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Splenic Uptake of Tc-99m Sulphur Colloid in Malignant Melanoma

Goldman (*1*) reported the observation that ten of 22 patients with malignant melanoma, in whom no hepatic abnormality could be detected by scan or liver chemistry, showed augmented splenic radioactivity in Tc-99m sulphur colloid scans. In the same report, none of 60 patients with carcinoma at various sites demonstrated such an increase in splenic uptake. Anterior and left anterior oblique scans of the spleen were carried out using a rectilinear scanner, and counts per minute were recorded over the area of highest activity. Rates of particle extraction in normal patients were demonstrated graphically by additional printouts stored on magnetic tapes during sequential gamma-camera liver imaging over a 15-min period. Criteria for increased splenic uptake included splenic density exceeding that of the liver on the anterior projection, and more counts per minute recorded over splenic "hot spots" on the left anterior oblique scan of the liver, compared with the anterior scan.

Shortly thereafter Klingensmith (*2*) described a patient in whom increased splenic uptake (using criteria similar to those of the Goldman study) was noted. In this patient the abnormal increase in spleen density disappeared following resection of a primary melanoma that was confined to the globe of the eye.

Both investigators theorized that malignant melanoma may produce a factor that increases uptake of Tc-99m sulphur colloid in the reticuloendothelial cells of the spleen.

We have recently reviewed our experience with 34 scans in 24 patients who were put on an adjuvant immunotherapy program for malignant melanoma, with the presumption that no distant or visceral disease was present. In all of these patients at least one scan was done before the onset of treatment.

In only two patients was increased splenic uptake noted. One was a patient in whom occult hepatic disease, which was not previously appreciated, was seen on liver scan. In the second such patient, demonstration of increased splenic uptake was followed at 5 mo by a scan with decrease in overall density of uptake in the spleen, but with the appearance of a discrete filling defect presumably representing a metastatic lesion. Four of these 24 patients had uptake considered to be at the upper limit of normal, and one patient demonstrated "small normal" category of splenic uptake.

An additional patient of interest was seen separately from this study. In this patient, also on immunotherapy, diffuse enlargement and increase in density of spleen was followed by splenectomy, which demonstrated what was initially thought to be "Hairy Cell" leukemia by the pathologist who saw the slides. It was later shown that this diffuse splenic enlargement was in fact due to a miliary distribution of splenic metastases from melanoma.

In summary, in a brief review of 24 patients in whom only primary and/or regional melanoma was thought to be present, no patients were found in whom splenic enlargement or increased density of uptake, demonstrated by spleen scan, could not be explained by probable splenic metastases. This is clearly contrary to the experience of Sober (*3*) and others who have recently reported identification of 50 patients with increased splenic uptake on scan in a series of 148 patients with early melanoma without known visceral disease. Only one of 165 patients with other malignancies, in their experience, demonstrated such an increase in splenic uptake.

Our findings suggest that excess splenic uptake observed in melanoma is either a nonspecific phenomenon related to previously unappreciated diffuse hepatic disorder (e.g., cirrhosis, hepatitis, or metastases) or nonspecific stimulation of the RE system (e.g., by septicemia). An additional explanation is that it may relate to the technical problem of estimating absolute counting rates in three-dimensional organs that are looked at in an essentially two-dimensional pattern. If true increase in splenic uptake of the sulphur colloid does occur, it may be a relatively uncommon event, probably not useful for diagnostic or prognostic purposes.

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Skeletal Uptake of Tc-99m HEDP in Primary Hyperparathyroidism

Using Tc-99m labeled phosphate compounds, bone scanning and simple quantification have been performed in patients with hyperparathyroidism, but contradictory results have been obtained (*1–3*).

Sy (*1*) described four patients with primary hyperparathyroidism whose scans with Tc-99m polyphosphate showed relatively increased skeletal uptake of radiopharmaceutical in calvarium, mandible and long-bone epiphyses, but he did not quantify his results. However, Weigmann et al. (*2*), using Tc-99m pyrophosphate, found that most of their 20 patients with primary hyperparathyroidism had apparently normal bone scans, and also their ratios of bone to soft tissue were not significantly different from a control group. Krishnamurthy et al. (*3*), also using Tc-99m pyrophosphate, found that seven of their 12 patients with primary hyperparathyroidism had bone-scan abnormalities that were located mainly at the extremities. They also measured urinary excretion of Tc-99m pyrophosphate in nine of those patients over a 4-hr period and found this to be higher than in a control group. This implies that (unless soft-tissue uptake is altered) total skeletal uptake of the radiopharmaceutical is reduced in such cases.

TABLE 1. WHOLE-BODY RETENTION OF Tc-99m HEDP (MEAN ± S.E.M.)

	4 hr	8 hr
Primary hyperparathyroidism (n = 4)	59.5 ± 1.9	50.2 ± 3.0
Control group (N = 8)	40.0 ± 1.7	27.9 ± 1.2
Wilcoxon rank sum test	$p < 0.01$	$p < 0.01$

We have performed bone scans on seven patients with primary hyperparathyroidism using Tc-99m HEDP, and our provisional observation is that although "mild" cases of primary hyperparathyroidism appear normal, more severe cases show higher uptake of the tracer, with patterns of abnormality similar to those described by Sy (*1*). We have also measured the ratios of bone to soft tissue (using lumbar vertebra 2 to adjacent soft tissue below the kidney) in five patients (mean 3.9 ± 0.3 s.e.m.) and, in agreement with Weigmann (*2*), have not found this to be significantly different from our control group of 30 patients (mean 4.1 ± 0.1). This is perhaps not surprising in view of our relatively crude means of quantification, in which we select only a small area of bone in an attempt to detect what may be a small yet significant change in total skeletal uptake.

Using a conventional shadow-shield whole-body monitor, we have also measured whole-body retention of Tc-99m HEDP over an 8-hr period in four patients. The Wilcoxon rank sum test shows this retention to be increased as compared with that of a control group (Table 1). Thus, our patients with primary hyperparathyroidism, unlike Krishnamurthy's (*3*), had significantly decreased urinary excretion of the tracer, and we can offer no explanation for this other than our use of a different radiopharmaceutical.

We find, therefore, that there is overall increased skeletal uptake of Tc-99m HEDP in primary hyperparathyroidism. Bone-to-soft-tissue ratios are not sensitive enough to detect this in many cases, whereas the whole-body monitor can make a precise measurement of total-body retention of the tracer.

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Comments on Tc-99m DTPA Scintillation Camera Renography

We read with much interest the paper by S. P. Nielsen et al. (*1*).

Since we have presented a similar work (*2*), we would like to comment on some aspects of the method used by the authors.

Our method deals with the direct determination of the separate glomerular filtration rate, using the Tc-99m DTPA complex, a scintillation camera, and a minicomputer.

Data are acquired for 20 min, with 20-sec frames. Cardiac, renal, and perirenal areas are selected. A blood sample serves for the normalization of the precordial curve, thus providing a plasma curve. We use the perirenal area to correct the renal curve for extrarenal background, since the perirenal curve best approximates a curve taken from a nephrectomy site—better, for example, than regions under or above the kidneys. These data permit calculation of the separate glomerular filtration rate (SGFR) if the data are restricted to the first 3 min—the period during which there is no significant escape of tracer from the kidney area. The relationship is as follows:

$$\text{SGFR (ml/min)} = \frac{1}{P} \cdot \frac{dR}{dt}(t) \cdot \cdot \cdot (t < 3 \text{ min}),$$

where R (t) is the renogram corrected for nonrenal activity and P (t) is the plasma concentration of tracer.

Between 80 and 180 sec, six very similar values of SGFR are obtained; the mean represents SGFR expressed in milliliters/minute.

Comparisons were made on more than 200 pathological cases. Good correlations were found with total and separate creatinine clearance, as well as with the $HgCl_2$ uptake test. Normal values, established on 25 patients, were in agreement with normal inulin clearance.

Nielsen and his colleagues base their procedure on two assumptions: (A) that in the uptake phase, the activity increases linearly with time (i.e., the slope is constant) and (B) that the blood-background curve is flat during the interval used for calculation (1–2 min to 4–5 min).

The first assumption is based only on the general behavior

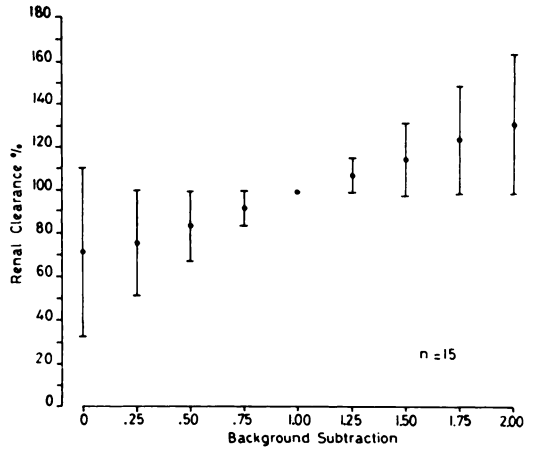

FIG. 1. Percentages of clearance variations (mean ± 1 s.d.) as a function of the amount of background subtraction. The subtractions were all performed on 15 patients.