Iron Requirements in Infancy and Childhood

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A critical characteristic of iron nutrition in infancy, as compared to adults, is the greater dependency of the infant on external sources of iron for daily red cell production. Dallman et al. (1) have calculated that in a 1-year-old, 10-kg infant, dietary iron must provide 30% of the needs for hemoglobin iron turnover as compared to only 5% in the adult male (Table 1). This imposes disproportionate requirements of iron to the infant. In addition, infants may (a) consume diets with a low iron content or poor iron availability; (b) be born with decreased iron reserves, as is the case with premature infants; (c) grow too rapidly and have excessive demands; or (d) have increased iron losses. The sum of these factors explains the high occurrence of iron deficiency observed at this age.

The main factors determining iron requirements in infants and children are the iron endowment at birth, the requirements for growth, and the need to replace losses.

IRON ENDOWMENT AT BIRTH

The human fetus has been described as a good parasite with respect to iron nutrition. Most studies, based either on the measurement of ferritin in the newborn (2,3) or the later development of anemia (4,5), suggest that iron status at birth is little dependent on the iron nutrition status of the mother. It is only under the most unusual circumstances of severe iron deficiency in the mother that the iron endow-

| TABLE 1. Greater dependence on dietary iron in the infant compared to the adult male*
<table>
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<tr>
<td></td>
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<tr>
<td>Hemoglobin iron (mg)</td>
</tr>
<tr>
<td>In circulation</td>
</tr>
<tr>
<td>Turnover/day</td>
</tr>
<tr>
<td>Dietary iron</td>
</tr>
<tr>
<td>Assimilated/day (mg)</td>
</tr>
<tr>
<td>Hgb iron turnover (%)</td>
</tr>
<tr>
<td>1-year-old infant (Wt: 10 kg)</td>
</tr>
<tr>
<td>270.0</td>
</tr>
<tr>
<td>2.3</td>
</tr>
<tr>
<td>0.7</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>Adult male (Wt: 70 kg)</td>
</tr>
<tr>
<td>2.200</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
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</tbody>
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*From Dallman et al. (1).
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ment of the newborn may be affected (6). It must be remembered, however, that severe maternal iron deficiency can be associated with intrauterine growth retardation or premature delivery, thus indirectly affecting the iron reserves of the newborn (6,7).

Chemical analysis of fetuses and stillborn term infants have shown a linear relationship between body weight and total body iron, so that premature and term infants have an average of 75 mg/kg iron at birth (8) (Fig. 1). An important feature about the distribution of this iron is that about 75% of it is in circulating hemoglobin, constituting a true iron reserve due to the fact that hemoglobin concentration is much higher in the newborn than later in infancy. Thus fetal bleeding during delivery or bleeding during the postnatal period will have a marked effect on iron reserves and on subsequent susceptibility to development of iron deficiency.

Requirements for Growth

Calculations of iron requirements for growth are based on estimations of total body iron of normal infants and children at different ages. Growth is maximum during the first year of life when a term infant triples his birth weight. However, not all iron compartments increase their size proportionally during this period. As already mentioned, the physiologic fall in hemoglobin concentration in the first 2 months of life and the redistribution of this iron to storage compartments is of great significance. Iron stores, however, become depleted at about 4 months of age in term infants and at 2 to 3 months in preterm infants. At this time the infant becomes dependent on external iron sources for maintenance of an adequate iron nutrition status. These different postnatal stages of iron balance and erythropoiesis are depicted in Fig. 2 (1).

Based on existing data on the iron content of various tissues, blood volume, and weight of organs, calculations can be made of the total body iron content and the

![Graph](image-url)
iron present in various compartments at different ages. An example of such calculations made by Smith and Rios (9) is shown in Fig. 3. Although these estimations may be subject to some error, they provide a solid basis for calculating requirements for growth (Table 2). The main source of uncertainty in these calculations lies in the definition of a normal or optimal level of iron stores at different ages. The error introduced in the final results, however, may be of relatively little importance since the size of the main iron compartment, circulating hemoglobin, can be accurately calculated from existing data. Mean requirements of absorbed iron for growth calculated in this manner are about 0.4 mg/day from 0 to 12 months of age. Requirements are higher in the second semester (6–12 months), when the infant needs about 0.53 mg/day of iron for growth (Table 3). Growth rate decreases after the first year of life, resulting in decreased requirements for growth of 0.29 mg/day between 1 and 2 years and 0.23 mg/day between 2 and 8 years of age.

Adolescence is another critical period in the growth process. During this period there is a rapid expansion of the blood volume and an increase in hemoglobin concentration in boys. The mean iron requirement in an adolescent boy can amount to about 1 mg/day during the year of peak growth (1).

**IRON LOSSES**

Physiologic iron losses in man are small. Studies in adult men have shown mean daily losses of about 0.9 mg (10). Mechanisms for regulating iron excretion are very limited, so that even under extreme circumstances of iron deficiency or iron
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![Bar chart showing distribution of body iron at different ages.](chart.png)

**FIG. 3.** Distribution of body iron at different ages. Values were calculated from data in the literature for body weight and length, organ weight, hemoglobin levels, blood volume, and amount of iron in different tissues. (From Smith and Rios, ref. 9.)

**TABLE 2.** Estimated total body iron content at different ages

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (kg)</th>
<th>Body iron (mg/kg)</th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>3.27</td>
<td>75</td>
<td>245</td>
</tr>
<tr>
<td>6 months</td>
<td>7.85</td>
<td>37</td>
<td>290</td>
</tr>
<tr>
<td>1 year</td>
<td>10.15</td>
<td>38</td>
<td>386</td>
</tr>
<tr>
<td>2 years</td>
<td>12.59</td>
<td>39</td>
<td>491</td>
</tr>
<tr>
<td>8 years</td>
<td>25.30</td>
<td>39</td>
<td>987</td>
</tr>
</tbody>
</table>

*50th percentile values for boys, from data of the National Center for Health Statistics.

*From estimations by Smith and Rios (9).

overload, excretion does not vary more than two- or threefold (10). Most iron is lost in the gut as a consequence of physiological bleeding and cell desquamation (11).

Information on iron losses in infants and children is very limited. Garby et al. (12) measured iron lost in the feces using a radioisotopic method in 3 infants and obtained a mean value of 0.03 mg/kg. Elian et al. (13) determined the apparent blood loss in the feces of 25 normal infants 2 to 17 months of age using $^{51}$Cr-labeled red cells and found a mean value of 0.64 ml/day (range: 0.17–2.5 ml).
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TABLE 3. Estimated requirements of absorbed iron for boys (mg/day)

<table>
<thead>
<tr>
<th>Age:</th>
<th>0–6 months</th>
<th>6–12 months</th>
<th>1–2 years</th>
<th>2–8 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requirements for growth</td>
<td>0.25</td>
<td>0.53</td>
<td>0.29</td>
<td>0.23</td>
</tr>
<tr>
<td>Iron losses</td>
<td>0.24</td>
<td>0.37</td>
<td>0.46</td>
<td>0.56</td>
</tr>
<tr>
<td>Total requirements</td>
<td>0.49</td>
<td>0.90</td>
<td>0.75</td>
<td>0.79</td>
</tr>
</tbody>
</table>

*Calculated from data by Smith and Rios (9).
^Estimated at 0.04 mg/kg from 0–2 years and 0.03 mg/kg from 2–8 years.

This corresponds to approximately 0.25 mg of iron per day. Values of the same order were obtained by Hoag et al. (14) using ⁵⁹Fe-labeled red cells. Smith and Rios (9) estimated mean total iron losses during the first 2 years of life at 0.04 mg/kg, which seems reasonable if one adds to the measured intestinal losses the small amounts lost through the skin and urine.

Physiological iron losses in infancy are frequently dismissed as an unimportant factor in the calculations of iron requirements, when in fact they account for approximately one-half of the iron needs during the first 2 years of life (Table 3). Losses in some cases may be much higher because of the wide variation in the amount of blood lost through the gut by normal infants (13). In addition, iron losses can be increased markedly by such common events as the feeding of fresh cow’s milk to young infants (15,16) or the occurrence of diarrhea (13).

REQUIREMENTS OF ABSORBED IRON

Requirements of absorbed iron can be calculated on the basis of the requirements for growth and the need to replace iron losses. An example based on the previous discussion is shown in Table 3. Requirements of absorbed iron are estimated at approximately 0.5 mg/day from 0 to 6 months of age, 0.9 mg/day from 6 to 12 months, and 0.7 to 0.8 mg/day from 1 to 8 years.

Similar figures have been obtained by others. Schulman (17) estimated the needs of absorbed iron in the first year of life, after stores are depleted, to be 0.8 mg/day. Using a somewhat different method, Fomon (18) estimated these needs at 0.7 mg/day during the first year of life and 0.8 mg/day from 1 to 3 years of age, even though he probably underestimated iron losses.

All of these estimates are mean values. The somewhat higher recommendation by FAO/WHO (19) of 1 mg of absorbed iron throughout infancy and childhood is probably justified due to the considerable individual variation that can occur.

RECOMMENDED IRON INTAKES

Recommended intakes of iron should be those that can meet the needs of absorbed iron. Amounts needed will vary, depending on the bioavailability of the ingested iron. Absorption of food iron in infants and children can be as low as 1 to 2% or as high as 50%, as in the case of breast milk iron. Most existing recommendations
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(20) are based on an estimated 10% absorption of food iron. In 1970, FAO/WHO (19) recognized the importance of animal tissues on food iron availability, estimating a mean iron absorption of 10% when animal tissues represented less than 10% of total calories, and a mean absorption of 20% when they represented more than 25%. In view of more recent information (21), these estimates of food iron availability appear too high and result in low recommended intakes of 5 to 10 mg/day in infants and children. In addition, it is only animal tissue (meat) that has an enhancing effect on nonheme iron absorption; other animal products of importance in pediatric nutrition such as eggs and milk lack this effect.

The Committee on Nutrition of the American Academy of Pediatrics recommends intakes of 1 mg/kg/day for term infants, up to a maximum of 15 mg, and 2 mg/kg/day for low-birth-weight infants (22). Recommendations based on body weight for infants and children have been justifiably questioned (18) on the basis that requirements of absorbed iron are not dependent on body weight.

Based on the detailed calculations of Monsen et al. (21), it can be estimated that infants and children will absorb about 10% of the iron in a good availability diet and about 5% in a poor availability diet. On this basis it would appear that, depending on the quality of the diet, intakes of 10 to 20 mg/day are needed to meet the requirement of 1 mg absorbed iron throughout most of infancy and childhood.

REFERENCES

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DISCUSSION

Dr. Finch: Quantitative studies of placental iron procurement in the rat (American Journal of Clinical Nutrition, in press) have shown the limits of fetal iron supply. Fetuses of iron-deficient mothers were iron-deficient and many died and were resorbed in utero. However, considering that the rat has about 10 fetuses, and extrapolating these results to the one human fetus, it would seem most unlikely that there could be a deficient iron supply to the human fetus despite the most severe maternal iron deficiency.

Dr. Chandra: Dr. Finch, you mentioned fetal resorption, but you didn't tell us about the fetuses in whom the intraterine growth was affected and whether there was higher incidence of congenital malformations among them. Such observations have been made in a number of other nutrient deficiencies.

Dr. Finch: The fetuses that were examined on the 20th day of pregnancy were as anemic and iron-deficient as the mother. The fetuses that were reduced in number were also small. In this current study we do not have information concerning fetal abnormalities, but in a previous report (Teratology 1980;22:329), Shepard et al. did note some defects. It was quite apparent, however, that the imposition of iron deficiency in the rat was far more detrimental to the fetus than to the mother. In the human, because of the difference in levels of iron requirements, it will be the mother who suffers rather than the fetus.

Dr. Chandra: Dr. Stekel, you have mentioned that the requirements of iron might be dependent, among other factors, on the mode of feeding. You have hinted that untreated cow's milk, for example, increases fecal losses of iron and therefore increases the requirements. At a previous conference on this topic, a statement was made that exclusively breast-fed infants have never been shown to have developed iron deficiency. I don't know if such a strong statement can be upheld.

Dr. Stekel: As it will be surely discussed in greater detail during this workshop, there is some evidence that availability of iron from breast milk is higher than that from cow's milk. Still, the relatively low iron concentration in breast milk, even with 100% absorption, is not enough to support indefinitely the iron requirements of the infant. Thus, I think that statement is quite strong and probably relates only to the young healthy term infant during the first 4 to 6 months of age. I think that after this age even the breast-fed infant will require an extra source of iron.

Dr. Fomon: The data of Smith and Rios (1974) [ref. 9, this chapter] presented in your Table 2 and Fig. 3 estimate body iron to be 37 mg/kg at age 6 months and 39 mg/kg at age 8 years. This is an increase in quantity of iron per unit of body weight of 5%. I believe this is too small an increase. Iron in circulating hemoglobin and storage iron are almost certainly greater per unit of fat-free body mass in the 8-year-old than in the 6-month-old and fat-free
body mass comprises a substantially greater percentage of body weight at age 8 years than at age 6 months.

**Dr. Dallman:** Dr. Stekel mentioned two areas that are possibly controversial. The first problem is, what constitutes normal iron reserves for an infant or child? One's first reaction might be to regard the usual circumstance of almost absent iron stores in rapidly growing children as pathological. Yet, we find this in healthy, well-nourished populations of children that only very rarely go on to develop anemia. It therefore seems that rapidly growing children may be considered to have adequate iron nutrition despite the virtual absence of stores.

The other topic deals with the guidelines of Monsen et al. (1978) [ref. 21, *this chapter*] for estimating iron absorption from adult diets on the basis of their meat and ascorbic acid content. Perhaps these values need to be increased for the child in the view of studies that suggest that infants and children absorb a greater percentage of dietary iron than adults.

**Dr. Stekel:** First, a short comment on Dr. Fomon’s intervention. I know that he has made his own calculations for requirements based on estimations of the iron content of the body per kilogram of fat-free body mass at different ages. I really do not know what is the right answer. I do not know of any experimental data that can support either way of making these calculations. I don’t think we have the gold standard, which would be data on total body chemical analysis of children at different ages.

Regarding Dr. Dallman’s comment, I think this is really one of the main problems in trying to determine what are the requirements for growth. We have a fairly good idea of what a normal hemoglobin concentration is, but we have very little idea of what normal iron stores in infants should be. As Dr. Dallman just commented, the fact is that apparently normal infants in affluent countries, being fed what can be considered very good diets, have relatively low iron stores. Whether higher levels would be desirable is not known.

**Dr. Cook:** We should discuss desirable iron stores in the population rather than in the individual. In the individual person, there is no difference of clinical relevance between iron stores of 100 and 1,000 mg; in both cases, there is enough iron to supply the needs of the bone marrow. A desirable level of storage iron in the population should ensure that the vast majority have some iron reserves. In adult women in the United States, estimates of storage iron suggest that if the median store in the population is 300 mg, then maybe 20% have absent stores. Perhaps a desirable level is one at which no more than 10 to 15% of the population have absent stores.

**Dr. Dallman:** Judging from the low serum ferritin values in groups of children that are virtually free of anemia, it seems that iron stores can fall into a lower and narrower range than in women without necessarily having a substantial risk of anemia and the associated physiological consequences.

**Dr. Stekel:** In calculating requirements, I believe that the variation imposed by the normal range of iron losses may be more important than that derived from variations in growth, since most children will grow within a relatively narrow range. I think we need to learn a lot more about what is the normal range of iron losses. This may help explain why requirements in different individuals in a population can differ so much and why 20 to 30% of children who appear to have similar growth and a similar diet will develop iron deficiency anemia. We know very little about iron losses in children; it has been a very neglected area.

**Dr. Dallman:** I would like to ask Dr. Cook or Dr. Hallberg whether the difference between absorption in children and adults is due solely to lower iron reserves in children or whether there may be a difference in gastrointestinal function.

**Dr. Cook:** When extrapolating from adult to childhood absorption levels, one may need to assume higher absorption values for the infant and child. The question is whether differences in absorption between children and adults is due solely to a difference in iron status or whether there is some difference in gastrointestinal function. We have observed in studies of food iron absorption in adults that there is an age-dependent fall-off in absorption over
the range of 20 to 60 years. This observation was first reported with inorganic iron by the Cardiff group and we have confirmed it with both heme and nonheme iron absorption. We are not able to determine why—whether it is a fall-off in mucosal cell function or perhaps related to a change in gastrointestinal secretion. I know of no data that would help sort out whether in the age range of 1 to 20 years there is a similar decline in gastrointestinal function, although I doubt this. I think the major difference in absorption levels between children and adults relates to differences in iron status.

Dr. Stekel: In this respect, Dr. Cook, I notice that in your presentation and in your recent publication on the absorption of iron from soya formulas in infants, you relate results to a reference dose absorption of 60%, which in a way would bear in this discussion. I would like to ask you if you used this figure because you think that infants with iron stores similar to adults absorb more iron or because you think that infants are more iron-deficient than adults.

Dr. Cook: When we select a single figure for the reference dose absorption, we defeat our purpose because the reference does allow an estimate of absorption at all levels of iron status. We should get away from the system of using 40 or 60 or 20% and simply express absorption of the test dose as a ratio of the reference dose. Then everyone can make their own conversions. If I remember correctly, the choice of 60% reference dose in our paper was to reflect that, in general, children are more iron-deficient than adults. This is not, however, a very solid basis for using a reference value of 60% in infants versus 40% in adults.

Dr. Dallman: These issues assume practical importance when recommended allowances for iron are calculated. If one assumes an iron absorption of 10% for infants in the United States, as was done some years ago, estimates of dietary iron needs are probably excessive. I don't have any better percentage to substitute, but I think that the validity of recommended allowances has to be verified whenever possible by experimental data, i.e., by actually determining what intakes of iron in various diets are successful in preventing iron deficient anaemia and the associated handicaps of iron deficiency.

Dr. Stekel: You may be thinking about the kind of figures that one comes up with in these calculations, with the higher values in the range of 20 mg, which is a very high figure. On the other hand, if one considers children living in countries where the diet contains little meat and poor vegetable-iron sources, 20 mg of iron may be necessary to absorb 1 mg, i.e., 5%. Therefore, it is difficult to come up with fixed figures for recommended intakes. One should consider rather the amount that needs to be absorbed and calculate intakes depending on the type of diet available.

Dr. Guesry: I should like to come back to the point raised by Dr. Finch concerning the regulatory mechanisms controlling the passage of iron from the mother to the fetus. In rats, this mechanism does not appear to exist and mothers suffering from iron deficiency give birth to iron-deficient offspring. In humans, however, there is a mechanism which regulates the passage of iron, and iron-deficient mothers give birth to babies with fair iron stores. Could Dr. Finch comment on this mechanism.

Dr. Finch: It is likely that the supply to the fetus is a simple matter of a very large transferrin receptor mass in the placenta which can take up as much as one-third of the plasma iron with which it comes into contact. If we assume that maximum iron requirements of the human fetus are 6 mg/day and assume a cardiac output of 5 liters/min and 10% of this going to the placenta, it is apparent that there would be no difficulty in the fetus obtaining its needed iron even if maternal plasma levels are 5 or 10 mg/100 ml plasma.

Dr. Fomon: I understand that there is a large difference between the rat fetus and the human fetus, and Dr. Finch seems to indicate quite clearly the reasons why the human fetus may be to a large degree protected.

Dr. Finch: I think that the studies that have been carried out are reassuring in terms of the safety that the human fetus appears to have. If a number of fetuses were appreciably
increased, obviously the human would have increased requirements approaching that of the rat. While there may be some point where increasing human requirements due to multiple pregnancies along with a marked restriction in plasma-iron content by the mother would cause a limitation in iron supply, there appears to be a greater margin of safety than we would have suspected.

**Dr. Dallman:** In regard to Dr. Fomon's earlier questions about the reasons for variability in iron stores in newborn infants, there was an interesting recent paper by MacPhail et al. (Scand. J. Haematol. 1980;25:141) showing a reciprocal relationship between hemoglobin concentration and serum ferritin in the newborn. Those infants that had the highest hemoglobin concentration tended to have the lowest serum ferritin and vice versa. The implication of these results was that the amount of iron crossing the placenta to the fetus tended to bear a constant relationship to the fetal weight. However, the distribution of iron in the fetus between stores and hemoglobin seemed to be partly regulated by other factors such as adaptation to altered oxygen availability.

**Dr. Chandra:** We know that iron deficiency is a problem principally of developing countries. I should like to mention another factor, infection, which might complicate any of the calculations that are being discussed. We recognize that the incidence of infection in the maternal-placental-fetal unit in developing countries is very high. Are there any studies that have looked at this question? We should also examine iron absorption in relationship to changes in gut microflora.

**Dr. Hallberg:** It is difficult to establish what is “normal” iron absorption in infants and children from studies made in adults. Infants and children are growing and their iron stores are proportionally less than in adults. If we want to compare the ability of a child and an adult to absorb food iron, we need to use the reference doses and the same level, e.g., 40%. However, to calculate the amount of iron absorbed from a diet by a child, one must take into account the facts of growth and lower iron stores.

**Dr. Finch:** To extend the discussion further, a change in iron requirements has a marked effect on iron stores. The male individual who gives one unit of blood a year has his “normal stores” dropped to half of their initial value. Blood donors who give more frequently may have no anemia, but may have a virtual absence of iron stores. The dynamics of iron balance at higher requirements as you are dealing with in infancy needs to be further examined.