The Quantitative Distribution of the Erythron and the RE Cell in the Bone Marrow Organ of Man

By Wil B. Nelp and Rae Ellen Bower

During the past few years several radioisotope technics have been developed to delineate the functioning bone marrow organ of man. Using rectilinear scanning or camera imaging devises one may map out the spatial distribution of the reticuloendothelial (RE) cells of the marrow after intravenous injection of radioactive colloids. Initially studies of this sort were done using gold-198 colloids. The amount of radioactivity given was generally restricted to 1 or 2 millicuries to minimize radiation exposure to the other organs of the reticuloendothelial system, primarily the liver and the spleen, which accumulated the majority of the administered dose. More recently sulfur colloids labelled with technetium-99m have become available for visualizing the bone marrow organ. This isotope, with a short 6 hour half-life and no beta particle emission, has significantly lowered the radiation exposure to the patient such that administration of 10 millicuries of activity results in no more than 0.3 rad exposure to the total marrow and 2–3 rads exposure to the liver and spleen. This represents 20 to 25 times less radiation exposure than 2 millicuries of $^{198}$Au colloid and deposits about 5 times more gamma photons in the marrow organ which can be used to increase the speed of imaging as well as the information content of the resultant image. Thus it is feasible that many nuclear medicine laboratories may conveniently use this technic to study patients with diseases affecting the bone marrow organ.

It is also possible to visualize the bone marrow organ by imaging the distribution of intravenously administrated radioactive iron-52. Although this approach may be more ideal insofar as it directly depicts the functioning erythron of the marrow, $^{52}$Fe (half-life 8 hours) is produced in a cyclotron and its use is restricted to a few laboratories that have cyclotron facilities immediately available.

If one uses radiocolloid to study the marrow organ it is of basic importance to establish what the distribution of the RE cell is in relation to the hematopoietic elements of the marrow. In histologic studies of normal individuals there is a rather constant quantitative relationship of the hematopoietic and reticuloendothelial elements of the marrow. Studies in normal animals in which the skeleton has been removed have also shown a nearly identical...
Fig. 1.—Technetium-99m-sulfur colloid photoscan of an adult male depicting the normal distribution of activity in the bone marrow organ. Note activity is restricted to proximal femurs and humeral heads. Pelvis and spine are also seen. Midportion of scan is partially cut out due to high concentration in liver and spleen. Cervical spine and skull also show marrow activity.

quantitative distribution of the erythron and the RE cell.\textsuperscript{4,5} In normal man simultaneous radiocolloid and $^{52}\text{Fe}$ imaging studies have shown very similar spatial distributions of the two cell systems, although in certain diseases causing depression of marrow activity this identity may be questioned.\textsuperscript{6} Our clinical experience with $^{99m}\text{Tc}$-sulfur colloid photoscanning also shows a marrow distribution pattern which is comparable to that described for the distribution of the functioning erythron (Fig. 1).

The present study was done to acquire additional information on the quantitative relationship of the distribution of the RE cell and the erythron in
Table 1.—Recovery of Colloidal Gold-198 and Iron-59

<table>
<thead>
<tr>
<th>Bone</th>
<th>% Recovered in Excised Skeleton</th>
<th>% of Injected Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>198Au</td>
<td>59Fe</td>
</tr>
<tr>
<td>Sacrum</td>
<td>18.2</td>
<td>17.7</td>
</tr>
<tr>
<td>Ilium</td>
<td>41.1</td>
<td>43.8</td>
</tr>
<tr>
<td>Ischium</td>
<td>5.6</td>
<td>6.3</td>
</tr>
<tr>
<td>Pubis</td>
<td>7.6</td>
<td>8.2</td>
</tr>
<tr>
<td>Femur</td>
<td>23.6</td>
<td>23.4</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Fibula</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Patella</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Feet</td>
<td>0.9</td>
<td>0.2</td>
</tr>
<tr>
<td>½ Specimen</td>
<td>1.58</td>
<td>16.31</td>
</tr>
<tr>
<td>Total Specimen</td>
<td>3.16</td>
<td>32.6</td>
</tr>
</tbody>
</table>

A patient who had a hemicorpectomy provided a unique opportunity to compare the localization of radiocolloid and radioactive iron throughout the marrow organ of the surgically excised pelvis and lower extremities.

**METHODS AND MATERIALS**

The patient was a 52 year old man who had recurrent carcinoma of the rectum. The primary lesion was surgically resected three and one-half years earlier. Because of local extension, pain, obstruction of the right ureter and loss of bladder control from sacral nerve root invasion a hemicorpectomy was performed after operative exploration indicated all tumor tissue was restricted to the region of the pelvic floor.

Preoperatively the patient had a temperature of 38.5°C. Urinalysis was normal and a urine culture was sterile. The hematocrit was 34 per cent, the white blood count was 19,900 per cu.mm. with a differential count showing 94 per cent polymorphonuclear cells, 2 per cent lymphocytes and 4 per cent monocytes. The red cells and the platelets were normal on the peripheral blood smear. The blood urea nitrogen was 24 mg. per cent. Serum electrolytes, bilirubin, albumin and globulin were normal. Twenty-four hours prior to operative removal of the lower body the patient received 500 uCi of colloidal gold-198 (average particle size 40 millimicrons) and 50 uCi of 59Fe which was preincubated for 15 minutes with 5 ml of the patient’s plasma to permit binding of the 59Fe to transferrin.

Postoperatively the lower skeleton was removed from the surgical specimen. This included the pelvis with the total sacrum and all bones of the lower extremities. Muscle mass was normal in the lower extremities. The tumor had invaded the sacral nerve roots and tumor was present in the coccyx and occupied about one-half of the marrow of the fourth and fifth sacral vertebrae. No other tumor was present in the skeleton. Histologic sections of the marrow from the ilium and femur were interpreted as normal.

The distribution of colloidal gold and 59Fe within the marrow was determined as follows. The sacrum was cut into two equal sections along the posterior midline. The pelvis was separated and the right ischium, pubis and ileum were saved for sectioning. All bones of the right lower extremity were likewise removed for sectioning. The bones of the left half of the skeleton were not processed for radioactive counting but were sectioned longitudinally to examine the gross appearance of the marrow which appeared normal and essentially the same as the contralateral bones.

The bones of the right side (with the exception of the bones of the feet and the
patella) were cut into numerous sections (sacrum 19, ischium 14, pubis 10, ilium 37, femur 51, tibia 19, fibula 6) and the concentration of $^{198}$Au and $^{59}$Fe in each small segment was measured with a sodium iodide scintillation detector and a gamma ray spectrometer. The amount of radioactivity in each segment was compared to a standard fabricated in a similar geometric configuration so that the per cent of the injected dose and the per cent of the recovered dose of both $^{198}$Au and $^{59}$Fe could be calculated for each bone segment.

**RESULTS**

In the right half of the excised skeleton 1.58 per cent of the injected $^{198}$Au colloid and 16.31 per cent of the injected $^{59}$Fe was recovered. Assuming that both halves of the skeleton accumulated equal amounts of the iron and colloid, twice the above amounts or 3.16 per cent of the $^{198}$Au and 32.6 per cent of the $^{59}$Fe were contained in the entire specimen. Table 1 lists the amount of the injected dose in each bone and also lists the radioactive content of the bone as a per cent of the dose recovered from the excised skeleton (columns 1 and 2). For example, of the radioactive $^{198}$Au recovered in the skeleton 18.2 per cent was in the sacrum, 41.1 per cent was in the ilium, etc. By comparing columns 1 and 2, one can see the relative quantitative distribution of the $^{198}$Au colloid in the RE cells and the $^{59}$Fe in the erythron was similar throughout the skeleton.

Analysis of small segments of the individual bones emphasized the similarity of the distribution of the $^{198}$Au colloid and the $^{59}$Fe. Figure 2 shows the relative distribution of both isotopes in the 37 segments of the right ilium. The per cent of the ileal dose (considering the amount of radioactivity re-
covered in the ilium as 100 per cent) in each segment was strikingly similar for both $^{198}$Au (RES) and $^{59}$Fe (erythron). Similarly identical distribution patterns were seen for the segments analyzed for the pubis, ischium, sacrum and femur (Fig. 3).

Figure 4 depicts the quantitative spatial distribution of the functioning marrow in the femur. In this instance the distribution of $^{198}$Au colloid is depicted (RES). The distribution $^{59}$Fe (the erythron) was essentially the same (Fig. 3). One can see that 38 per cent of the marrow activity was in the proximal femur above the lesser trochanter. Distally, marrow activity decreased so that the lower third contained less than 10 per cent of the activity present in the femur. This pattern is characteristic of that seen in marrow photoscans, where in the normal adult one expects to see activity only in the upper one-third of the femur (Fig. 1).

**Discussion**

These studies confirm the identical spatial distribution of the RE cell and the erythron in the marrow organ of man. Similar studies in normal animals and simultaneous photoscans of $^{55}$Fe and $^{99m}$Tc-colloid in man indicated this same type of relationship. A minor discrepancy in the quantitative distribution of the two components (RES and erythron) might be present in the small bones of the feet. In this subject the foot bones contained 0.9 per cent of the recovered $^{198}$Au-colloid and only 0.2 per cent of the recovered $^{59}$Fe.
In normal rabbits the tarsals also consistently contained slightly more colloid than iron.5

The data also provides an indication of the initial deposition of intravenous 59Fe in the marrow of man. According to early studies of the bone marrow space in man by Mechanik7,8 and estimation of functioning marrow within this space,9 it has been calculated that the pelvis and lower limbs contain about 55 per cent of the total marrow space and about 40 per cent of the functioning marrow. In this study 33 per cent of 59Fe was recovered in this space.

After an intravenous injection of transferrin bound 59Fe in man it is not certain how much of the dose is initially deposited in the erythron but it is possibly 70 per cent or greater. Studies in animals (rat, rabbit and monkey) by Donohue and associates10 indicated that 49 to 84 per cent of injected 59Fe was in the skeleton 5 to 12 hours following injection. Still at this time (particularly in rats and rabbits) some of the 59Fe had returned to the blood labelled to erythrocytes. If the functioning marrow mass in the present subject was approximately 40 per cent of the total and 33 per cent of the 59Fe radioactivity was recovered in it, this would indicate that about 84 per cent of the 59Fe was transferred to the total marrow erythron during the first 24 hours.

In addition 3.2 per cent of the 198Au was recovered in approximately 40 per cent of the functioning marrow, thus by calculation 8 per cent of injected colloid was localized in the total marrow organ. This figure agrees with estimates of the marrow distribution of intravenously injected 198Au-colloid as judged by photoscanning studies, and is similar to the 11.5 per cent recovered from the marrow of young rabbits.5

SUMMARY

Studies of the quantitative distribution of the RES and the erythron in the
bone marrow of the pelvis and lower extremities were performed in a 52 year old male undergoing hemicorpectomy. $^{198}$Au colloid and transferrin bound $^{59}$Fe were injected 24 hours prior to disarticulation of the lower skeleton. Thirty-three per cent of the injected $^{59}$Fe and 3.2 per cent of the injected $^{198}$Au-colloid was recovered in the excised skeleton. By calculation approximately 84 per cent of the injected $^{59}$Fe and 8 per cent of the $^{198}$Au was deposited in the total body marrow. The spatial distribution of $^{198}$Au and $^{59}$Fe activity was essentially the same in each bone and in multiple small sections of them. The results support the concept that in normal situations the quantitative distribution of the RES and the erythron in the bone marrow organ of man is essentially identical and that radioisotope photoscanning of the marrow using radiocolloids does depict the quantitative distribution of the erythropoietic marrow.

SUMMARIO IN INTERLINGUA

Studios del distribution quantitative del sistema reticuloendothelial e del erythron in le medulla ossee del pelve e del extremitates inferior esseva effectuate in un masculo de 52 annos de etate subjicite a hemicorpectomia. Colloide a $^{198}$Au e $^{59}$Fe ligate a transferrina esseva injicite 24 horas ante le disarticulation del skeleto inferior. Trenta-tres pro cento del injicite $^{59}$Fe e 3,2 pro cento del injicite colloide a $^{198}$Au esseva retrovate in le excidite skeleto. Esseva calculate que approximativemente 84 pro cento del injicite $^{59}$Fe e 8 pro cento del $^{198}$Au esseva deponite in le medulla ossee total. Le distribution spatial del activitate de $^{198}$Au e de $^{59}$Fe esseva essentialmente le mesme in cata osso e in multiple micre sectiones ossee. Le resultatos supporta le conception que in situationes normal le distribution quantitative del sistema reticuloendothelial e del erythron in le organo de medulla ossee del homem es essentialmente identic e que photoscrutinage radioisotopic del medulla con le uso de radiocolloides representa le distribution quantitative del medulla erythropoietic.

ACKNOWLEDGMENTS

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REFERENCES

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