EFFECT OF PHLEBOTOMY AND pH ON
IRON ABSORPTION FROM THE COLON

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A large fraction of an orally administered dose of iron is absorbed into the body during the first 2 hr (1,2). This has been termed the "rapid phase" of intestinal iron absorption, and it correlates with the passage of the iron bolus through the lumen of the duodenum and jejunum (2). During the subsequent 24-48 hr an additional amount of iron is absorbed into the body. This has been termed the "slow phase" of intestinal iron absorption and correlates with the presence of iron in the lumen of the distal small bowel and colon and that retained within the cells of the duodenal and jejunal mucosa. While it has been suggested that the iron absorbed into the body during the slow phase of iron absorption arises from iron retained in the mucosa of the upper small bowel (3), the role of iron absorption by the colon has never been fully evaluated in vivo. Ohkawara and coworkers (3) presented evidence in man that some iron absorption can occur from the large bowel, and Panayotopoulos and coworkers (4) suggested that such iron absorption could be facilitated if the iron administered were in a solution of low pH. There appears to be little data in the literature concerning the influence of other factors, such as phlebotomy, on colonic absorption of iron.

The present work was undertaken to evaluate the role of the colon in intestinal iron absorption to determine whether colonic absorption of iron played a significant role in the slow phase of iron absorption and to study the effects of phlebotomy and pH on such colonic absorption of iron.

MATERIALS AND METHODS

Fasted mongrel dogs were used in all studies. The dogs were of both sexes and weighed between 12 and 15 kg each. During the course of the absorption study plasma iron turnover rates were determined following the intravenous injection of 50 μCi 59Fe-ferrous citrate (carrier-free, Nuclear Science and Engineering Corp., Pittsburgh, Pa.). The 50 μCi 59Fe was added to a carrier dose of 4 mg of ferrous sulfate adjusted to pH 2 with dilute hydrochloric acid, and this solution was used to evaluate intestinal absorption of iron (New England Nuclear Corp., Boston, Mass). This latter solution was injected directly into the duodenum or into the cecum at the time of laparotomy. In additional experiments this iron solution was mixed with a homogenate of luminal contents from the distal ileum (obtained from normal dogs) prior to its direct injection into the colon. The animals were studied prior to and 3-8 days subsequent to obtaining a 350-450-ml phlebotomy. Prior to phlebotomy, hematocrits varied from 38 to 43% and following phlebotomy, they varied from 28 to 35%. Plasma 59Fe radioactivity was determined during each 30-min interval during the first 2 hr by counting in a deep-well scintillation counter (5), and plasma 59Fe activity was determined in a gas-flow counter by counting with and without appropriate beryllium filters (6). The amount of 59Fe absorbed into the plasma during the initial 2-hr period was determined using the method of Hallberg (7), and the amount of 59Fe absorbed from the intestinal tract into the entire body over a 2-week period was determined using the previously described whole-body counter technique (8).

RESULTS

The data presented in Fig. 1 represent the average values for the various groups of dogs. The number in each group is given in parenthesis along the abscissa. The amount of iron absorbed into the
The effect of phlebotomy and pH on iron absorption following direct administration of iron into colon and duodenum. Ordinate is expressed as percent of administered dose absorbed into body occurring during first 2 hr calculated by Hallberg's double-isotope technique (open bars) and for iron absorbed over 2-week period calculated using whole-body measurements (solid bars). Groups correspond to data obtained when iron solution administered was pH 2 or pH 6 (when iron was mixed with ileal contents prior to its administration). Left-hand portion of figure shows results of iron absorption studies following administration of iron directly into cecum and right-hand portion shows results after iron administration directly into duodenum in dogs prior to and subsequent to phlebotomy.

The effect of pH on the relative amount of iron absorbed during the rapid phase of intestinal iron absorption as opposed to the slow phase is best appreciated by examination of the results of iron absorption from the colon following phlebotomy. In such dogs when the pH of the iron administered was low (pH 2), colonic absorption of iron occurred essentially entirely during the initial 2-hr period. When the pH was raised to 6 by buffering with distal ileal contents, approximately two thirds of the iron was buffered with contents of the ileum to pH 6. It therefore appears that a significant portion of the iron absorbed into the body during the "slow phase" of intestinal iron absorption could have occurred from iron contained in the colon. In these animals subsequent to phlebotomy the amount of iron at pH 2 absorbed into the body in 2 weeks following administration into the duodenum was markedly increased to 30.8% of which 24.0% appeared in the plasma during the initial 2-hr period. Thus approximately 6.8% was absorbed during the "slow phase." It is noteworthy that these animals absorbed 15.7% of the administered dose from the colon when the administered dose was at pH 2 and 13.9% when the administered dose was at pH 6. At pH 2 essentially all of the colonic absorption of iron occurred during the rapid phase of iron absorption but at pH 6 only 4.3% or approximately one third of the iron absorbed from the colon occurred during the rapid phase, the remaining two thirds occurring during the slow phase of intestinal iron absorption.

DISCUSSION

That intestinal absorption of iron is increased following phlebotomy is well known, and it was not surprising to find that when the iron was administered into the duodenum following phlebotomy a significantly larger fraction was absorbed into the body compared to that measured prior to phlebotomy. However, the finding of markedly increased colonic absorption of iron following phlebotomy was not anticipated from presently available information. While phlebotomy resulted in a threefold increase in the amount of iron absorbed into the body when it was administered into the duodenum, such phlebotomy resulted in a seven- to tenfold increase in the amount of iron absorbed from the colon. Indeed the amount of iron absorbed from the colon when it was buffered with distal ileal contents (pH 6) was greater than the amount of iron absorbed into the body of these same dogs prior to phlebotomy when it was administered directly into the duodenum (13.9% as compared to 11.3%).
absorbed into the body occurred subsequent to the first 2 hr and only one third occurred during the first 2 hr of the study.

It appears from these results that colonic absorption of iron may be a significant component of the slow phase of intestinal iron absorption, provided that the incubation of iron with ileal contents simulates changes in the form of iron which may occur as it passes through the upper intestinal tract. Perhaps a valid analysis of the "phases" of intestinal iron absorption would be to view the processes not as occurring in different anatomical sites but as the same processes dependent only upon the pH in the immediate vicinity of the iron. Thus when iron is initially present in the lumen of the upper small bowel at low pH, it is quite soluble, and rapid absorption of iron occurs. As the iron bolus passes into the distal small bowel, the pH progressively increases associated with a decreasing solubility of the iron. The iron retained in the mucosa of the upper small bowel appears to be within intracellular spaces in which the pH approximates neutrality. The slow phase of iron absorption can be thought of as occurring from relatively insoluble iron located in all sites in which the pH is relatively high such as within the intracellular spaces of the duodenal and jejunal mucosa and in the luminal contents of the colon.

SUMMARY

Colonic absorption of iron in dogs may be of sufficient magnitude to account for a large component of the iron absorbed during the slow phase (after the first 2 hr following administration) of intestinal iron absorption. In the present experiments phlebotomy resulted in a threefold increase in iron absorption when the iron was administered directly into the duodenum whereas it caused a seven- to tenfold increase in colonic absorption when the iron was administered directly into the colon. Following phlebotomy when the pH of the iron introduced into the colon was low (pH 2), essentially all of the iron absorbed into the body occurred within the first 2 hr. When the pH was elevated (pH 6), only a third of the iron absorbed from the colon into the body occurred during the first 2 hr, the remaining two thirds being absorbed subsequent to this time. It is suggested that the rapid or slow phase of intestinal iron absorption may be thought of as related to the relative pH of the iron at the time iron absorption is occurring rather than with regard to location in specific anatomical sites. The significant colonic absorption of iron following phlebotomy in the present experiments suggests the possible use of colonic iron administration in the treatment of iron deficiency secondary to blood loss.

REFERENCES