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A MODIFIED ^{59}Fe FERROKINETIC PROCEDURE

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FOREWORD

This report was prepared in the Internal Medicine Branch, Clinical Sciences Division, under task No. 775502. The work was accomplished between November and December 1968. The paper was submitted for publication on 27 January 1969.

A Packard series 5000 Auto-Gamma spectrometer system was used in this study. The external counting of in vivo ^{59}Fe was done using a Picker-Nuclear multiprobe system (No. 620-058).

The authors thank Sergeant Robert Hayes for his voluntary assistance in the testing of this modified procedure.

This report has been reviewed and is approved.

JOSEPH M. QUASHNOCK
Colonel, USAF, MC
Commander

ABSTRACT

In an effort to reduce the exposure dose from the ^{59}Fe ferrokinetic procedure, the injection dose was reduced from 6 μc. to 0.6 μc. Although the count rate was reduced, counts above background were obtained. The blood volume, plasma iron clearance, and red cell iron uptake were measured and found to be within normal limits. Measurement of ^{59}Fe in the spleen, heart, liver, and sacrum by external counting produced curves closely similar to those found with the higher dose. The total-body exposure dose was reduced from 110 mrem to 11 mrem.

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I. INTRODUCTION

The increasing concern with the cumulative effect of exposure to low doses of radiation has caused a re-examination of sources of such radiation. Diagnostic radioisotope procedures are a source of low exposure doses, and it is in the interest of a radioisotope laboratory to attempt to reduce these whenever practical. Two ways in which this can be done include: decreasing the amount of activity used, or substituting another radioisotope producing a lower exposure dose. The second method is usually the most practical alternative, but often the isotope presently used has many unique advantages. In this case, the only way to reduce the dose is to reduce the levels of activity. In this report this approach is tested on the ^{59}Fe ferrokinetic procedure and the practical limitations outlined.

II. MATERIALS

Iron-59

Radioactive iron was supplied as ferric chloride-^{59}Fe. The solution was prepared in distilled water, with NaOH or HCl used to adjust the pH to 7.4. Radioiron has a half-life of 44.5 days and emits both gamma rays and beta particles. The specific activity of the solution used was 10 μc./mg. or 30 μc./ml.

Gamma spectrometer

This was a well-type, NaI scintillation crystal spectrometer and was calibrated for full-scale energy of 1 Mev, at a gain setting of 40%, with additional calibration for settings of: 0.5 Mev, gain 80%; 2 Mev, gain 20%; and 4 Mev, gain 10%. The coarse gain dial setting was 0 to 2, and the fine gain setting was 2.3 in order to provide a 1% counting window.

External counting system

The gamma spectrometer system used to scan the various organs consisted of the following individual components: two scintillator probes containing 2 x 2 inch NaI crystals, with attached 36° flat field collimators; a high voltage supply; a dual channel analyzer; a dual rate computer; a wide-chart recorder; and a high speed printer.

Dosimetry

The total-body exposure dose is dependent on: the amount of activity injected, the type of radiation, the energy of the radiation, and the effective half-life. This last factor is the product of the physical half-life and the biologic half-life. Since radioiron emits both beta and gamma radiations, the exposure dose is the sum of the doses produced by these radiations. The formula for calculation of the gamma dose is:

$$D_\gamma = 0.0346 \times \tau \times \bar{g} \times T\tfrac{1}{2}\ \text{(effective)} \times \frac{\mu c.}{gm.}$$

For ^{59}Fe, τ equals 6.24, $\bar{g}$ equals 126, and T½ (effective) equals 42.7 days. If the dose used is 6 μc. of ^{59}Fe, the gamma dose equals 83 mrads. The formula for calculation of the beta dose is:

$$D_\beta = 73.8 \times \bar{E}_\beta \times T\tfrac{1}{2}\ \text{(effective)} \times \frac{\mu c.}{gm.}$$

For ^{59}Fe, $\bar{E}_\beta$ equals 0.118, and the T½ (effective) equals 42.7 days. If 6 μc. is the dose, the D_β equals 27 mrads.

Therefore, the total-body exposure dose is 83 mrads plus 27 mrads, which equals 110 mrads. If the dose is 0.6 μc. of ^{59}Fe, as in the procedure presented in this paper, the total dose is 11 mrads.

III. METHOD

In a previous report, we have presented a standard method for ^{59}Fe ferrokinetics (1). The first step in this procedure is to withdraw a blood sample sufficiently large to provide 6 ml. of plasma. Next, 12 μc. of ^{59}Fe are added to the plasma and the plasma is incubated at room temperature for 45 minutes. This is the step that we have modified in our improved procedure. Instead of 12 μc., we have added 1.2 μc. of ^{59}Fe. After incubation, the plasma is divided into two 3-ml. samples. One 3-ml. sample is diluted to 1,000 ml. with saline to prepare the plasma volume standard.

The second 3-ml. sample of plasma, labeled with 0.6 μc. of ^{59}Fe, is injected back into the patient. Blood samples are drawn at 15, 30, 45, 60, 90, and 180 minutes after injection. The venous hematocrit is determined at the same time the 15-minute sample is drawn. All blood samples are separated and the plasma retained. Additional blood samples are drawn at intervals over a 10-day period, beginning at 24 hours. These samples are not separated; the whole blood activity is determined. The venous hematocrit is determined at each point.

Blood volume is measured using the 15-minute plasma sample, the hematocrit, and the plasma volume standard. The first step is to find the plasma volume. Since 3 ml. of labeled plasma were injected, a 3-ml. volume of the plasma standard and 3 ml. of the 15-minute plasma sample are counted in the gamma spectrometer. The samples are counted to 10,000 counts and the ratio of the plasma/standard is determined. This ratio is multiplied by 1,000 to determine the plasma volume. The total blood volume is found by dividing the plasma volume with the plasmacrit (equal to 1 — corrected hematocrit).

The raw venous hematocrit is corrected for trapped plasma and for the difference between the venous and body hematocrits using a multiplication factor of 0.91 $\times$ 0.96, or 0.874 (2, 3). The red cell volume is calculated by subtracting the plasma volume from the total blood volume.

The plasma samples collected from 15 to 180 minutes postinjection are used to determine the plasma clearance rate for iron. The samples, all of the same volume, are counted and the counts plotted versus the time in minutes postinjection. The time necessary to reduce the count rate to one-half is the half-clearance time ($T\frac{1}{2}$).

The whole blood samples, collected at intervals from 24 hours to 10 days postinjection, are used to determine the red cell uptake curve. Equal volumes of whole blood are counted, and the count rate per milliliter of red cells is determined using the hematocrit (corrected for trapped plasma by using a factor of 0.96). The count rate per milliliter of red cells is then multiplied by the red cell volume to give the count rate per entire red cell mass for each time interval. A sample of the plasma standard is counted, and the count per milliliter of standard is determined. This is multiplied by 1,000 to give the amount of ^{59}Fe activity injected into the patient. The activity of the red cell mass is then divided by the activity injected to give a percentage. The percentage is plotted versus days to show the time when the maximum incorporation into new red cells occurs. This is the point at which the rising curve becomes a plateau.

In addition to these measurements of blood, the concentration of ^{59}Fe in the liver, spleen, heart, and sacrum, and the changes with time are measured using an external counter. Organs are measured to insure that the bulk of the ^{59}Fe moves to the bone marrow to be reincorporated into new red cells, and is not stored in the liver or spleen. The procedure used is that of Strong et al. (4). Counts are made at 15 minutes, 2 hours, 4 hours, 6 hours, and at intervals to 10 days postinjection. The counts are divided by a constant ^{59}Fe standard prepared from the same batch of ^{59}Fe used for injection. Since the internal ^{59}Fe and the ^{59}Fe standard are decaying at the same rate, dividing the individual count rates by the standard

count rate eliminates the need for decay correction. The ratios obtained are then further standardized by dividing all values postinjection by the 15-minute ratio. These ratios are then plotted versus time by organ to show the change in ^{59}Fe concentration.

IV. RESULTS

The modified procedure was tested on a volunteer subject—male; 22 years old; height, 72 inches; weight, 64.4 kg. In order to obtain good counting statistics (10,000 counts), it was necessary to count some samples for 50 minutes. Total blood drawn was 88 ml. The subject's uncorrected hematocrit was 53%, and this value remained constant throughout the 10-day course of the study. The values found are shown in table I.

Figure 1 shows the change in ^{59}Fe concentration (with time) of the heart, liver, spleen, and sacrum. These curves show that the bulk of the ^{59}Fe concentrates in the sacral area (bone marrow) with no appreciable iron storage in the other organs.

TABLE I

Ferrokinetic values found using a 0.6 μc. dose

Parameter	Value
Plasma volume	2,426 ml. or 37.67 ml./kg.
Red cell volume	2,847 ml. or 44.21 ml./kg.
Total blood volume	5,273 ml. or 81.88 ml./kg.
Plasma clearance ($T_{1/2}$)	71 minutes
Red cell uptake	8 days (maximum incorporation of 82%)

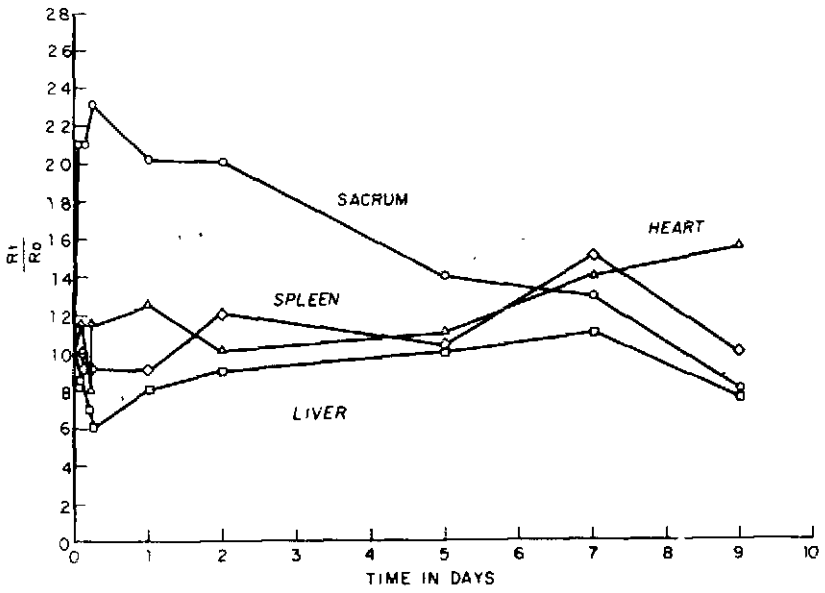

FIGURE 1

The change in ^{59}Fe concentration (with time) in the liver, spleen, heart, and sacrum.

V. DISCUSSION

The radioisotope laboratory must constantly seek to reduce the exposure dose to patients. The effect of proposed lower doses on the usefulness of the procedure must be determined. In a practical test, we have found that accurate results can be obtained using a lower dose of ^{59}Fe. One inconvenience of the method is the lower count rates found compared with the normal dose. The total number of samples to be measured is small, however, and the longer counting times required should pose few problems for most laboratories. If the lengthened counting time is a problem, the ^{59}Fe dose can be increased to some intermediate position between 0.6 and 6 μc., thus allowing shorter counting times but still decreasing the total exposure.

In routine use, the ferrokinetic procedure is used once with a given patient and is not combined with other isotopic procedures. In this case, the exposure dose of 110 mrads may be acceptable. However, if the procedure is to be repeated or performed with other radioisotope tests, a reduction in the exposure dose of ^{59}Fe from 110 to 11 mrads would be highly desirable.

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