Pancreatic Scanning Using Retrograde Injection of Technetium-99m-Labeled Compounds

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With increased clinical availability of endoscopic retrograde pancreatography, a method for retrograde injection of radionuclides into the pancreas became available. A dog model was developed to evaluate resolution and toxicity of retrograde imaging prior to human use. Two groups of technetium-99m-labeled compounds were used. The first included ionic carriers—pertechnetate and pyrophosphate—and the second included particulate carriers—sulfur colloid and albumin microspheres. Parenchymal visualization, absorption patterns, and toxicity in dogs were studied. The results suggest that pyrophosphate, sulfur colloid, and albumin microspheres would all be feasible technetium carriers for use in humans.

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Over the past 5 years endoscopic retrograde pancreatography (ERP) has developed from primarily a research technique to a readily available clinical procedure for evaluation of pancreatic disease (*1–5*). In competent hands the procedure is relatively easy and usually requires less than 30 min for completion. Endoscopic retrograde pancreatography reveals the main pancreatic duct (MPD) and usually the major side branches in over 90% of the cases attempted (*6*). Although providing detail of the MPD, the procedure is limited to diagnosing only those diseases that directly or indirectly affect the MPD.

By adding parenchymal visualization to the ERP, we anticipated extending the usefulness of this procedure and overcoming one of its major limitations. Direct injection of a technetium-99m-labeled compound into the MPD at the time of ERP is a simple procedure with no apparent added morbidity or mortality to the patient. Therefore, a dog model was developed to evaluate four commonly used Tc-99m compounds: Group 1, *ionic* (pertechnetate and pyrophosphate); and Group 2, *particulate* (sulfur colloid and albumin microspheres). Preliminary evaluation in patients has revealed focal parenchymal defects in instances of pancreatic malignancy or pseudocyst.

MATERIALS AND METHODS

Three groups of adult mongrel dogs were studied. Each dog was anesthetized for the surgical cannulation of the main pancreatic duct by means of a duodenotomy and direct placement of the cannula. This permitted injection of only the major portion of the gland, since the area drained by the minor pancreatic duct was not injected. The minor portion thus served as control for distribution of the compounds as well as their effect on the parenchyma of the gland. Neither pancreatic duct was cross-clamped at any time. Animals were anesthetized during all imaging procedures. The chosen doses of radionuclide were similar to those in clinical use.

Group 1. Four adult mongrel dogs were each injected with one of the four labeled compounds and serially imaged for 1 hr. They were then killed and the pancreases removed for further imaging. This group was designed to provide a preliminary screening study for the compounds and for early histologic evaluation of the effects of technetium-labeled compounds on the pancreas.

Group 2. Four adult mongrel animals were given a retrograde injection of Renografin 60 under a pressure of 120 mm Hg for 4 min to induce chemical

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pancreatitis (7). The following day the dogs were injected with the labeled technetium compounds and serially imaged for 24 hr. They were then killed and the pancreases removed and imaged again. This group of animals was designed to evaluate the effects of ERP with the labeled compounds in animals with acute pancreatitis, and to see whether this would alter the distribution or absorption pattern. One dog in this group died 12 hr after retrograde injection of labeled pyrophosphate, preventing serial imaging. However, the pancreas was removed and the isolated organ was imaged. Histologic examination confirmed severe chemical pancreatitis.

Group 3. Each of the four animals in this group was injected with one of the four labeled compounds and serially imaged for 24 hr. The dogs were allowed 7 days to recover and were then killed and their pancreases removed. This group allowed relatively long-term evaluation of the effect of the injected radionuclides on the parenchyma of the pancreas.

Blind histologic evaluation was performed on the injected pancreases in all animals by one of us (SES).

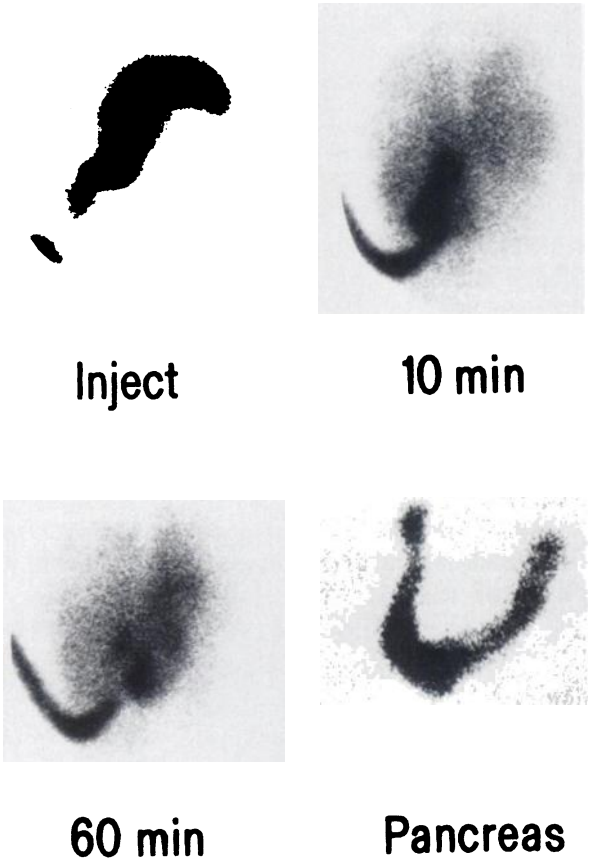

FIG. 1. Retrograde injection of Tc-99m as pertechnetate into main pancreatic duct of normal dog, with serial imaging for 1 hr. Note that injected portion of pancreas is significantly obscured 10 min after injection. Uniform distribution in excised pancreas is presumed to represent blood pool only.

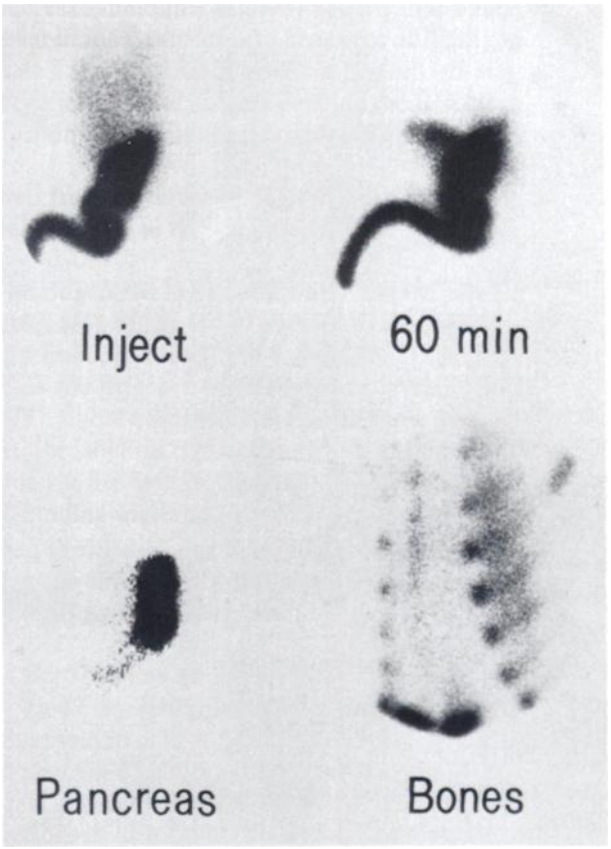

FIG. 2. Retrograde injection of technetium-99m pyrophosphate into main pancreatic duct of normal dog, with serial imaging for 1 hr. Deterioration is slower than with pertechnetate, and injected portion of pancreas can be visualized up to 1 hr later.

RESULTS

Eight normal dogs, and three dogs with chemically induced acute pancreatitis, were studied to evaluate both ionic and particulate carriers of Tc-99m. Both kinds of carrier were injected and the animals followed serially for up to 24 hr in both normal animals and in those with acute pancreatitis.

The ionic carriers of technetium-99m included pertechnetate and pyrophosphate. This group showed homogeneous parenchymal activity with systemic absorption presumably through the ductal–interstitial–venous pathway (8).

Figure 1 shows rapid absorption of the pertechnetate, with identification of the injected portion of the pancreas significantly impaired 10 min after injection. The image at 1 hr fails to identify the pancreas clearly. The removed pancreas (1 hr after injection) shows uniform distribution throughout both the injected and uninjected portions. No attempt was made to image the gland in the same relationship as in situ.

The result suggests essentially complete absorption, with the image of the removed organ showing only blood pool and not the injected portion of the gland.

Figure 2 also shows an ionic carrier of Tc-99m pyrophosphate injected into the main pancreatic duct. There is systemic absorption, but this is slower than with pertechnetate, and because of bone concentration and renal excretion, the blood background remains low enough for imaging up to 1 hr following injection. The removed gland, imaged in relation to its position in situ, shows only parenchymal visualization of the injected portion of the gland. Uptake of the pyrophosphate in bone did not interfere with pancreatic imaging.

The particulate carriers, Tc-99 sulfur colloid and Tc-99m albumin microspheres (Fig. 3), show essentially identical, homogeneous distribution throughout the injected portion of the gland. In contrast to the ionic materials, these carriers showed no significant systemic absorption even 24 hr after the injection. No redistribution of the compounds could be identified in the noninjected portion of the gland. Some drainage of the tracer into the duodenum did occur with both groups, but this was cleared promptly from the bowel and did not present a diagnostic problem. This is also seen in the previous figures and explains the bulbous collection of activity at the bottom of most of the images.

Histologic examination was performed on the pancreases of both normal dogs and those with acute pancreatitis. In this experiment only the caudal lobe of the dog's pancreas was injected. Comparisons were then made between the injected caudal lobe and the uninjected cephalic lobe. In the dog these structures are separate, and an internal control can therefore be obtained in each animal. No changes were observed between the two lobes of the pancreas in any of the animals receiving the Tc-99m-labeled compounds. The pancreatic acinar tissue was well preserved. There was no inflammatory reaction either in the acinar tissue, the ducts, or the periductal tissue. In the dogs that had had a chemical pancreatitis induced by the injection of renografin, the cephalic lobe was entirely normal whereas the caudal lobe contained polymorphs in the acinar tissue and ducts. In one animal there was moderate necrosis of the pancreatic tissue. These observations are compatible with those found in previous studies of chemically induced pancreatitis.

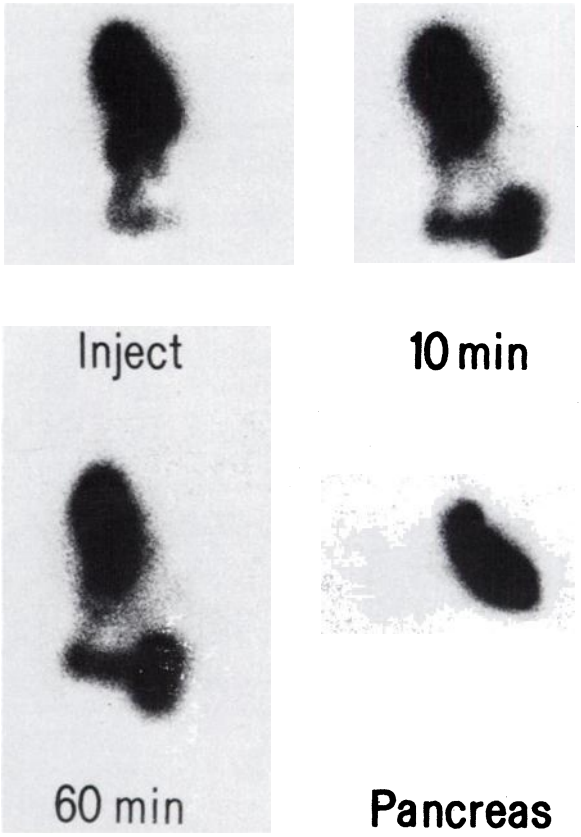

FIG. 3. Retrograde injection of technetium-99m sulfur colloid into main pancreatic duct of normal dog, with serial imaging for 1 hr. Note homogeneous distribution throughout injected portion of gland, without significant systemic absorption.

DISCUSSION

The incidence of pancreatic carcinoma is slowly increasing, and this cancer is now the fourth most common cause of cancer death in men and the sixth in women. Although selective angiography and ERP have made the diagnosis of pancreatic malignancy somewhat less difficult, early diagnosis is still rarely possible. The addition of parenchymal visualization through ERP would, we hope, allow diagnosis of lesions before their effects could be visualized by retrograde contrast studies. Acinarization or dispersal of contrast material into the glandular elements of the pancreas can be achieved using the usual radiographic contrast materials (*6*). But since this requires increased injection pressure and larger doses of contrast material, acinarization is performed intentionally in only a few selected cases. Normally ERP gives excellent anatomic delineation of the MPD and of its major side branches. Nevertheless, the anatomic variability of the major side branches somewhat limits their usefulness in interpretation and stresses the need for parenchymal visualization.

A dog model was chosen first to evaluate the addition of parenchymal visualization to the ERP because of the work on contrast toxicity from retrograde pancreatic injection currently in progress by one of the authors (SES). In this work, both normal dogs and those with induced acute pancreatitis are

TABLE 1. COMPARISON OF Tc-99m-LABELED COMPOUNDS

Carrier	No. dogs*	Visualization		Absorption from pancreas	Comments
		Early	Late		
Pertechnetate	3	Excellent	Poor	Rapid	Too much blood background
Pyrophosphate	2†	Excellent	Satisfactory	Fairly rapid	Feasible
Sulfur colloid	3	Excellent	Excellent	Minimal	Feasible
Microspheres	3	Excellent	Excellent	Minimal	Feasible

* One animal each from groups 1–3.
† One animal from group 2 died before serial imaging was obtained.

being studied to evaluate parenchymal uptake, retention, absorption, and toxicity.

Retrograde injection of the labeled compounds revealed rapid parenchymal assimilation of all radionuclides, with excellent parenchymal visualization. As anticipated, the ionic compounds were rapidly absorbed into the blood stream, but because of this rapid absorption, the high blood background, and gastric secretion, delayed images were difficult to interpret. The somewhat slower rate of absorption of pyrophosphate, along with its lower blood background, made possible acceptable delayed images for up to 12 hr. The particulate materials, sulfur colloid and albumin microspheres, remained within the pancreatic parenchyma with essentially no extrapancreatic loss demonstrable for up to 24 hr after injection (Table 1).

The most common morbid complication of ERP is chemically induced acute pancreatitis. Studies were performed here in dogs with this condition to show that there results no appreciable difference in parenchymal visualization or absorption patterns of the labeled compounds. Histologic evaluation of the pancreas failed to reveal any changes other than those expected from the chemical pancreatitis—namely polymorph infiltration and focal necrosis. No other histologic changes in the pancreas were observed either in normal animals or in those with induced pancreatitis.

The dog model developed here has provided evidence of rapid uptake of the labeled compounds, excellent parenchymal visualization, variable absorption rates depending upon the nature of the chemical carrier, and no histologic evidence of tissue toxicity. These findings suggest that retrograde injection of technetium-labeled pyrophosphate, sulfur colloid, or albumin microspheres may be feasible for use in patients.

Abnormalities observed to date in humans utilizing Tc-99m sulfur colloid have included focal defects in the head and body of the pancreas secondary to malignancy in one instance and to a large pseudocyst in another. No untoward side effects were observed in either patient.

ACKNOWLEDGMENT

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REFERENCES

1. KASUGAI T, KUNO N, KUZI M, et al.: Endoscopic pancreatocholangiography. II. The pathological endoscopic pancreatocholangiogram. *Gastroenterology* 63: 227–234, 1972

2. OGOSHI K, NIWA M, HARA Y, et al.: Endoscopic pancreatocholangiography in the evaluation of pancreatic and biliary disease. *Gastroenterology* 64: 210–216, 1973

3. RUPPIN H, AMON R, ETTL W, et al.: Acute pancreatitis after endoscopic/radiological pancreatography (ERP). *Endoscopy* 6: 94–98, 1974

4. SILVIS SE, NEBEL O, ROGERS G, et al.: Endoscopic complications. Results of the 1974 American Society for Gastrointestinal Endoscopy Survey. *JAMA* 235: 928–930, 1976

5. SUGAWA C, RAOUF R, BRADLEY V, et al.: Peroral endoscopic cholangiography and pancreatography. The surgeon's helper. *Arch Surg* 109: 231–237, 1974

6. VARLEY PF, ROHRMANN CA, SILVIS SE, et al.: The normal endoscopic pancreatogram. *Radiology* 118: 295–300, 1976

7. OLSON RC, VENNES JA, SILVIS SE: Pancreatitis secondary to endoscopic retrograde cholangiopancreatography (ERCP). *Gastrointest Endosc* 22: 232, 1976

8. WALDRON RL, LUSE SA, WOLLOWICK HE, et al.: Demonstration of a retrograde pancreatic pathway: Correlation of roentgenographic and electron microscopic studies. *Am J Roentgenol* 111: 695–699, 1971