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Intestinal Iron Absorption Studies Using Iron-52 and Anger Positron Camera

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INTRODUCTION

Iron absorption from the gastrointestinal tract following an oral dose occurs in two phases; an early rapid phase occurring within the first two hours and accounting for about 40 to 60% of the total dose absorbed, and a later and a much slower phase occurring over the subsequent 24 to 48 hours (1-5).

In animals, it has been shown that the upper small intestinal tract, particularly the duodenum, is responsible for the rapid phase (1). The same is postulated to be true in man, since during the first two hours, the time at which the rapid phase occurs, iron is thought to be in contact only with the upper small intestinal mucosa.

The site accounting for the slow phase of iron absorption is not clearly defined. It has been suggested from animal experimentation that such absorption occurs from iron retained in the small intestinal mucosa mainly duodenum and jejunum (1) (6). However, it is possible that in man iron absorption can occur in the large bowel (7).

The purpose of this communication is to present a technique for use directly in humans, whereby, the rate of iron absorption into the plasma as a function of time is correlated with its distribution in the gastrointestinal tract, and to demonstrate its use in localizing the sites of the rapid and slow phases of iron absorption in man.

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MATERIALS AND METHODS

Forty μC of ^{52}Fe, a cyclotron produced positron emitting isotope with a half-life of 8.2 hours, is given orally as ferrous chloride with 4 mg carrier ferrous sulfate to fasting normal subjects.

Just prior to the oral dose and at the conclusion of the experiment, iron turnover studies are performed using 2 μC of transferrin bound ^{59}Fe injected I.V., or alternatively, when the total absorbed oral dose is to be measured using ^{59}Fe and the whole body counter, 20 to 30 μC of ^{55}Fe are injected I.V. for continuous plasma iron turnover studies.

Photoscans of the abdomen using the Anger Positron Camera are taken throughout the study.

Blood samples are taken at approximately ½ hour intervals, and their plasma content of ^{52}Fe determined using a thallium activated sodium iodide crystal, scintillation counter. The separation of ^{52}Fe counts is done by counting the fresh blood samples, holding them for seven days, and then counting them again at which time the ^{52}Fe has virtually completely disappeared. Iron-55 is counted using a gas flow counter.

Since the rate of ^{52}Fe absorption into plasma at any one time is the sum of the rate of change in the plasma ^{52}Fe at that time, plus the rate of removal of ^{52}Fe from the plasma to bone marrow and other tissues, it is possible to calculate the rate of absorption of ^{52}Fe into the plasma as a function of time. This is done by using the rate of change of ^{52}Fe plasma levels and the plasma iron turnover rate as measured by ^{59}Fe or iron-55 (8).

RESULTS AND COMMENTS

Figure 1 shows the appearance in the plasma of orally administered ^{52}Fe and the plasma ^{59}Fe turnovers prior to and at the end of a representative study on a normal human subject (S.A.). The calculated per cent ^{52}Fe absorbed and transferred into circulating plasma per ½ hour intervals is represented as a bar graph on the top of the figure.

It is seen that in this subject (S.A.) the maximum rate of ^{52}Fe absorption occurs between 30 and 60 minutes, and slowly decreases thereafter.

The next three figures show photoscans of the abdomen in this same subject (S.A.). In the upper portion of the figures the rate of the ^{52}Fe absorbed is plotted as a bar diagram representing the per cent of the oral dose absorbed per ½ hourly intervals. The shaded area above each picture represents the rate of absorption during the time interval the photoscan was taken.

In Figure 2a, one can see that at 0-to-30 minutes the ^{52}Fe is present in the stomach duodenum and upper jejunum. Absorption has already started at this time. In Figure 2b, 30-to-60 minutes after oral administration of ^{52}Fe further progress of the ^{52}Fe into the jejunum is seen. At this time the rate of ^{52}Fe absorption is maximal. At 60-to-90 minutes (Figure 2c), still further progress of the ^{52}Fe in the jejunum is seen. By this time the rate of absorption has started to decrease.

It is clear from Figure 2 then, that at the time of maximal ^{52}Fe absorption the orally administered ^{52}Fe is present in the upper small intestinal tract and stomach.

Figures 3 and 4 show the course of the ^{52}Fe in the distal small intestinal tract and colon.

At 1-to-1½ hours (Fig. 3a) the bolus of ^{52}Fe has reached the distal jejunal area. At 2-to-2½ hours (Fig. 3b) the ileum is visualized. The rate of ^{52}Fe absorption at this time has further decreased. At 2½-to-3 hours (Fig. 3c) the ^{52}Fe content of the stomach has decreased markedly, the duodenal loop is no longer visualized but the jejunal area is well outlined. At 3-to-3½ hours (Fig. 4a) the bolus of ^{52}Fe has moved further down in the ileum with much less remaining in the proximal jejunum. There is at this time virtually no ^{52}Fe visualized in the stomach and the duodenum but the jejunal area continues to be well outlined. At 5-to-5½ hours (Fig. 4b) the ^{52}Fe can be seen in two places, the ascending colon and the jejunum, and the rate of ^{52}Fe absorption has decreased considerably. At 8-to-8½ hours (Fig. 4c) further movement of ^{52}Fe into the colon is seen. The jejunal area is still well outlined. The absorption rate is small but still detectable.

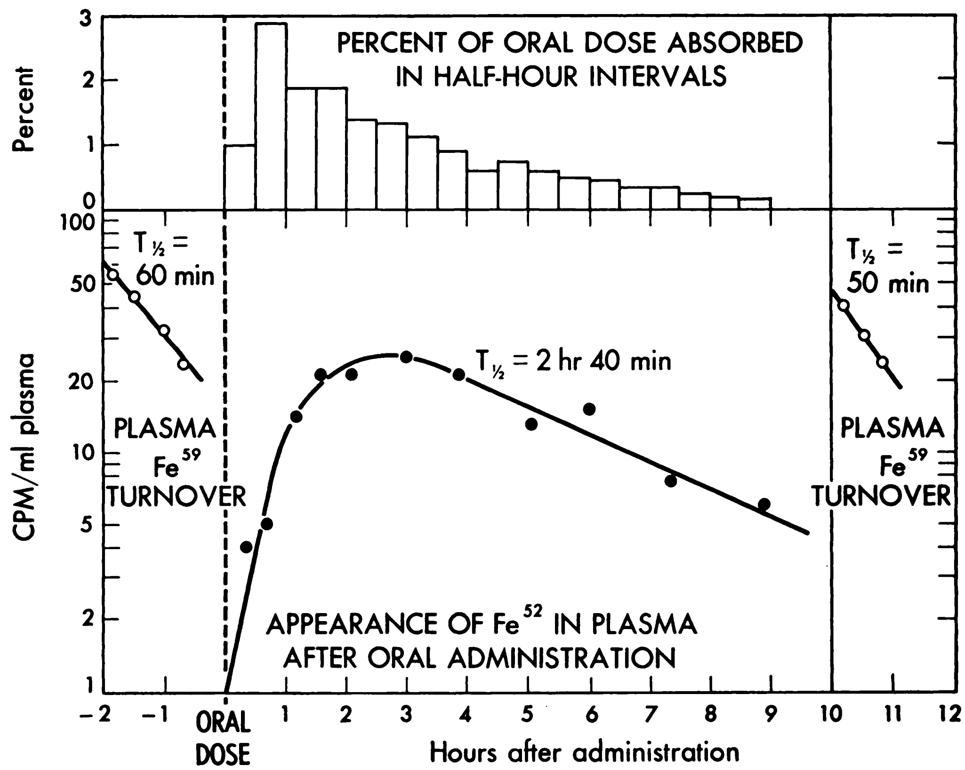

Fig. 1. Determination in a normal subject (S.A.), of the appearance of ^{52}Fe in plasma after oral administration, plasma ^{59}Fe turnover prior and at the conclusion of the experiment, and per cent of oral dose absorbed in half-hour intervals.

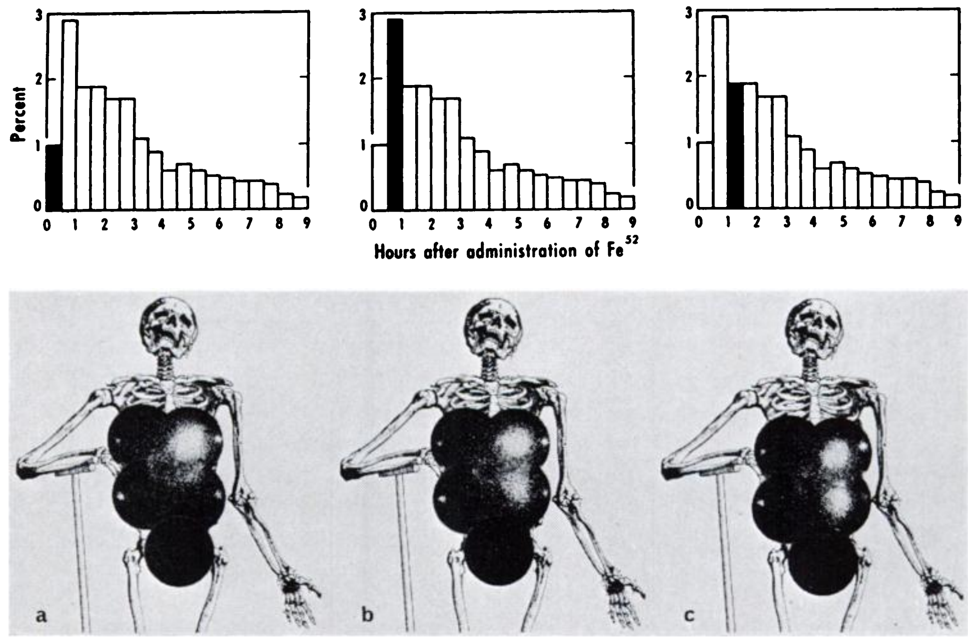

Fig. 2a. Photoscan of the abdomen in a normal subject (S.A.) at 0-to-30 minutes and the per cent radioiron absorbed at this time. 2b. Photoscans of the abdomen in a normal subject (S.A.) and the per cent radioiron absorbed at 30-to-60 minutes. 2c. Photoscans of the abdomen in a normal subject (S.A.) and the per cent radioiron absorbed at 60-to-90 minutes.

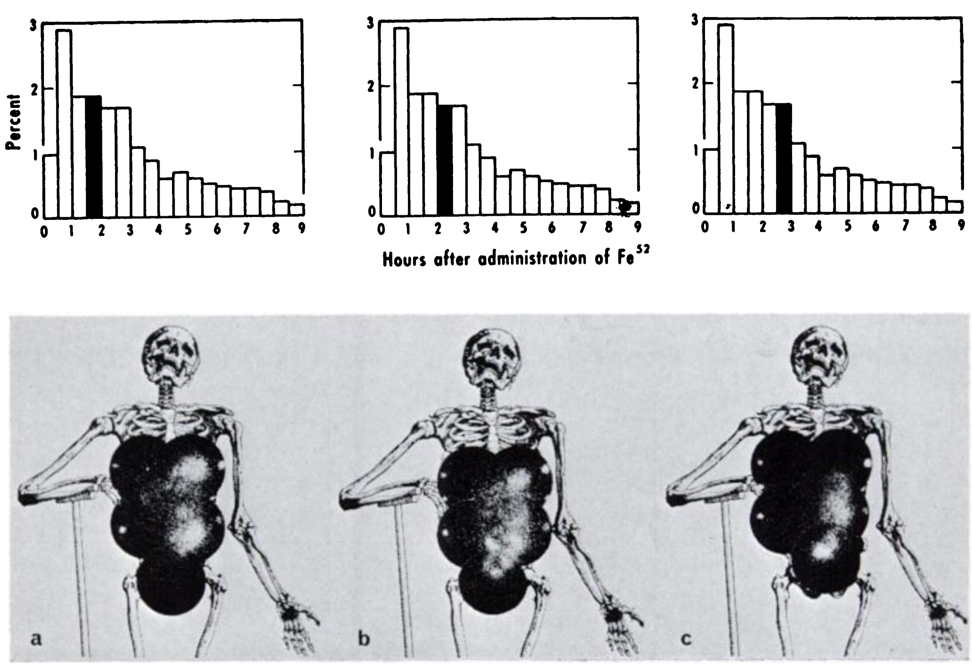

Fig. 3a. Photoscans of the abdomen of a normal subject (S.A.) and the per cent radioiron absorbed at 1½-to-2 hours. 3b. Photoscans of the abdomen of a normal subject (S.A.) and the per cent radioiron absorbed at 2-to-2½ hours. 3c. Photoscans of the abdomen of a normal subject (S.A.) and the per cent radioiron absorbed at 2½-to-3 hours.

The relative localization of the ^{52}Fe in the stomach, duodenum, jejunum, ileum and colon as judged by ^{52}Fe positron pictures was confirmed in two studies by comparison with x-ray visualization of the bowel following a barium meal. A significant difference with barium as contrasted to ^{50}Fe in these two studies was that when the bolus of barium reached the colon there was no significant residual barium in the small intestinal area as opposed to iron-52.

To date a total of six normal subjects have been studied using this technique and all have shown patterns of iron absorption similar to the subject shown in Figures 1, 2, 3 and 4.

Thus, the delayed phase of iron absorption occurs in man during the time that the orally administered iron is demonstrated to be in only two locations: 1) in the proximal small bowel, presumably adherent to the mucosa (1). 2) in the distal small bowel and colon presumably in the lumen. Since prior studies indicate that although possible, the absorption of iron from the distal bowel is probably insignificant (9), these results suggest that in man the delayed phase of iron absorption is related to the iron retained in the proximal small bowel, subsequent to passage of the iron contained bolus.

CONCLUSION

A technique has been demonstrated whereby the rate of intestinal absorption of labelled substances is correlated with its distribution in the gastrointestinal

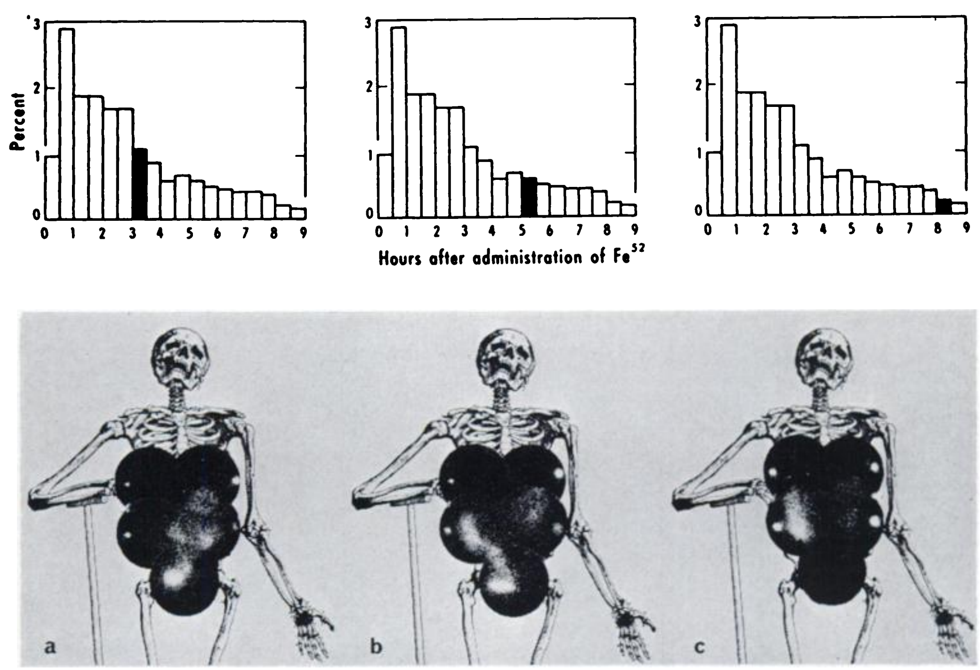

Fig. 4a. Photoscans of the abdomen in a normal subject (S.A.) and the per cent radioiron absorbed at 3-to-3½ hours. 4b. Photoscans of the abdomen and the per cent radioiron absorbed in a normal subject at 5-to-5½ hours. 4c. Photoscans of the abdomen in a normal subject (S.A.) and the per cent radioiron absorbed at 8-to-8½ hours.

tract. Its use in the study of iron absorption has been discussed. The technique should be equally applicable to study of the intestinal site of absorption of virtually any appropriately labelled substance.

The maximal rate of intestinal iron absorption occurs at the time iron is seen to be in the upper gastrointestinal tract. Iron retention in the proximal bowel occurs in man and may account for the slow phase of iron absorption.

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