LOCULATION AS A CONTRAINDICATION TO INTRACAVITARY ^{32}P-CHROMIC PHOSPHATE THERAPY

Taylor, Baily, Halpern, and Ashburn (*1*) postulate that prior to intraperitoneal instillation of therapeutic radiocolloids an abdominal radionuclide scan should be obtained using the technique described by Tully, Goldberg, and Loken (*2*). Although intraperitoneal radionuclide therapy has been used for many years, its clinical value for the control of microscopic seeding in the peritoneal cavity is still questioned. Taylor et al suggest that ^{99m}Tc scanning may be helpful for the assessment of radiocolloid distribution prior to radiotherapy.

We have been instilling ^{32}P-chromic phosphate intraperitoneally for treatment of ovarian carcinoma as a prophylactic measure, and in advanced ascitic malignant disease therapeutically. For abdominal localization ^{99m}Tc-pertechnetate was administered simultaneously with the therapeutic radionuclide. Scintillation camera images were obtained to determine nuclide distribution. In five cases studied, four were imaged with ^{99m}Tc and one with ^{198}Au. All showed an uneven distribution of the radionuclide in the peritoneal cavity (Figs. 1–3) despite a variety of maneuvers to disperse the radioactivity evenly. In each case (only one had ascites) the radionuclides were administered in carrier fluid medium, a 10% dextran solution. The carrier solution was intended to disperse the colloid evenly in the peritoneal cavity (500 cc used), but in our experience the loculation of radionuclide in the peritoneal cavity has been the rule rather than the exception (Figs. 1–3).

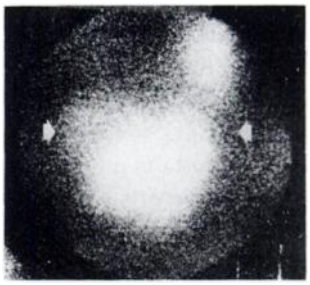

FIG. 3. Anterior abdominal scan in patient with pancreatic carcinoma, performed after intraperitoneal injection of ^{198}Au-radiocolloid. Patient was known to have loculations from extensive multiple surgical procedures. Arrows indicate iliac crests.

FIG. 1. Posterior lower-abdomen scan in patient with ovarian tumor, performed immediately after surgery. Intraperitoneal injection of ^{32}P-chromic phosphate and ^{99m}Tc-serum albumin was used. Arrow indicates coccyx.

FIG. 2. Anterior abdominal scan in patient with ovarian tumor, performed after surgery. Intraperitoneal injection of ^{32}P-chromic phosphate and ^{99m}Tc-serum albumin was used. Radiopharmaceutical has localized in left abdomen. Arrow indicates right costal margin.

Some insight into the factors responsible for uneven distribution of intraperitoneal radionuclides can be obtained from the experience of M. A. Meyers, a diagnostic radiologist, in peritoneography (*3*). The normal and pathologic distribution patterns of contrast fluids in the peritoneal cavity had been studied by Meyers (*3*) who found them to have numerous levels, collections, and recesses. Fluid injected into the upper abdomen descended in cascades (*4*) and collected in numerous pockets. In patients with abdominal tumors or previous surgery, additional compartments may develop; these may be expected to

appear as "hot spot" loculations on the scan. These focal collections of radioactivity remain despite maneuvers and changes in patient position (supine, prone, recumbent, sitting, and standing positions were used to reposition the radiocolloid).

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AUTHORS' REPLY

We agree with Drs. Vider, DeLand, and Maruyama that "uneven distribution" is common, but we do not equate uneven distribution with loculation. The fact remains that the purpose of administering ^{32}P-chromic phosphate or ^{198}Au-colloid is to deliver a reasonably homogeneous absorbed radiation dose throughout the peritoneal space. Furthermore, injection into a small loculated space could result in tissue necrosis. Thus, we believe it prudent to evaluate the peritoneal space before injecting a therapeutic dose of radiocolloid.

Ovarian carcinoma is frequently bilateral and microscopic seeding may occur on both sides of the pelvis and abdomen. Intracavitary therapy in patients with ovarian carcinoma, therefore, is more likely to be successful if there is wider dispersion than that indicated in Fig. 2 of Dr. Vider's letter. In our institution, surgeons routinely place drains on both sides of the abdomen of patients with ovarian carcinoma selected for ^{32}P-chromic phosphate therapy. If the preliminary ^{99m}Tc scan indicates failure of the pharmaceutical to cross the midline, assuming no loculation, then the therapy dose is divided and administered through both drains, thus achieving a much wider dispersion. In summary, we suggest that intracavitary ^{99m}Tc-sulfur colloid administration prior to intracavitary therapy is useful not only to exclude loculation, but also to provide the basis for optimal intracavitary therapy.

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PREPARATION OF ^{99m}Tc-FIBRINOGEN

We wish to comment on the labeling of fibrinogen with ^{99m}Tc as reported by Wong and Mishkin (*1*). Preparation of fibrinogen labeled with various emitters for in vivo studies is a significant objective (*2,2a*). However, studies in this laboratory have shown that the most important consideration in preparing radiolabeled fibrinogen is that the product must retain its structural integrity and biologic activity (*3–5*). Fibrinogen is one of the most sensitive plasma proteins, with a pronounced tendency to aggregate spontaneously (*6*). It must be handled with extreme care throughout isolation, purification, and radiolabeling.

According to present concepts, the native configuration of a protein is most stable under the pH conditions, ionic strength, and temperature associated with the native state. Changing those conditions may result in reversible or irreversible denaturation of the protein. Irreversible denaturation will also occur if the protein's primary structure is modified or if the rearrangement of the denatured state into the native configuration requires high energy, as in some cases of protein aggregation (*6*). Mihalyi has concluded from optical rotation studies that the pH zone of stability of fibrinogen is quite narrow, extending from the isoelectric point of 5.5 up to about pH 10 (*7*). Denaturation takes place readily at pH values beyond this range. Thus, the method reported by Wong and Mishkin (*1*), in which fibrinogen is subjected to a medium with pH below 3, should not be recommended. In fact, their own results suggest irreversible denaturation of the ^{99m}Tc-fibrinogen, as indicated by the precipitation of protein when their ^{99m}Tc-fibrinogen solution is readjusted to pH 7, which is within the physiologic pH range. This denaturation is probably caused not by the pH readjustment with buffer or plasma, but rather by the labeling conditions. The use of acidic media for labeling proteins often re-