ATTENTION AND IRON DEFICIENCY IN EGYPTIAN SCHOOL CHILDREN

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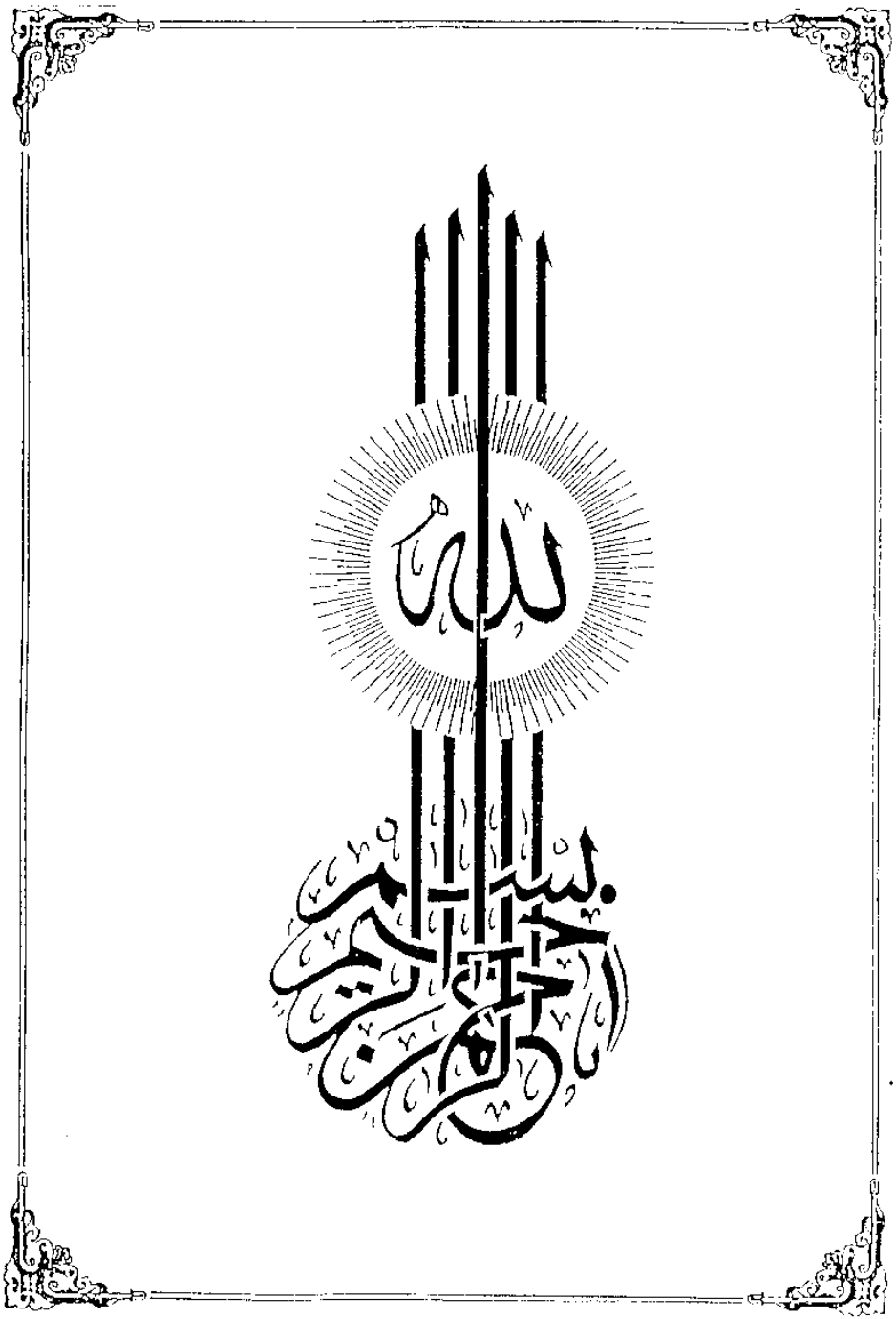
To all our martyrs everywhere,

whom we did not even try to rescue.



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My first word should be (Al Hamdu Lillah), then

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REVIEW OF LITERATURE

Introduction

Iron deficiency is a common problem throughout childhood. During this period the composition of the diet is often unfavorable for iron absorption. This is particularly true for developing countries in which cereals are usually the major constituent of the diet. Economic factors often limit the intake of meat, poultry or fish, foods that would enhance the absorption of iron from cereal. Cultural patterns also frequently favor giving the father and other adults first access to these more expensive foods of animal origin. If unrefined cereal products are used, their high fiber content may also restrict the absorption of iron as well as other trace minerals.

In developed countries the availability of dietary iron is often restricted by an excessive use of milk. Milk, not only displaces other more iron-rich foods from diet, but also is rich in calcium and phosphorus which form insoluble complexes with iron.

In tropical semi-tropical parts of the world where children are often barefooted, infestation is a common problem. Intestinal blood loss can then become a major factor contributing to iron deficiency (Layrisse and Roche, 1964). Pin worm

infestation may also result in substantial blood loss (Layrisse et al., 1967) and is common in temperate climates. In order to prevent iron deficiency in hookworm areas more dietary iron is generally required than elsewhere with acceleration of growth particularly during the years of sexual maturation imposes increased requirements of iron primarily for production of hemoglobin. For example, during the peak years of their adolescent growth spurt body gain, an average of 10 kgm (Tanner et al., 1966), can be calculated to require a net increase of about 300 mg of iron merely to maintain a constant concentration of hemoglobin in an expanding blood volume. However, the concentration of hemoglobin also increases between 0.5 and 1 g/dl/year at this age (Daniel, 1973) (Krabbe et al., 1978) which means more need of iron.

Iron deficiency is the state in which the content of iron in the body is less than normal no matter what is the cause. It occurs in varying degrees of severity which merge imperceptibly into one another. The term iron depletion has been applied to the earliest stage of iron deficiency, in which storage iron is decreased or even absent but serum iron concentration and blood hemoglobin and hematocrit levels are normal (Finch et al., 1968). The designation iron deficiency without anemia describes a somewhat more advanced stage of iron deficiency characterized by decreased or absent storage iron, usually low serum iron concentration and transferrin

saturation, without frank anemia. A still more advanced stage of iron deficiency is termed iron deficiency anemia, which is the third stage and occurs when the production of essential iron compounds including hemoglobin are restricted (Scrimshow, 1984). It is characterized by decreased or absent iron stores, low serum iron concentration low transferrin saturation and low hemoglobin concentration and hematocrit value (Fairbank and Beutler, 1983). Although iron deficiency anemia is a more advanced state of iron deficiency than in iron depletion, yet in certain rare disorders such as pulmonary hemosedrosis or paroxysmal nocturnal hemoglobinuria (Fairbank and Butler, 1983), iron deficiency anemia may occur without iron depletion.

Iron deficiency anemia develops when the transport of iron by transferrin falls short of that required by erythropoetic cells. Red cell production is limited when transferrin saturation falls below about 16 % (Bainton, 1964). Iron is required by all mammalian cells and plays a central role in oxidative energy metabolism, thus iron deficiency sufficient to affect erythropoiesis is preceded by a latent phase during which symptomless biochemical aberrations are measurable. These observations include reduction in serum iron, increase in free erythrocyte protoporphyrin and decrease in tissue heme enzymes. In much of the world iron deficiency is the commonest of all medical ailments, and is second only to protein calorie malnutrition elsewhere (James, 1987).

Status of iron	Characteristics
I. Iron depletion (prelatent iron deficiency (Heinrich, 1970)	- Transferrin saturation normal - Plasma iron normal - Hemoglobin normal - Hematocrit normal - Iron stores are decreased or absent
II. Iron deficiency without anemia latent iron deficiency	- Transferrin saturation decreases - Plasma iron decreases - Hemoglobin normal - Hematocrit normal - Iron stores are absent
III. Iron deficiency anemia	- Transferrin saturation decreases - Plasma iron decreases - Hemoglobin concentration decreases - Hematocrit percent decreases - Iron stores are absent

Hypochromic anemias are disorders in which erythropoietic stem cell kinetics and DNA synthesis are normal but cytoplasmic synthesis of hemoglobin is impaired. Erythroid division and maturation proceed out of synchrony with the lagging synthesis of hemoglobin leading to creation of mature red cells that are deficient in hemoglobin. The mechanisms that coordinate cellular division with hemoglobin accumulation are unclear, but it appears that when the cumulative amount of hemoglobin in mature erythroblasts falls short of about 20 pg/cell an extra division occurs thus hypochromia is generally accompanied by microcytosis: the red cells are pale and small and deficient in homoglobin content (MCH) and in volume (MCV).

Similar-appearing anemias such as thalassemia are sufficiently frequent to warrant care in differential diagnosis. As iron deficiency is exceedingly prevalent, is treatable, and is often the first indication of gastrointestinal bleeding it is important to recognize deficiency early.

CAUSES OF IRON DEFICIENCY

Causes of iron deficiency can be classified under:

I. Decreased intake of iron

II. Malabsorption of iron

III. Blood loss

I. Decreased intake of iron

Iron deficiency ensues when the intake of iron from the diet falls short of physiologic requirements. During infancy dietary deficiency of iron usually results from total dependency on unsupplemented milk, in the first year of life. Infants require about 150 mg of iron in addition to that provided initially by the mother. Premature infants need nearly twice that amount during the first year to keep pace with the expanding erythron and to compensate for their congenital shortage of storage iron. Milk products are poor sources of iron (Burman, 1972) and prolonged feeding with breast milk or bottled milk requires iron supplementation. Iron needs are proportional to growth rates, hence simple dietary inadequance causes iron deficiency most often during the 2 major physiologic spurts in growth rate, infancy and adolescence. The

highest requirement for iron is during infancy and the recommended daily intake during the first year of life is 1.5 mg/kg body weight. During childhood the total body requirement for iron remains steady at 5 to 10 mg daily, but during adolescence dietary iron needs increase several folds. In adultstypical western diets contain about 6 mg of iron per 1000 calories, about 7 % of ingested food iron is assimilated. Thus adult men and women generally absorb about 0.4 to 1.4 mg of iron per day. From a ferrokinetic standpoint the average male adult is in a steady state. To balance losses he assimilates daily about the same amount of iron as is available from his average dietary intake. In men, therefore, the development of iron deficiency is indicative of pathologic iron loss. With rare exceptions, the occurrence of iron deficiency in adult men can be equated with blood loss, and the diagnosis of iron deficiency in an adult man makes as search for the cause of blood loss obligatory. In normal adult men, the loss of iron from sweating, exfoliation of skin and gut cells, and traces of blood loss totals less than 1 mg/day. In normal young adult women iron loss via menstruation averages an additional 1 mg/day. Normal young adult women lose about 3 to 4 times as much as adult men. Pregnancy makes particularly severe demands on a woman's iron status. Each pregnancy involves loss of iron to the fetus (about 270 mg), blood lost during delivery (100-150 mg) plus blood lost in the decidum (50 mg). On the average if prorated over the full 9 month term of pregnancy

the net loss of iron is increased to about 2.5 mg/day. Iron loss to the fetus is greatest during the final trimester when net maternal need exceeds the capability of the intestine to absorb dietary iron (de Leeuw et al., 1966). Consequently, iron supplementation should be a routine prenatal precaution; iron deficiency is so prevalent worldwide, particularly among multiparous women and nutritionally improverished countries or regions, that routine iron fortification of common foods such as bread and cereals is advisable (Vazques-Seoane et al., 1985). The extent to which foods should be enriched with iron is debated but currently in the United States and Great Britain the taken amount of iron added to "Fortify" flour (3.0 mg and 1.6 mg respectively per 100 gm flour) is unlikely to protect women against iron deficiency (AMA Council 1972) (Layrisse and Martinez-Torres, 1971). An increased fortification of staple foods with iron has been recommended (Hablberg, 1982) to compensate for lower consumption of iron rich foods by our increasingly fastidious and diet-absessed society.

II. Malabsorption of iron

Normally iron is absorbed by means of specific mucosal receptors located in the duodenum and upper jejunum (Linder and Munro 1977) (Whiby, 1970). To be absorbed food iron either must

be in the form of heme or must be converted to soluble ferrous salts or chelates. The heme of hemoglobin as steak myoglobin, for example, is hydrolyzed free from the apoprotein by gastric Hcl and intraluminal proteases and then autooxidizes to hemin (ferriheme). Hemin enters upper intestinal mucosal cells intact, after which the iron is released by heme oxygenase for entry into the blood stream bound to transferrin (Weintraub et al., 1968) (Raffin et al., 1974). The efficiency of intestinal absorption of non-heme food iron is subject to numerous intraluminal factors. Most natural dietary iron is aggregated in the ferric state. Factors favoring conversion of ferric food iron to soluble and absorbable ferrous forms include gastric acid reducing agents, and low molecular weight weak chelators (Crosby, 1968). Conversely, compounds that form insoluble complexes with iron such as phosphates and phytate (hexaphosphoinositol), prevent absorption. Ferrous irons are actively transported into mucosal brush border cells by receptor-mediated endocytosis. Depending on the degree of mucosal hunger for iron, the internalized, reoxidized atoms are either transferred directly to intacellular transferrin for delivery to the plasme (Halliday et al., 1976) (Pinkerton, 1969) or incorporated into mucosal ferritin (Sheehan and Frenkel, 1972). If the ferritin iron is not relinquished to transferrin during the brief (3-4 days) lifespan of the deciduous mucosal cell, it is sloughed off within the exfoliated cell (Awad and Wells, 1982). Thus body iron is regulated within narrow limits through modulation of the rate of iron absorption, the mechanisms coordinating iron