had not been recognized as such, would have caused an error in diagnosis.

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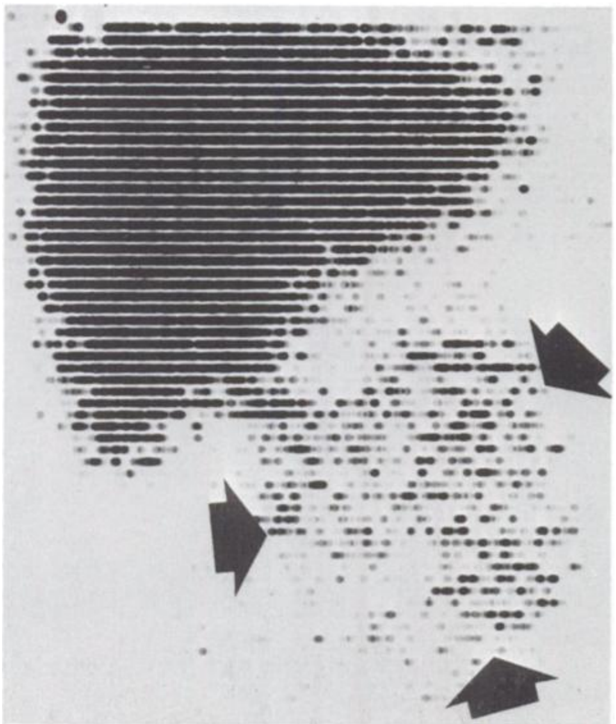


FIG. 1. Normal 1-hr ^{131}I rose bengal abdominal scan. Typical diffuse pattern of small-bowel activity is indicated by arrows. Compare with more localized renal excretion in Figs. 2-5.

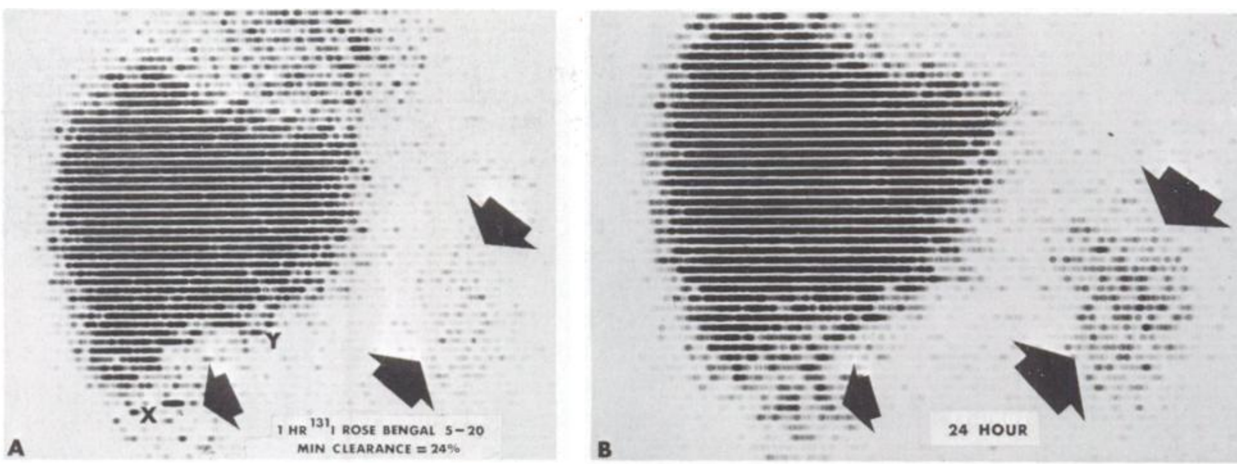
Patients with severe intrahepatic disease such as cirrhosis often show renal activity on the scan as well (Fig. 4). Quantitative studies show that there is almost as much urinary excretion of the radionuclide in cirrhotics as in those patients with extrahepatic obstruction (Table 1; also see Discussion below). Therefore, the demonstration of renal activity on a ^{131}I-rose bengal scan does not, in itself, establish a diagnosis of extrahepatic obstruction.

There are three basic ways in which an individual performing and interpreting the scan can distinguish renal from intestinal activity:

1. By recognizing the bilaterality of the extrahepatic activity. This may be difficult because the right kidney is often tucked up and behind the liver (Figs. 2, 4, 5).

2. By observing no change in position of the activity on follow-up studies (Figs. 2B, 3B, 4B). Small bowel activity would necessarily change from one study to another. Intensification of the renal activity might be noted, however (Figs. 2B and 4C).

3. By performing a lateral scan, particularly at 24 hr, which would identify the kidney in its proper location posterior to the liver (Figs. 2C, 3C, 4D and 5B).



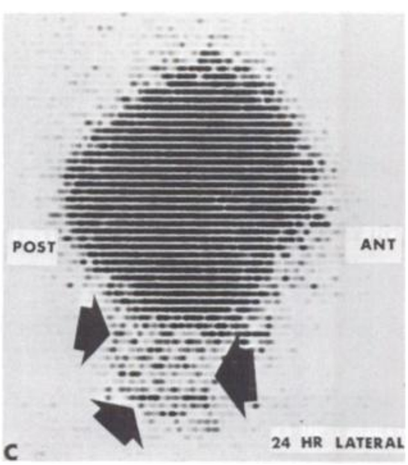
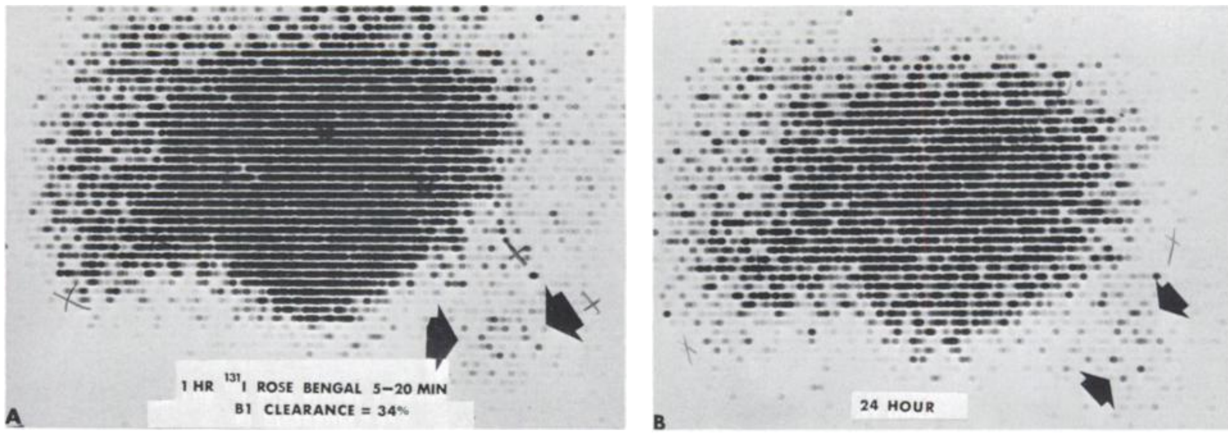


FIG. 2. Radioiodinated rose bengal scans on 68-year-old female with pancreatic carcinoma. 2A: 1-hr study demonstrates typical pattern of renal excretion (arrows). Because of its presence on this early scan, confusion with intestinal activity could easily lead to mistaken impression of patent biliary tract. 20/5 min clearance is 24%. 2B: serial scans, including this 24-hr study, reveal intensification, but no change in position of extrahepatic activity, confirming fact that activity represents kidneys (arrows). Upper half of right kidney is obscured by overlying hepatic activity. Failure of dye to leave liver supports impression of extrahepatic obstruction despite moderately impaired liver function (20/5-min blood clearance of 24%). 2C: 24-hr right lateral scan shows kidney in normal position posterior to liver.



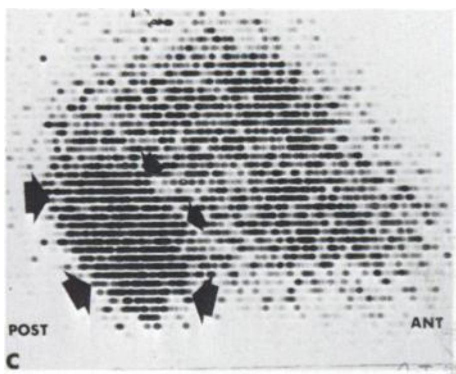


FIG. 3. ^{131}I-rose bengal abdominal scans on 68-year-old male with gastric carcinoma and metastatic disease to liver and perihepatic lymph nodes. 3A: 1-hr study reveals left-sided extrahepatic activity that represents renal excretion (arrows). Differentiation from intestinal activity could not be made on basis of this study alone. Note large metastatic deposit in the right lobe of liver. 20/5-min blood clearance is 34%. 3B: 24-hr scan reveals no change in position of extrahepatic activity on 1-hr study (arrows). Right kidney is obscured by overlying liver. Liver is still densely filled with radioactive dye. 3C: 24-hr right lateral scan demonstrates posteriorly located right kidney (arrows) which was masked on supine study by overlying hepatic activity.

If any doubt still exists, one can perform an intravenous urogram or ^{197}Hg-chlormerodrin renal scan and see if the position of the kidneys corresponds to what is seen on the rose bengal scan.

In Nordyke's original method of performing the ^{131}I-rose bengal examination, a wide-angle abdominal probe is used to detect intestinal activity. While the head-probe chart recording shows a progressive decline because of falling blood activity, the abdominal-probe recording shows an upward turn as the dye enters the intestine (*4–7*). In extrahepatic biliary obstruction, the abdominal recording should parallel the head recording and continue to fall. It appears as if the scanning method is superior to the probe counting method because renal activity could conceivably cause an upward turn on the chart recording in a patient with extrahepatic obstruction. The probe technique obviously can not differentiate kidney from intestinal activity.

DISCUSSION

Ghadimi and Sass-Kortsak studied the renal excretion of radioiodinated rose bengal in normal dogs as well as after surgical ligation of the common bile duct (*8*). They found that the normal 96-hr urinary excretion is less than 7% of the injected dose whereas about 38% of the radioactive substance contained in the dose appeared in the 96-hr cumulative urine when the common duct was ligated. Jacobson and Brent found a 48-hr urinary excretion of 5.1% of the injected dose in the normal rat (*9*).

Quantitative urinary excretion of radioiodinated rose bengal in children was also studied by Ghadimi and Sass-Kortsak (*8*). Normal children excreted less than 5% of the injected dose in 72 hr. Children with atresia of the extrahepatic ducts excreted 30.0–47.0% of the injected dose in 72 hr while those with acute obstructive jaundice and patent extrahepatic ducts excreted 26.1–32.8% of the injected dose over the same time period. Several children studied after subsidence of jaundice excreted smaller amounts of the injected dose in their urine compared to the above figures. Brent and Geppert also demonstrated this increased urinary excretion of radioiodinated rose bengal during infantile jaundice (*10*).

Quantitative urinary-excretion studies of this type were performed in adults using a Nuclear Chicago well counter (Model 3037B) and scaler (Model 183). The results are given in Table 1. The normal radionuclide excretion is similar to that previously reported in animals and human children. Both hepatocellular disease and extrahepatic biliary obstruction markedly increase this renal excretion. The greatest amount of urinary activity was found in the first 24 hr with a steadily decreasing amount from that point on (Table 1). Therefore, it is also clear from these quantitative studies that differentiation between intrahepatic and extrahepatic causes of jaundice cannot be made on the basis of comparative urinary-excretion data.

Jacobson and Brent have presented evidence in the rat and rabbit that there is continuous dissociation of ^{131}I from the rose bengal molecule *in vivo* by comparing thyroid uptake and excretion after administration of Na^{131}I- and ^{131}I-tagged rose bengal (*9*). They found that the release of radioactivity from the thyroid of rats that received the radioactive dye was greatly delayed compared with that from rats receiving Na^{131}I. The amount of uptake of radioactivity in the rat thyroid after ^{131}I-rose bengal injection also "considerably exceeded the amount that would be expected from accumulation of free iodide in the rose bengal solution at the time of injection" (*11*). Chemical and chromatographic de-

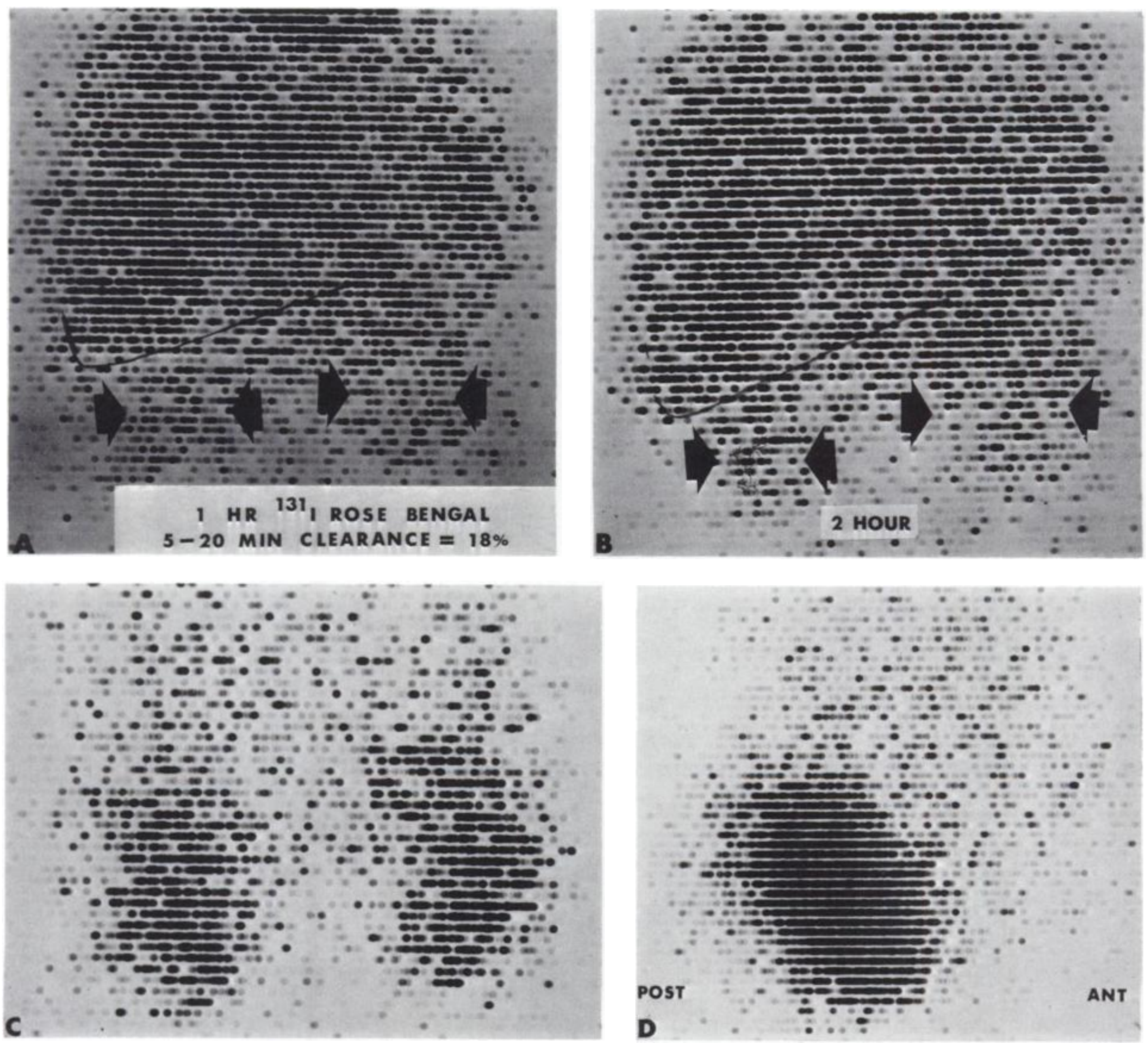


FIG. 4. Radioactive rose bengal abdominal scans on 67-year-old female with severe Laennec's cirrhosis. 4A: 1-hr study reveals extrahepatic activity that is bilaterally located and corresponds in position to what was felt to represent kidneys (arrows). The palpable liver edge is represented by solid oblique line. Poor liver function (20/5-min blood clearance of 18%) is reflected by both patchy appearance of the liver and good visualization of cardiac blood pool at top of scan. 4B: 2-hr study fails to show any change in position of extrahepatic activity, strengthening impression that it represents renal activity (arrows). 4C: 24-hr supine scan clearly delineates both kidneys. Liver has now emptied of activity. 4D: 24-hr right lateral scan again demonstrates typical renal excretion.

TABLE 1. URINARY EXCRETION OF ^{131}I-ROSE BENGAL

Groups	Excretion (% of injected dose) at 24 hr	48 hr	72 hr	Total 72-hr excretion
Group A (normals)				
1	2.6	1.3	0.6	4.5
2	3.0	1.1	0.6	4.7
3	1.5	1.0	0.4	3.9
4	1.8	—	—	—
5	1.6	—	—	—
Group B (extrahepatic obstruction)				
1. CA of pancreas	12.4	6.7	4.9	24.0
2. CA of pancreas	6.9	5.8	4.9	17.6
3. CA of pancreas	4.4	5.8	3.8	14.0
4. Common duct stones	6.9	5.1	2.6	14.6
5. CA of pancreas	17.8	—	—	—
Group C (intrahepatic disease)				
1. Hepatitis	3.4	2.6	1.6	7.6
2. Laennec's cirrhosis	7.0	3.0	1.5	11.5
3. Laennec's cirrhosis	6.2	3.4	1.6	11.2
4. Laennec's cirrhosis	5.6	3.1	1.2	9.9
5. Laennec's cirrhosis	4.0	—	—	—

terminations by one of the manufacturers indicate that only a fraction of a percent of the iodine in solution is unattached. Moreover, cold storage for 2 or 3 weeks does not materially increase the free ^{131}I content (*11*).

Human evidence for this continuous dissociation of ^{131}I from rose bengal is also available. Marked thyroid activity (7.8% of injected dose) has been noted in a child with biliary atresia 1 week after the intravenous infusion of the radioactive dye (*9*). In the same patient, daily 24-hr urine samples contained exponentially decreasing amounts of ^{131}I.

Since the above animal and human data support the contention that there is dissociation of ^{131}I from rose bengal *in vivo,* it is reasonable that intrinsic hepatocellular disease or biliary-tract obstruction allows greater time for increased dissociation of this sort by prolonging the normal transit of rose bengal. This also appears to suggest indirectly that the increased urinary activity noted in these patients is mostly in the form of dissociated free ^{131}I. However, further investigative analysis of the urine itself is necessary to supply more direct support to this hypothesis. In any event, the increased radiation to the thyroid gland in these patients should be kept to a minimum by adequate prophylaxis with a loading dose of free iodine most often in the form of Lugol's solution.

SUMMARY AND CONCLUSIONS

Extrahepatic biliary-tract obstruction as well as severe intrahepatic disease causes increased renal excretion of radioiodinated rose bengal. Experimental evidence indicates that there is continual dissociation

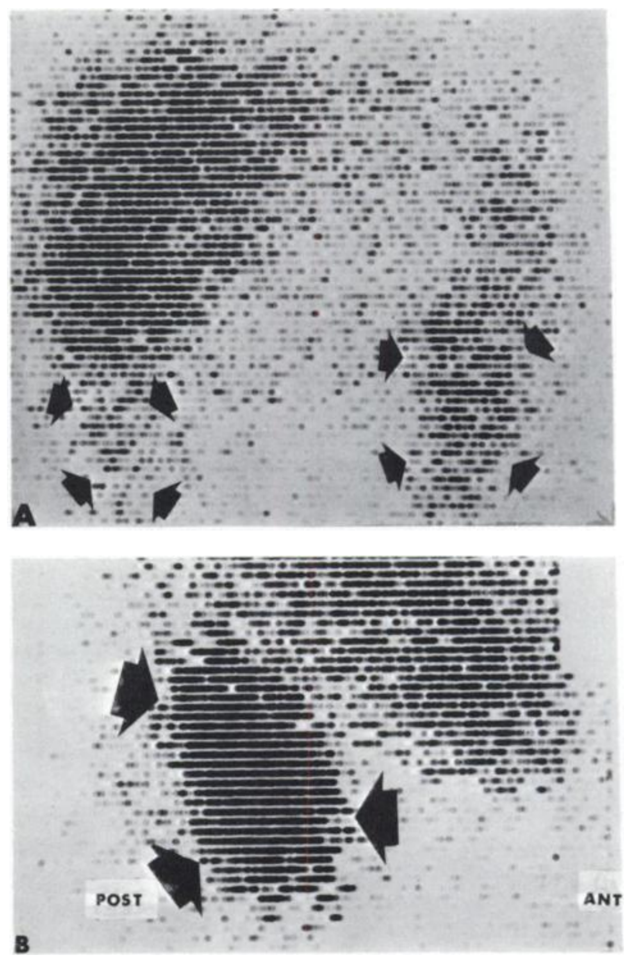


FIG. 5. ^{131}I-rose bengal abdominal scans on 65-year-old male with hepatoma. 5A: 24-hr supine study shows bilateral extrahepatic activity (arrows) that was less clearly seen on earlier studies. Note large space-occupying defect in left lobe of liver. 5B: 24-hr right lateral study reveals clearly delineated kidney in its expected position posterior to liver (arrows).

of ^{131}I from rose bengal *in vivo* and indirectly suggests that a good portion of this urinary excretion may be in the form of free ^{131}I.

The importance of recognizing renal activity on rose bengal abdominal scans lies in the need to differentiate it from intestinal activity and to avoid an erroneous impression of a patent biliary tract where obstruction actually exists.

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