The Significance of Transferrin for Intestinal Iron Absorption

By Helmut A. Huebers, Eiko Huebers, Eva Csiba, Walter Rummel, and Clement A. Finch

A mechanism is proposed by which apotransferrin is secreted from mucosal cells, loaded with iron in the intestinal lumen, and then the intact complex is taken into the cell. Within the cell, iron is released and transferred to the blood stream, whereas iron-free transferrin returns to the brush border to be recycled. We have investigated this hypothesis by measuring intestinal absorption of radioiron and \(^{125}\text{I}\)-labeled plasma transferrin using tied-off gut segments in normal and iron-deficient rats. There was no absorption of diferric transferrin from the ileum, but high absorption from the duodenum and jejunum segments. Jejunal absorption occurred as a function of the dose offered and showed saturation kinetics. In normal animals, 4 \(\mu\)g of the 50 \(\mu\)g of transferrin iron was absorbed over 1 hr. In iron-deficient animals, mean values reach as high as 13 \(\mu\)g in the blood stream whereas iron-free transferrin returns to the mucosal lumen and then the intact complex is taken into the cell. Within the cell, iron is released and transferred to the blood stream, whereas iron-free transferrin returns to the brush border to be recycled. We have investigated this hypothesis by measuring intestinal absorption of radioiron and \(^{125}\text{I}\)-labeled plasma transferrin using tied-off gut segments in normal and iron-deficient rats. There was no absorption of diferric transferrin from the ileum, but high absorption from the duodenum and jejunum segments. Jejunal absorption occurred as a function of the dose offered and showed saturation kinetics. In normal animals, 4 \(\mu\)g of the 50 \(\mu\)g of transferrin iron was absorbed over 1 hr. In iron-deficient animals, mean values reach as high as 13 \(\mu\)g.

**SUBCELLULAR FRACTIONATION**

Studies during absorption of ferric iron revealed the involvement of two iron-binding proteins in the intestinal mucosa of rats. They have been isolated and characterized as mucosal ferritin and transferrin. The amount of mucosal transferrin increases in iron deficiency, whereas the amount of mucosal ferritin is reduced. A parallel observation has been the involvement of two iron-binding proteins in the intestine. This factor has been called "elutable factor" because it can be washed away. Furthermore, it can be transferred from one rat to another. When the elutable factor is washed off the absorptive cell surface by perfusion, iron absorption decreases. Readdition of the elutable factor restores iron absorption almost to normal. The possibility has been raised that transferrin itself might be this elutable factor. In an attempt to substantiate this, the absorptive behavior of iron bound to plasma transferrin was compared with a variety of other chemical forms of iron.

**MATERIALS AND METHODS**

**Isotopes and Chemicals**

The radioiron (\(^{59}\text{Fe}\)) was purchased from New England Nuclear, Boston, Mass., as ferrous sulfate, specific activity 13-22 \(\mu\)Ci/\(\mu\)g of iron, dissolved in 0.5 \(M\) HCl (1 Ci = 3.7 \(\times\) 10\(^{10}\) becquerels). Radioiodine (\(^{125}\text{I}\)) for protein iodination was a product of Amersham Arlington Heights, Ill. (\(^{125}\text{I}\) as sodium iodide, specific activity 13-17 \(\mu\)Ci/\(\mu\)g of iodine).

Ferrous ammonium sulfate, \((\text{NH}_4)_2\text{Fe(SO}_4\text{)}_2 \times 6 \text{H}_2\text{O},\) and ferric ammonium sulfate, \(\text{NH}_4\text{Fe(SO}_4\text{)}_2 \times 12 \text{H}_2\text{O,}\) were purchased from Baker Chemical Company, Phillipsburg, N. Y. Rat plasma transferrin was isolated from iron-saturated rat plasma. Human lactoferrin was a gift from P. Masson (University of Leuven, Belgium). Human serum albumin was purchased from Sigma Chemical Company, St. Louis, Mo. The preparation of \(^{59}\text{Fe}\)-tagged rat liver ferritin was based on the method of Huebers et al.

Tagging of these proteins with radioiron was accomplished as described earlier. Tagging with radiiodine was carried out on the purified proteins according to the procedure of McFarlane, followed by extensive dialysis against buffered saline.

The radioactivity of \(^{59}\text{Fe}\) and \(^{125}\text{I}\) was measured simultaneously in a scintillation spectrometer (Packard, Model 5330, Packard Instrument Co., Inc., Downers Grove, Ill.) with proper correction (of about 12%) for the \(^{59}\text{Fe}\) cross-count into the \(^{125}\text{I}\) channel.

**Animals**

Male Sprague-Dawley rats, 8-12 wk of age weighing 200-30 g, were employed. They were on a standard Purina chow diet containing 350 mg of iron/kg. In order to produce iron deficiency, rats were placed on a low-iron diet at the age of 6 wk and periodically bled to accelerate iron depletion. Iron overload was produced by placing animals on a high iron diet containing 1% of iron as ferrous sulfate. Within about 2 wk, these animals usually had a transferrin saturation of over 70%. Before evaluation of intestinal absorption, the animals were fasted overnight but access to water was maintained.

**Gut Loop Technique**

A standardized method of measuring absorption has been developed. Animals were anesthetized with ether and the abdomen opened by a 3-4 cm cut along the linea alba. Twenty centimeters of...
upper jejunum or ileum, or in some studies a 5-cm segment of duodenum, was isolated. One end was ligated and the other was ligated after a solution of ionized iron alone at pH 2.0 or stabilized with various proteins at pH 7.4 had been introduced. The amount of iron employed in a volume of 0.5-1.5 ml varied from 4 to 50 μg; the amount of protein varied from 3 to 36 mg. Labeling was achieved by "Fe (0.2-1 μCi) and 125I (0.2-2 μCi). The wound was then closed by clips and the animal kept in a temperature-controlled environment until sacrificed 10-60 minutes later.

At that time, 7-8 ml blood was removed through the abdominal aorta. Blood samples were immediately placed on ice and centrifuged at 4°C. Meanwhile, the animal was exchange transfused with 2-3 blood volumes of a 0.9% saline warmed up to 37°C. The tied-off gut segment, the liver, femurs, kidneys, and spleen were removed for determination of radioactivity in an automatic gamma counter (Packard, Model 5330). Isotope radioactivity in the red cells and in the plasma was also determined.

Results were expressed as (1) total uptake, i.e., activity found in the washed out gut segment and carcass; (2) gut uptake, i.e., activity present in the washed gut segment; and (3) carcass uptake, i.e., radioactivity found in the carcass after the gut had been removed. Absorption was considered to be identical with carcass activity. Gut activity was not included since it represented adsorbed iron as well as intracellular iron that might later be lost in the feces.

Mucosal Analysis

The gut loop, removed from the animal, was opened and perfused with 50 ml ice-cold saline. Radioactivity of the washed gut loop was determined and the mucosa was scraped off with a glass slide. After addition of 10 parts (v/w) 0.9% saline, a mucosal homogenate was prepared using a glass Teflon homogenizer. From this homogenate, a nonparticulate fraction was obtained by centrifugation at 100,000 g for 1 hr (Spinco L50, Beckman Instruments, Palo Alto, Calif.). The distribution of the radiouclide between the particulate and nonparticulate fraction was determined. Analysis of the tagged components in the nonparticulate fraction was done using gel chromatography on Sephadryl S200 and on Sephadex G-50. Electrophoretic separations were carried out by electrophoresis on polyacrylamide and by isoelectric focusing. If necessary, the samples were concentrated by ultrafiltration (Amicon ultrafiltration cell 8MC, PM 10 filter, Amicon Corporation, Lexington, Mass.).

Iron and Protein Determinations

Plasma iron was determined according to a scaled-down procedure requiring only 0.3-0.5 ml plasma but was carried out otherwise as described by the International Standardization Committee.

Total iron-binding capacity was performed by the method of Cook et al. Reticulocyte counts were carried out employing brilliant cresyl blue for staining and the number of reticulocytes in 1000 red cells was determined. Hematocrits were determined by the microhematocrit technique and hemoglobin by the cyanmethemoglobin method. The ferritin iron concentration was determined after overnight incubation in 3N HCl and 37°C, using the colorimetric method referred to above.

Protein determination was carried out using the Bio-Rad Protein Assay kit (Bio-Rad Laboratories, Richmond, Calif.) with bovine plasma gamma globulin and/or bovine plasma albumin (BSA) as standards.

Statistics were carried out according to standard methods. Data were analyzed with the Student's unpaired t-test. Significance was assumed at p < 0.05.

The variations of multiple determinations were expressed as ± 1 SD.

RESULTS

Measurement of the Absorption of Various Chemical Forms of Iron

Results of the absorption of iron from various chemical forms injected into jejunal segments of normal and iron-deficient rats after a 1-hr absorption period are depicted in Table I. If given to normal animals as a 20-μg dose of ionized iron (pH 2.0), the absorption of the ferrous form was considerably more than that of ferric salts (2.7 versus 4.7 μg, p < 0.05). Similar differences for both forms of iron were observed in the mucosal uptake (5.0 versus 9.7 μg, p < 0.01). In the iron-deficient group, iron absorption was increased over that of normal animals, and no difference was observed relating to the valency of iron. Increasing the ferric iron dose to 28 μg did not enhance iron absorption, but nearly tripled mucosal activity in normals and doubled it in iron-deficient animals. Iron adsorbed to the intestinal mucosa was not distinguished from intracellular iron.

In a second study, iron bound to various proteins in the ferric form was injected at neutral pH. Very low absorption resulted from lactoferrin, with no increase

<table>
<thead>
<tr>
<th>Chemical Form</th>
<th>pH</th>
<th>Dose</th>
<th>Iron Uptake (μg)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Normal Rats</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Carcass</td>
</tr>
<tr>
<td>Fe²⁺</td>
<td>2.0</td>
<td>0.2</td>
<td>4.7 ± 0.9</td>
</tr>
<tr>
<td>Fe³⁺</td>
<td>2.0</td>
<td>0.2</td>
<td>2.7 ± 0.3</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>7.4</td>
<td>5</td>
<td>0.03 ± 0.01</td>
</tr>
<tr>
<td>Ferritin</td>
<td>7.4</td>
<td>5</td>
<td>1.8 ± 0.2</td>
</tr>
<tr>
<td>Transferin</td>
<td>7.4</td>
<td>0.2</td>
<td>4.0 ± 0.6</td>
</tr>
<tr>
<td>Fe²⁺ plus Albumin</td>
<td>7.4</td>
<td>0.2</td>
<td>3.5 ± 0.6</td>
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</table>

*Mean values ± 1 SD, n = 6-8.
in the presence of iron deficiency. The low absorption from ferritin also showed no increase with iron deficiency. In contrast, iron absorption from transferrin had the expected inverse relationship to the iron status of the experimental animal and was at least as efficiently absorbed as ionized forms of iron injected at pH 2. A similar response was seen when ferric iron was kept in solution in a complex with albumin. However, the increment with iron-deficient rats was less marked than that seen with transferrin iron. The amount of iron taken up in the gut wall was usually lower when iron bound to protein was injected (Table 1).

The dose dependence of the intestinal absorption of the iron and protein part of the transferrin molecule was assessed using a dually labeled (\(^{59}\)Fe and \(^{125}\)I) diferric rat plasma transferrin (Fig. 1). The amount of iron absorbed in 1 hr was found to be concentration dependent and gave a curve with saturation characteristics for both normal and iron-deficient rats (Fig. 1A). At higher iron concentrations, about three times as much iron was absorbed by the iron-deficient group. The dose dependence in the washed gut loop at the termination of the experiment, however, showed a linear relationship to the amount of luminal iron. In contradistinction to the amount taken up into the carcass (absorption), the amount in gut segments of normal rats was approximately twice as high as that found for iron-deficient animals.

The accumulation of \(^{125}\)I originally bound to transferrin in the gut wall was less than the corresponding values for iron and did not show significant differences between normal and iron-deficient rats (Fig. 1B). Some of the \(^{125}\)I was found in the carcass. In normal animals, this cumulative activity amounted to 8% and 12% of uptake in the duodenum and jejunal mucosa, respectively, while in iron-deficient animals it amounted to 7% and 13%. However, virtually all of the absorbed \(^{125}\)I radioactivity was found in the small molecular fraction in the plasma, presumably reflecting catabolism of transferrin in the mucosal cell.

The ability of different portions of the small intestine to absorb transferrin-bound iron was tested with a saturating dose of \(^{59}\)Fe and \(^{125}\)I diferric transferrin (50 \(\mu\)g Fe, 36 mg protein). After the 1-hr absorption period, iron absorption in normal rats was highest in the duodenum (10.2 \(\mu\)g Fe) followed by the jejunum (3.9 \(\mu\)g Fe) (Table 2). Virtually no absorption of iron could be demonstrated when the transferrin dose was injected in segments of the distal ileum. In iron-deficient animals, there was an overall increase in absorption and the increment over normal absorption was most pronounced in the jejunum.

The apparent protein absorption (measured by \(^{125}\)I radioactivity) was highest for the jejunum, followed by the duodenum and the ileum. In contradistinction to iron, the absorption of the protein part of the transferrin from ileal segments could be easily documented (Table 2).

For studying the kinetics of iron absorption from the

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{The dose dependence of intestinal iron and protein uptake from \(^{59}\)Fe-\(^{125}\)I-tagged transferrin in normal and iron-deficient rats. (A) The injection of \(^{59}\)Fe-\(^{125}\)I-tagged test dose (4-48 \(\mu\)g Fe, 3-34 mg protein) was injected into tied-off jejunal segments (20-22 cm) of rats weighing about 200 g. After 60 min, the animals were sacrificed and radioiron and radioiodine in the gut segment ("gut") and in the carcass ("absorption") were determined and expressed in micrograms of iron (A) and milligrams of transferrin (B) per rat. Mean values ± SD: n = 6. Open circles: iron deficient rats; solid circles: normal rats.}
\end{figure}

\begin{table}
\centering
\caption{Intestinal Iron Absorption in Different Parts of the Small Intestine in Normal and Iron-Deficient Rats (Dose: 50 \(\mu\)g iron as \(^{59}\)Fe-\(^{125}\)I-Transferrin)*}
\begin{tabular}{llllllll}
\hline
 & \multicolumn{3}{c}{Normal Rats (n = 6)} & \multicolumn{3}{c}{Iron-Deficient Rats (n = 6)} \\
 & Carcass & Gut & Total & Carcass & Gut & Total \\
\hline
Uptake in \(\mu\)g Fe & & & & & & & \\
\(^{59}\)Fe & & & & & & & \\
Duodenum & 10.2 ± 0.8 & 2.4 ± 0.2 & 12.6 ± 0.7 & 15.8 ± 1.0 & 2.3 ± 0.5 & 18.0 ± 1.2 & \\
Jejunum & 3.9 ± 1.1 & 5.6 ± 0.8 & 9.5 ± 0.8 & 12.9 ± 2.2 & 6.9 ± 1.4 & 19.8 ± 3.3 & \\
ileum & ≤0.01 & 0.34 ± 0.06 & 0.34 ± 0.06 & ≤0.01 & 0.34 ± 0.12 & 0.34 ± 0.12 & \\
\hline
Uptake in mg Transferrin & & & & & & & \\
\(^{125}\)I & & & & & & & \\
Duodenum & 2.1 ± 0.3 & 1.2 ± 0.1 & 3.3 ± 0.3 & 2.0 ± 0.1 & 1.6 ± 0.5 & 3.6 ± 0.4 & \\
Jejunum & 3.2 ± 0.7 & 2.1 ± 0.6 & 5.3 ± 0.3 & 3.4 ± 0.5 & 1.6 ± 0.5 & 5.1 ± 0.5 & \\
ileum & 0.9 ± 0.2 & 0.4 ± 0.04 & 1.3 ± 0.1 & 0.7 ± 0.2 & 0.4 ± 0.1 & 1.1 ± 0.2 & \\
\hline
\end{tabular}
\footnote{Mean values ± SD, n = 6.}
\end{table}
iron bound to transferrin and for the determination of
the amount bound by the mucosal tissue at different
intervals during the absorption test, a dose of 50 µg
iron (36 mg transferrin) as diferric transferrin was
injected into jejunal segments. After a lag phase of
about 10 min, iron absorption proceeded in a linear
fashion up to 1 hr (Fig. 2A). Similar behavior was
found for the apparent protein absorption (Fig. 2B). In
contrast, gut activity of 59Fe and 125I leveled off 30 min
after the injection of the test dose.

The addition of 5 and 20 mg of human serum
albumin to the dually-tagged 59Fe-125I-transferrin dose
did not affect the absorption of the iron or the protein
part of the transferrin molecule. A slight increase in
mucosal activity for both isotopes, however, was
noticeable after the addition of 20 mg human serum
albumin (Table 3).

**Molecular Changes in the Absorption of Transferrin**

Experiments were conducted to follow and quanti-
tate changes in the chemical properties of the radioiso-
topes used to tag the transferrin during its intestinal
absorption. For this purpose, 59Fe-125I-transferrin (28
µg Fe, 20 mg protein) was injected in tied-off jejunal
segments of normal and iron-deficient rats. After a
1-hr absorption period, the animal was sacrificed and
iron and protein absorption quantitated (data in Table
1 and Fig. 2). Samples of blood, jejunal fluid and
jejunal mucosa were collected and processed for sepa-
ration on gel chromatography and isoelectric focusing.
The nonparticulate fraction (100,000 g supernatant)
of mucosal homogenate contained 56% ± 8% (n = 12)
of the total 59Fe activity and 72% ± 6% (n = 12) of the
125I activity. There was no apparent difference between
normal and iron-deficient rats.

Chromatography on Sephadex G50 revealed that the
59Fe activity was found exclusively at the void
volume peak, whereas for 125I in the iron-deficient
group (Fig. 3D), a small percentage of radioactivity
was detected at low molecular weight material.
Further separation of the void volume peak by isoelec-
tric focusing showed differences between normal and
iron-deficient animals (inserts in Fig. 3). In normal
rats, the bulk of the 59Fe radioactivity was bound by
mucosal ferritin (arrow in Fig. 3A) whereas this peak
was not prominent in the iron-deficient group (Fig.
3B). In this state, most of the radioiron was present in
the same position as the 59Fe-tagged rat diferric trans-
ferrin, which consisted of slow (s) and fast (f) isotrans-
ferrins (as indicated in Fig. 3). By comparison with the
injected material, both in normal and in iron-deficient
animals, 125I radioactivity could be detected at the
position of the (s) and (f) species, indicating the
integrity of the transferrin found in the nonparticulate

<table>
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<th>Table 3. The Intestinal Absorption of Iron Bound to Transferrin: Effect of the Addition of Albumin (HSA)*</th>
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<tr>
<td>Iron-Deficient Rats</td>
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<tr>
<td>Jejunal Loop: 60 min.</td>
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<tr>
<td>Dose 18 µg Fe = 12.9 mg Tf</td>
</tr>
<tr>
<td>(A) Control</td>
</tr>
<tr>
<td>(B) Plus 5 mg HSA</td>
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<tr>
<td>(C) Plus 20 mg HSA</td>
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</table>

*Mean values ± 1 SD, n = 6.
fraction of the mucosal cell homogenate. The broad peak of $^{125}$I activity with higher isoelectric point (Fig. 3 C and D) was identified to contain the respective $^{125}$I-apotransferrin species of rat transferrin.

Analysis of the plasma activity of $^{59}$Fe and $^{125}$I was carried out on Sephadex G50. All of the $^{59}$Fe eluted at the void volume was shown to be transferrin bound by isoelectric focusing (Fig. 4). The $^{125}$I radioactivity in the plasma was almost completely associated with a low molecular weight fraction derived from the $^{59}$Fe-$^{125}$I-tagged transferrin (Fig. 4).

The residual activity of $^{59}$Fe-$^{125}$I-transferrin remaining in the lumen of the gut loop at the end of the 1-hr absorption period was excluded from the Sephadex G50 column (Fig. 5) and was shown to consist of a mixture of unchanged $^{59}$Fe-$^{125}$I-transferrin as well as $^{125}$I-apotransferrin by isoelectric focusing (insert, Fig. 5B).

For comparison, $^{59}$Fe bound to $^{125}$I human serum albumin (23 µg iron, 20 mg protein) and $^{125}$I-apotransferrin (20 mg protein) was subjected to the same absorption and analytical tests as outlined before for the $^{125}$I-$^{59}$Fe-transferrin. It was found that within the 1-hr absorption period, most of the $^{125}$I-tagged albumin appeared in low molecular weight fragments (Fig. 6B). The radioiron was found in two peaks, the first being identified as to contain small amounts of transferrin iron and apparently high molecular weight aggregates of $^{59}$Fe-(FeOH)$_3$ with albumin (Fig. 6A). The lower molecular weight radioiron peak has not yet been identified. In contrast to the findings with albumin, the gel chromatographic pattern of the gut eluate obtained 1 hr after the injection of apotransferrin showed only
These studies were carried out in the rat. Iron was administered in a tied-off jejunal, duodenal, or ileal loop in situ with intact blood supply. This technique permits standardization of luminal conditions and differentiation between mucosal uptake and transfer with a precision not usually achieved when iron is administered orally by a stomach tube. In earlier publications, it was shown that there is no significant difference in the overall absorption between iron administered in tied-off jejunal loops and iron administered by stomach tube.23,24

The absorption of inorganic iron is affected by its solubility within the intestinal lumen. Thus, it is to be expected that a low pH would be required for absorption of ferric iron.23,24 When a dose of 20 μg Fe¹⁴ was given to normal rats at pH 2.0, absorption was still considerably lower than that of ferrous salts, presumably because the increase in pH in situ converts the ferric iron more rapidly to nonabsorbable ferric hydroxide and/or its polymers (Table 1). To overcome

DISCUSSION

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these solubility problems common for both forms of inorganic iron, low molecular chelates have been employed to prevent precipitation. These chelates include citric acid, ascorbic acid, amino acids, and others.23 A high molecular excess of the ligand must be employed if there is to be stability of the soluble iron chelate at pH values around 7.23,24 Unfortunately, this gain in stability is compromised by a relatively poor availability for iron absorption.

The binding of iron to high molecular weight compounds (transferrin, albumin, lactoferrin, and ferritin) has proved effective in preventing precipitation of iron at pH 7.4. The molar ratios (iron/protein) were about twofold for transferrin, albumin, and lactoferrin and much higher for ferritin. Iron absorption from transferrin and albumin were both high and increased in the presence of iron deficiency, whereas the absorption of iron bound to ferritin and lactoferrin was low and showed no such effect (Table 1). A low absorption of ferritin iron is not surprising in view of previous studies.20 The ineffectiveness of lactoferrin as a vehicle for iron absorption is contrary to the suggestion of Cox and Peters,29 but consistent with other reports.30-32 We conclude that either iron bound to transferrin or albumin would be satisfactory for stabilizing iron within the intestine without compromising the absorptive availability for iron reported for low molecular iron chelators,23,24 although the effect of albumin seems to be time limited because of rapid proteolytic degradation in the gut lumen. This was not observed for the iron-transferrin complex (Fig. 6).

We have demonstrated in these studies that large quantities of unchanged transferrin were present in mucosal cell homogenates and to a small degree in the blood after iron bound to transferrin was placed in a jejunal loop. While the nature of the uptake process has not been defined, it may well be similar to that observed during endocytosis of transferrin by erythroid cells.33 The amount of iron absorbed from transferrin (4 μg/hr) from a small jejunal loop of normal rats is on a daily basis approximately two-thirds that required for normal absorption.34

A transferrin analog had been previously isolated from the mucosa or lumen in the upper intestine.34 It was found to be very similar to serum transferrin in its chemical characteristics but showed slight differences in amino acid composition and its isoelectric point. The highly significant increase in the amount of mucosal transferrin and the virtual absence of the iron storage protein mucosal ferritin in iron deficiency led to the concept that mucosal transferrin exerts a regulatory role in iron absorption as a function of its amount present within the mucosa and in the gut fluid.3,5,9,18,35

The source of the mucosal transferrin is still under debate. The suggestion by Isobe et al. that it may be stored or secreted by goblet cells may or may not be artifactual.36 Another possibility is that the protein is synthesized by mucosal cells or secreted by the liver in bile. Increased amounts of transferrin have been found in the bile of iron-deficient animals (B. Josephson et al., unpublished). Irrespective of the site of synthesis, the data of this study in combination with earlier observations1,5,9,18,35 allow us to propose a new model for intestinal iron absorption, where a similar functional behavior of mucosal transferrin and purified serum transferrin as employed in these studies is assumed (Fig. 7). Apotransferrin present in the luminal secretions from the intestinal mucosa reacts with food iron to form transferrin. After uptake of the transferrin iron complex and iron release, iron-depleted transferrin is returned in an intact form into the intestinal lumen. The resistance of transferrin and apotransferrin to proteolytic enzymes permits their functioning within the lumen. If quantitative aspects of the transferrin absorptive process are to be defined in more detail, it will be necessary not only to define the amount of mucosal transferrin, but also its rate of transit.

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The significance of transferrin for intestinal iron absorption

HA Huebers, E Huebers, E Csiba, W Rummel and CA Finch