

## INVESTIGATIVE NUCLEAR MEDICINE

### Effect of Complete Biliary-Tract Obstruction on Serial Hepatobiliary Imaging in an Experimental Model: Concise Communication

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**In order to determine the effect of biliary obstruction on hepatocyte clearance and bile flow, five dogs were imaged before, and three times a week after, surgical ligation of the common bile duct. The first postoperative study was performed 3 hr after surgery. Bile flow and duct function were evaluated from analog images; hepatocyte clearance (HC) was estimated in digital images from the ratio of liver to cardiac blood-pool counts at 3 min. Liver function tests were measured serially. 3 hr after surgery the HC index and liver function tests were still normal. Analog images showed no intestinal radioactivity, but accumulation was seen in the distending biliary tract. On the third postoperative day, all liver function tests were abnormal and the HC index was significantly decreased ( $p < 0.01$ ). The biliary tract was never seen beyond the first postoperative day. Thus, complete obstruction of the common bile duct does not stop bile flow or cause significant hepatocyte damage in the first few hours. By the third day of obstruction, however, no bile flow is detectible and significant hepatocyte damage has occurred.**

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Recent improvements in hepatobiliary radiopharmaceuticals have resulted in an expanded clinical role for radionuclide hepatobiliary imaging (1,2). It has been shown to be useful in the diagnosis of acute cholecystitis (3,4), biliary obstruction (5,6), biliary atresia (7,8), bile leaks (9), and postoperative abnormalities of the biliary tract (10).

In patients with cholestatic jaundice the level of obstruction can be assigned to the hepatocyte, intrahepatic duct, or extrahepatic duct with hepatobiliary imaging as long as some bile flow is present (5). Unfortunately, in as many as one third of patients there is no evidence of bile flow and the level of obstruction cannot be determined (5). However, if hepatocyte clearance is relatively good, obstruction can be recognized as being in the biliary tract rather than the hepatocyte, and usually in

the extrahepatic biliary tract, since intrahepatic cholestasis rarely results in complete obstruction (5). Thus, it would be useful clinically to know the temporal relationship between biliary-tract obstruction and secondary damage to hepatocyte function. We have studied this relationship in an experimental model of acute, complete obstruction of the common bile duct.

#### MATERIALS AND METHODS

**Animals and surgical procedure.** Five mongrel dogs, two males and three females, were studied; they weighed 13.6-26 kg. Following two control hepatobiliary studies, each dog was anesthetized with 2.2 mg/kg of xylazine given subcutaneously followed by 12.5 mg/kg of sodium pentobarbital i.v. A laparotomy was then performed and the common bile duct ligated.

**Imaging protocol.** Each hepatobiliary study was performed without anesthesia by injecting 2 mCi of Tc-99m diethyl iminodiacetic acid intravenously. With the dog supine under a gamma camera (10 in. diam), digital

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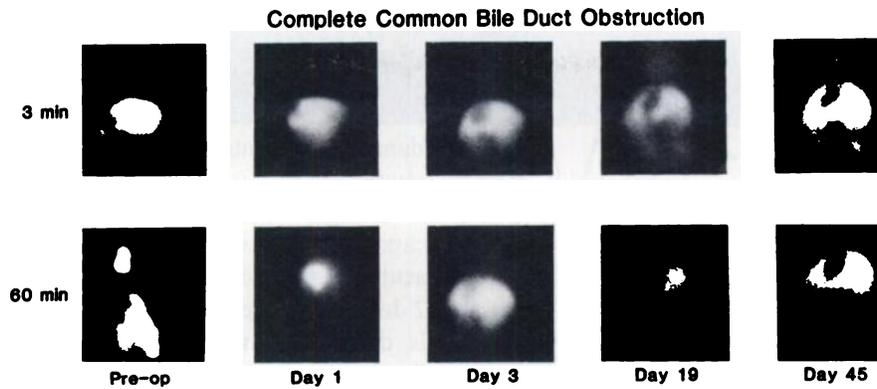


FIG. 1. Ventral images at 3 and 60 min after injection of Tc-99m diethyl IDA shown for preoperative control and postoperative studies on days 1, 3, 19, and 45. Control study shows good hepatocyte clearance, namely, high ratios for liver to background and liver to cardiac blood pool at 3 min, and passage of bolus into intestine and gallbladder by 60 min. Study at 3 hr after operation shows good hepatocyte clearance, visualization of dilated gallbladder, and no intestinal radioactivity. All subsequent studies show decreased hepatocyte clearance, nonvisualization of biliary tract (except as areas of decreased radioactivity), and no intestinal radioactivity.

images were acquired in 10-sec frames for 3.5 min following injection. Analog images were acquired for 2 min from 3 to 5 min after injection, and for 3 min from 60 to 63 min after injection.

Each animal was imaged on the day of operation, ~3 hr after surgery. Subsequently, hepatobiliary studies were performed three times a week until the experiment had to be terminated.

**Image analysis.** The analog images at 3 and 60 min were evaluated for the presence or absence of biliary tract and intestinal radioactivity. The digital images were summed into a 60-sec frame from 2.5 to 3.5 min and the ratio of left hepatic lobe to cardiac blood pool was determined, the regions of interest being placed within the borders of the left hepatic lobe and cardiac blood pool. This ratio was used as an index of hepatocyte clearance.

**Blood chemistry.** Blood for total and conjugated serum bilirubins (TB & CB), alkaline phosphatase (AP), and serum glutamic pyruvic transaminase (SGPT) was drawn at the time of each hepatobiliary imaging study.

## RESULTS

**Analog images.** All control studies showed high count ratios for liver to cardiac blood pool and liver to background at 3 min (Fig. 1). They all also demonstrated gallbladder and intestinal radioactivity at 60 min. The images on the first postoperative day (3 hr after surgery) showed areas of decreased radioactivity in the region of the gallbladder in the 3-min image, and radioactivity in a distended gallbladder at 60 min in all five dogs. A dilated biliary tract was also seen at 60 min in three of the five. Images from studies beyond the first postoperative day showed decreased radioactivity in the area of the gallbladder, no evidence of radioactivity in the biliary tract, gallbladder, or intestine, and a decreased ratio for liver to cardiac blood pool. The only significant difference between the 3- and 60-min images was increased

bladder radioactivity in the 60-min image.

**Digital images.** The count ratio for left hepatic lobe to cardiac blood pool (hepatocyte clearance index) in control studies was  $11.7 \pm 0.6$ , mean  $\pm$  s.e.m. (Fig. 2). The hepatocyte clearance index appeared decreased in the first postoperative study, but not to a significant degree. The index on the third postoperative day was  $6.0 \pm 1.38$  ( $p < 0.01$ ). Little change occurred after the third postoperative day (Fig. 2).

**Blood chemistry.** All liver function tests were within normal limits in the control period. On the first postoperative day, all liver function tests were elevated, but only the SGPT was above the normal range (Figs. 2 and 3). TB, SGPT, and AP all rose rapidly during the first 10 days, then leveled off. DB showed a more gradual rise (Fig. 2).

The correlation coefficients between the hepatocyte clearance index and TB, DB, SGPT, and AP were  $-0.80$ ,  $-0.75$ ,  $-0.72$ , and  $-0.72$ , respectively (all  $p < 0.01$ ).

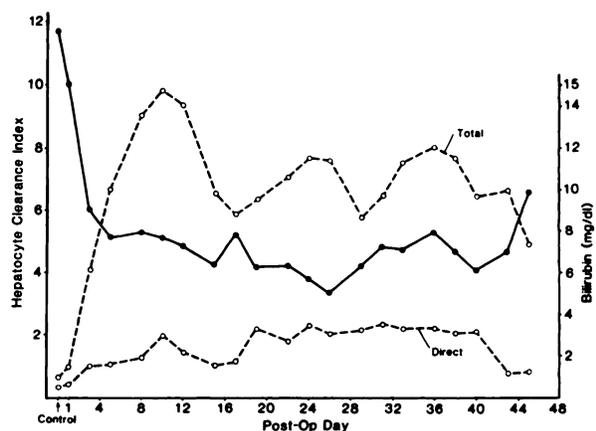


FIG. 2. Hepatocyte clearance index (solid line) and total and direct serum bilirubin levels plotted against time following ligation of common bile duct. Preoperative values are indicated.

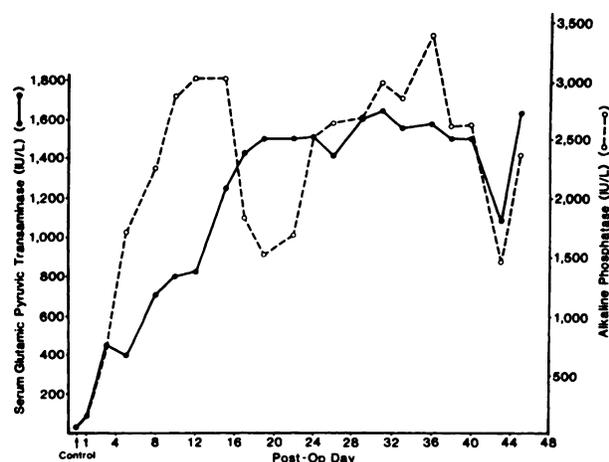


FIG. 3. Levels of serum glutamic pyruvic transaminase and alkaline phosphatase plotted against time following ligation of common bile duct. Preoperative control values are indicated.

#### DISCUSSION

Our findings indicate that complete acute obstruction of the common bile duct has little effect on hepatocyte clearance and bile flow for at least several hours. Hepatocyte damage would not be expected until bile-duct pressure rises significantly, and as long as the gallbladder can decompress the biliary tract by reabsorbing water, the pressure will not rise and bile flow will continue (Fig. 1). During this time the functional state of the hepatobiliary tract is probably similar to that in the fasting state with a tightly closed sphincter of Oddi. However, in three of five dogs some dilatation of the biliary tract was noted at this time.

By the third postoperative day no bile flow is present and hepatocyte clearance is decreased. Presumably the gallbladder has concentrated its contents to the point where the osmolarity is too high to allow continued reabsorption of water. At this point biliary-tract pressure will rise, resulting in secondary hepatocyte damage. Such damage approaches its maximum by the fifth postoperative day, but in all animals the hepatocyte clearance index and analog images continued to show some evidence of hepatocyte clearance throughout the imaging period. The chemical liver function tests showed a degree of abnormality paralleling the hepatocyte clearance index (Figs. 2 and 3).

Patient studies indicate that either complete biliary tract obstruction or severe hepatocellular disease can result in the findings of a severe decrease in hepatocyte clearance and an absence of bile flow (5). In general, therefore, these findings resist a clear interpretation. The present study was undertaken, in part, to determine how quickly complete biliary obstruction results in severe hepatocyte damage. While such damage occurred quickly in our experimental dog model, some hepatocyte

function and clearance persisted for several weeks following ligation of the common bile duct and cessation of bile discharge. Consequently the time required for complete obstruction to produce severe hepatocyte damage in patients cannot be estimated from the present study.

In summary, the gallbladder and biliary tract are capable of resisting pressure rise for several hours after acute, complete obstruction of the common bile duct. By 2 days after onset of obstruction, however, no bile flow is detectable and significant secondary hepatocyte damage has occurred. These results suggest that the findings of severe hepatocyte damage and absent bile flow in hepatobiliary imaging studies will be indeterminate between primary severe hepatocyte damage and complete extrahepatic biliary-tract obstruction with secondary severe hepatocyte damage, even when the clinical setting indicates an acute process.

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