# A COMPARISON OF $^{111}$In WITH $^{52}$Fe AND $^{99m}$Tc-SULFUR COLLOID FOR BONE MARROW SCANNING

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***Under most circumstances $^{52}$Fe, $^{111}$In, and colloid show a similar distribution of marrow. The lesser uptake of $^{111}$In by liver and spleen may occasionally be of value in permitting visualization of that portion of the spinal marrow obscured by these organs in the colloid scan. However, in red cell aplasia, when there is dissociation between phagocytic and erythropoietic functions, scanning with $^{111}$In gives no information about erythropoietic tissue distribution. Therefore, indium cannot be used as an analog for iron in the study of the hematopoietic system.***

The distribution of bone marrow can be demonstrated by radioisotope imaging with any of the radioactive colloids, such as $^{99m}$Tc-sulfur colloid, used for liver and spleen scanning. However this investigation has not gained widespread clinical acceptance for a number of reasons, the most important being that it shows only the distribution of phagocytic activity. In normal bone marrow, phagocytic and hematopoietic cells have a similar distribution and the scans are identical. This relationship is not always maintained in pathological conditions (*1,2*). In myeloproliferative disorders and aplastic states the distribution of hematopoietic marrow may become nonuniform. By scanning with a label for erythropoietic activity it becomes possible to detect both the sites and the extent of such activity and to select the most useful site for biopsy.

Iron-52 is the radioisotope of choice for imaging hematopoietic tissue because it directly labels erythroblasts. This is adequate for most purposes as under most conditions erythropoietic and other hemopoietic cells have a similar distribution. However, this isotope has a number of disadvantages, in particular, its restricted availability. It has recently been suggested that $^{111}$In may behave as an analog of iron (*3–5*). If this could be confirmed, the investigation could be made more generally available and the radiation dose to the patient would be considerably reduced. The present study reports on a comparison of this radionuclide with $^{52}$Fe and $^{99m}$Tc-sulfur colloid in a small group of patients selected because it was anticipated that they might reveal any possible differences between these agents.

## MATERIALS AND METHODS

Informed consent was obtained from patients having $^{52}$Fe scans as part of other studies. Most of these patients were also having $^{99m}$Tc-sulfur colloid scans. Whole-body scans were performed starting 15 min after the administration of 6 mCi of $^{99m}$Tc-sulfur colloid using an Ohio-Nuclear model 84 twin-headed whole-body scanner fitted with 55035L collimators. At the end of this examination, 2 mCi of carrier-free $^{111}$In in the form of ionic indium dissolved in 0.05 *N*

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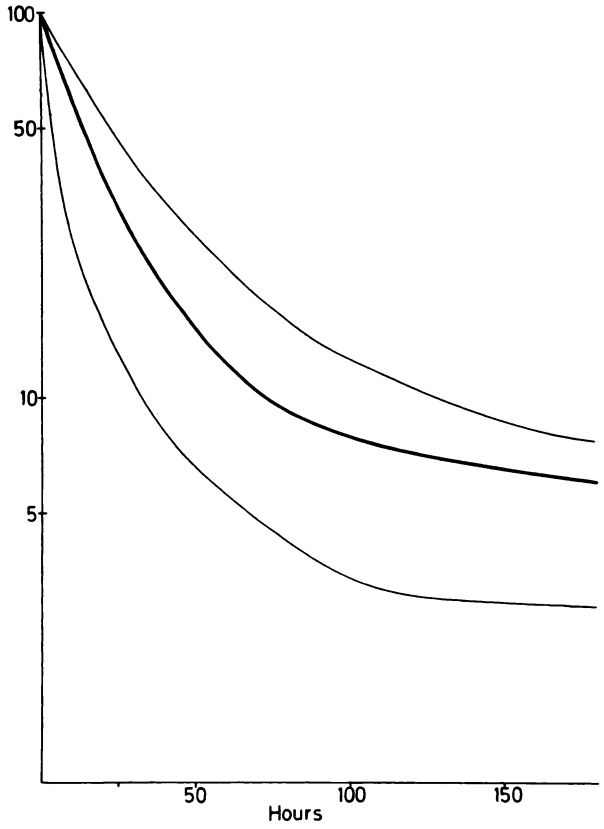


**FIG. 1.** Blood clearance of $^{111}In$ in man. Mean (heavy line) and observed range in six subjects without hematologic abnormality. Expressed as percentage of injected dose remaining in (measured) blood volume.

hydrochloric acid (*6*) were administered. The absence of colloidal $^{111}In$ was confirmed by thin-layer chromatography on silica gel. Repeat whole-body scans were performed on the same scanner 72 hr later, this time fitted with 55050M collimators. Two hundred microcuries of $^{52}Fe$-citrate (*7*) were then injected and a third whole-body scan performed 3 hr later on the same instrument on this occasion using 55050H collimators. With iron and technetium a 20% window was set centered around the peak. For indium a wide window was set to include both peaks.

Six patients were studied. In three the diagnosis was a preleukemic state associated with red cell aplasia. One patient had a myeloproliferative disorder which ultimately proved to be an idiopathic dyserythropoietic anemia. One patient had a reticulosarcoma previously treated by radiotherapy to the spine and left half of the pelvis and the sixth patient had myelosclerosis and had also developed a seminoma with biopsy-proven metastases to the paraaortic nodes.

As part of a previous study (*8*) the blood clearance of carrier-free $^{111}In$ was measured in six patients with various forms of malignant disease but without hematologic abnormality. Samples were taken at 5, 10, 15, 30, and 60 min, 2, 4, 6, 18, 24, 48, 72, 96, 120, and 144 hr.

## RESULTS

The blood clearance of indium has been described by the sum of several exponentials, the fastest component having a half disappearance time of approximately 10 hr (*9*) (Fig. 1). This is much slower than the blood clearance of iron ($t_{1/2}$ 90–120 min).

There was no detectable uptake of $^{52}Fe$ into the marrow or spleen of any of the patients with red cell aplasia (Fig. 2B). However both colloid (Fig. 2A) and indium (Fig. 2C) showed an expanded marrow in these patients. In the remaining three patients there was no significant difference in the distribution of marrow demonstrated by all three agents. In the patient with reticulum cell sarcoma who had received 3,600 rads to the spine and pelvis there was no de-

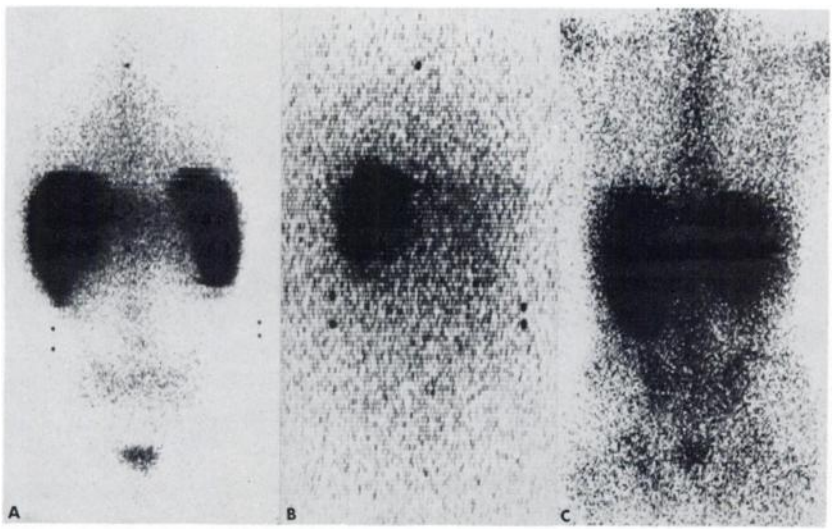


**FIG. 2.** (A) Colloid scan showing (expanded) marrow in preleukemia with red cell aplasia. (B) $^{52}Fe$ scan in same patient. No uptake in marrow or spleen is discernible. (C) $^{111}In$ scan. Marrow distribution resembles that seen with colloid, but note radioactivity around large joints.

tectable uptake of any of the agents in the irradiated areas. As sequential scans were not performed during treatment, it is not known whether the uptake of the various agents ceases at different dose levels of radiation.

There was relatively much more uptake of colloid than of indium in the liver and spleen of all patients, this being especially marked in the patient with reticulosarcoma whose spleen appeared very much larger with colloid than it did with indium. In every case there was accumulation of indium but not of the other radioisotopes around the large joints. Kidneys were visualized with indium only in those patients whose transferrin was almost saturated as a consequence of repeated blood transfusions and not in any other cases. The kidneys were not visualized in any of the 31 hematologically normal patients scanned with $^{111}$In in the previous study (*8*).

## DISCUSSION

Iron-52 is the radioisotope of choice for imaging hematopoietic tissue. However, it is cyclotron-produced and is not widely available. Moreover, when synthesized by alpha-particle bombardment of natural chromium, $^{55}$Fe comprises at least 14% of the radioactivity produced. This contaminant is responsible for over half of the absorbed dose and limits the amount of $^{52}$Fe that can be administered. With the doses used in the present study, the scan with $^{99m}$Tc sulfur colloid contained approximately double the number of counts collected in the $^{111}$In scan and four times the number collected in the $^{52}$Fe scan. The scans obtained with $^{52}$Fe are technically inferior to those obtained with $^{111}$In or $^{99m}$Tc partly because of this lower counting rate but also in part because there is significant septal penetration of the 511-keV photon of $^{52}$Fe even through the high-energy collimator used. Another limiting factor with indium and iron was the reluctance of the patients to undergo prolonged examination.

Although also cyclotron-produced, $^{111}$In can be obtained in high yield and without long-lived radioactive contaminants (*6*). Its half-life of 2.81 days is conveniently long to permit distribution to centers remote from the site of manufacture and to allow marrow uptake while its gamma emissions are ideal for use with conventional imaging devices. Following intravenous administration, indium in solution becomes bound to transferrin (*9*) although this does not happen immediately (*8*). Subsequently, some is incorporated into erythrocytes which enter the circulation (*9*). The percentage thus reappearing in the circulation is very much lower than that found with iron. There are a number of other important differences between the two elements. Iron may exist in either bi- or trivalent states whereas indium is only trivalent. Indium is always taken up by the normal spleen. Iron only appears early on in the spleen if extramedullary erythropoiesis is present. The two elements are handled differently at the placenta. Iron crosses into the fetus and is incorporated into fetal erythrocytes. Indium does not cross the placenta but accumulates there to a greater extent than does $^{125}$I-labeled transferrin (*10*). The space of distribution of $^{111}$In differs from that of colloid or $^{52}$Fe. In the first few minutes after injection $^{111}$In transferrin has been used to measure plasma volume. It subsequently equilibrates with a larger volume but it is not clear whether this represents the transferrin space or some purely hypothetical "indium space."

## ACKNOWLEDGMENTS

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