Review:
MEDICAL NUTRITION THERAPY IN ANAEMIC INFANTS AND CHILDREN
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Dr. Sandipan Sabde
MBBS, MD, DCH (KEM Hospital Mumbai), ECFMG (USA)
Consultant Neonatologist and Pediatrician
Shwas Paediatric Hospital, Latur 413512

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MEDICAL NUTRITION THERAPY IN ANAEMIC INFANTS AND CHILDREN

Introduction

Iron deficiency anaemia is a leading cause of infant morbidity and mortality worldwide. About two billion people (over 30% of the world's population) are anemic, mainly due to iron deficiency and in developing countries this figure is frequently exacerbated by malaria and worm infections.\(^1\)

Anaemia prevalence in young children is over 70% in most parts of India and Asia regardless of a policy being in place and a program that has been initiated for a long time. Numerous studies have confirmed that even moderate anaemia (hemoglobin \(< 100 \text{ g/L}\)) is related with depressed mental and motor development in children that may not be reversible. Therefore, primary prevention is a more appropriate goal than screening and treatment. Due to the well-documented sequelae of anaemia, there is a continuous necessity to develop strategies and educate caregivers about the prevention and management of iron deficiency anaemia. The irreparable damage that anaemia in childhood can cause particularly to the development of a young child on one hand and the knowledge and mechanism available for its control on the other, makes this silent morbidity completely unacceptable in modern times.\(^2\)

The term ‘nutritional anaemia’ includes all pathological conditions in which the blood hemoglobin concentration goes down to an abnormally low level, due to a deficiency in one or several nutrients. The main nutrients involved in the production of hemoglobin are iron, folic acid, and vitamin B. Iron deficiency is by far the first cause of nutritional anaemia worldwide. Folic acid deficiency is less prevalent and is frequently observed with iron deficiency.

Anaemia, like fever, is a sign and not a disease \textit{per se}. A large portion of iron deficiency is preventable with suitable and timely intervention. It exerts the substantial overall toll in terms of ill health and premature death. The effects of anaemia on children are the most devastating because their bodies are in phase of developing, including the brain, which is the fastest developing organ in infancy and early childhood.\(^2\)

Iron deficiency anaemia can usually be prevented at a low cost, and the benefit/cost ratio of implementing preventive programs is recognized as one of the highest in the realm of public health.\(^5\)

This article reviews in detail the magnitude of child anaemia and the mechanism for its incidence, and elaborates about what needs to be done, what difficulties we face, and how to overcome them, with the primary focus on iron deficiency anaemia (IDA).
Anaemia

Anaemia is the most common indicator used for screening iron deficiency, the terms ‘anaemia,’ ‘iron deficiency,’ and ‘iron deficiency anaemia’ are repeatedly used interchangeably. However, prior to the development of iron deficiency anaemia, there have been mild to moderate forms of iron deficiency, where various cellular functions are impaired. We need to differentiate between, iron deficiency, anaemia, and iron deficiency anaemia, to put each of them in their proper perspective.²

An abnormally low hemoglobin level due to pathological condition(s) is defined as anaemia. Iron deficiency is one of the most common, but not the only cause of anaemia. Other causes of anaemia include chronic infections, particularly malaria, hereditary hemoglobinopathies, and folic acid deficiency. It is worth noting that multiple causes of anaemia can coexist in an individual or in a population and contribute to the severity of the anaemia.²

Iron deficiency

Iron deficiency (ID) is defined by an abnormal iron biochemistry with or without the presence of anaemia. Iron deficiency is usually the result of inadequate bioavailable dietary iron, increased iron requirement during rapid growth, and increased blood loss for any reason. There are no current evaluations of the total ID cases, but it is estimated that most preschool children in developing countries are iron deficit.²

Iron-deficiency anaemia

Reduced immunity is commonly associated with iron-deficiency anaemia. In severe iron-deficiency anaemia, the capacity to maintain body temperature may also be decreased. Severe anaemia is also life-threatening. It is important to realize that anaemia resulting from iron deficiency characterizes a very late stage of iron deficiency.

Table 1. World Health Organization defined criteria for anaemia cut off as measured by the hemoglobin.²
Iron balance

In infants and children, a large amount of iron is essential for growth (i.e., considerably more iron must be absorbed than is lost from the body) e.g., a one-year-old infant loses about 0.2 mg of iron/day, calculated on the basis of body surface area, from values measured in adults. The amount required for growth is roughly 0.6 mg. Around 75% of the 0.8 mg of absorbed iron required per day during this period, is for growth.²

Prevalence of anaemia in Indian children

Childhood anaemia has major adverse consequences for health and development. Its prevalence in India continues to range from 70 to 90%.³

Anaemia has been problematic in India and the National Family Health Survey (NFHS) data showed the prevalence of anaemia among children less than five years of age to be about 70%. This prevalence is among children 6 to 59 months of age, with the highest concentration in that group being in children 6 to 35 months of age. As the data from the NFHS III study advocates, the highest prevalence is among the 6 to 23 months age group.²

A staggering increase in anaemia - lack of iron in the blood - across all ages has been found as per a survey of nine of India's poorest states (Assam, Bihar, Chhattisgarh, Jharkhand, Madhya Pradesh, Odisha, Rajasthan, Uttar Pradesh and Uttarakhand). Among children between 5 and 9 years of age, over 80% are anaemic in 9 states.⁴

Factors that increase the risk of anaemia

Conditions that are typically found when the prevalence of iron deficiency anaemia is high are charted in Table 2.¹

<table>
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<tr>
<th>Condition</th>
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<tr>
<td>Premature birth or intrauterine growth retardation (IUGR)</td>
<td>Low hepatic and bone marrow iron stores at birth</td>
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<tr>
<td>Early cord clamping</td>
<td>Decreased transfer of iron (as hemoglobin) at delivery</td>
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<tr>
<td>Prolonged exclusive breast-feeding</td>
<td>Decreased intake of dietary iron</td>
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<tr>
<td>Inappropriate use of whole cow’s milk</td>
<td>Decreased intake of dietary iron; intestinal blood loss</td>
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<tr>
<td>Timing of introduction and type of complementary food</td>
<td>Decreased availability and/or bioavailability of dietary iron</td>
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<tr>
<td>Frequent infections</td>
<td>Anorexia associated with infection can lead to decreased ingestion of iron-containing foods; infection can decreased erythropoiesis; parasitic infection can cause enteric blood loss</td>
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The amount of Iron present at birth depends on the length of gestational period and the weight of the baby. Human milk (which contains 0.2–0.3 mg/L of iron) does not provide enough iron over the first months of life, to meet the demands of rapid erythropoiesis, so iron stores are mobilized to meet the iron requirements of the infant. Iron stores are generally depleted by 6 months of age, yet from 4 to 12 months after birth the infant’s blood volume doubles. Thus, at this age, dietary sources of iron become critical to keep up with this rapid rate of red blood cell synthesis.

Pathophysiology of anaemia in children under three years of age

At birth, hemoglobin concentrations are generally higher than at any other time of life, due to the adaptation of the fetus to the hypoxic environment of the uterus. Moreover, the neonatal reserves of storage iron are comparatively generous. Therefore, most newborn infants are well supplied with iron. There is almost no change in the total body iron in the term infant between birth and four months of age. Therefore, the need for exogenous iron is modest during this period. The ample iron stores present at birth support to provide for synthesis of hemoglobin, myoglobin, and enzyme iron during the first 4 months. Extra iron from the hemoglobin breakdown is also made available to meet the iron needs because the concentration of hemoglobin declines from a mean of 17.0 g/dl at birth to a low of 11.0 g/dl at two months of age. This low point used to be called the early anaemia of infancy, and was separated from the ‘late anaemia of infancy,’ because it was unresponsive to iron treatment. However, a low birth weight baby would have a smaller amount iron stores and therefore would need additional iron as well as iron at an early age from the diet source.

A gradual shift happens from an abundance of iron to the marginal iron reserves after about four months of age, that characterize the period of continued rapid growth. This phase of vulnerability to iron deficiency is the major focus of concern. A large amount of iron required to maintain a near constant mean hemoglobin concentration of 12.5 g/dl within a rapidly expanding blood volume during 4-12 months. During this period, a large amount of iron, about 0.8 mg/day, must be absorbed from the diet. The rate and extent to which storage iron becomes short can be predictable from the changes in the concentration of serum ferritin and depends both on the magnitude of iron storage at birth and on the postnatal diet.

Mild maternal iron deficiency and anaemia have few significant consequences on the iron status of the newborn, but severe anaemia affects a lot. Prematurely clamped umbilical cord leads to increased risk of an infant developing iron deficiency.

The most common reason for iron-deficiency anaemia in infants and children is the insufficient supply of iron in the diet. The three main reasons for IDA in children are:
• a. Poor bioavailability of iron consumed, related to the low consumption of absorption enhancers and a high consumption of absorption inhibitors in the second year of life
• b. Insufficient intake of iron as compared to the need
• c. Increased requirement during the rapid growth stage of infancy and early childhood, between six and twenty-three months.

Children go through periods of rapid growth and the diet should provide sufficient iron to help the increased need for more red blood cells. There are other circumstances when children may get this anaemia. The infant may have been provided low or non-iron fortified formula or breast-fed through the later months without supplementation of iron. This happens in premature infants or low-birth weight infants. Otherwise, the infant or child may have a gastrointestinal disease such as a chronic infection, chronic diarrhea, celiac disease or an intestinal parasite. However, the low intake of iron in the diet is the most common factor in infants, children, and adolescents. Iron-deficiency anaemia is common in young children (infants and toddlers) because the child is rapidly growing at a time when the diet is typically low in iron content.²

Consequences of Iron Deficiency and Iron-Deficiency Anaemia in children

Longitudinal studies have shown that children who were anaemic in early childhood remain to have poor cognitive & motor development and decreased school achievement into middle childhood. For anaemic children less than 2 years of age, there is no good evidence from randomized controlled trials that iron treatment supports their cognitive and motor development. For children above 2 years of age, short-term treatment is linked with improvement in cognition but not in school achievement.¹

Another large study in preadolescents and adolescents described an association between iron status and standardized mathematics scores. Those with iron deficiency anaemia or iron deficiency without anaemia were 2.3 and 2.4 times more likely to have low mathematics scores than those with no iron deficiency. Researchers suggested that screening for iron deficiency appears to be warranted for all children and adolescents.¹

A child with IDA is likely to remain susceptible to infection and have lower immunity towards infection throughout childhood. Also, the overall appetite is reduced and this vicious cycle leads to a series of events.²
Prevention strategies

Dietary improvement

Efforts should be targeted to reduce poverty; improve access to diversified diets; improve health services and sanitation; and promote better care and feeding practices.

There are 3 interventions that if implemented successfully are likely to prevent anaemia. These include:

- Dietary modification to foods with more bioavailable iron;
- Fortification of foods targeted to full-term infants and children;
- Offering iron supplementation.

Dietary modification involves promotion of a diet with a wider variety of naturally iron-containing foods, especially red meat, poultry and fish. These foods have a high content of highly bioavailable heme iron and thus are most appropriate for infants and children above 6 months of age. Despite their widespread availability, they (red meat, poultry and fish) are not widely used (possibly because of the perceived unacceptable taste and smell of commercial products).

Enhancers of iron absorption

1) Haem iron is present in meat, poultry, fish, and seafood;
2) Ascorbic acid or vitamin C, present in fruits, juices, potatoes and some other tubers, and other vegetables such as green leaves, cauliflower, and cabbage; and some fermented or germinated food;
3) Condiments, such as soy sauce (note that cooking, fermentation, or germination of food reduces the amount of phytates).

Inhibitors of iron absorption

1) Phytates, present in cereal bran, cereal grains, high-extraction flour, legumes, nuts, and seeds;
2) Food with high inositol content;
3) Iron-binding phenolic compounds (tannins);
4) Foods that contain the most potent inhibitors resistant to the influence of enhancers include tea, coffee, cocoa, herbal infusions in general, certain spices (e.g. oregano), and some vegetables; and calcium, particularly from milk and milk products.

Factors in vegetable fiber may inhibit non-heme iron absorption. If taken with
meals, tea and coffee can reduce iron absorption by 50% through the formation of insoluble iron compounds with tannin. Iron in egg yolk is poorly absorbed because of the presence of phosvitin.6

Examples of simple but effective alterations in meal patterns that enhance iron absorption might include:

Include in the meal fruit juices such as orange juice, or another source of ascorbic acid such as tubers, cabbage, carrots, or cauliflower. Consume milk, cheese, and other dairy products as a between-meal snack, rather than at mealtime. Separate tea drinking from mealtime - one or two hours later as the tea inhibits iron absorption. Consume foods containing inhibitors at meals lowest in iron content, e.g. a breakfast of a low-iron cereal (bread or corn) consumed with tea or milk products; this meal pattern can provide adequate calcium without hampering iron nutrition.5

Fortified foods for young children

Normal-birth-weight infants who are exclusively breastfed do not need iron supplements for the first 4 to 6 months of life. When complementary feeding begins, and certainly after 6 months of age, infants need an additional source of iron to maintain adequate iron nutrition and prevent iron deficiency anaemia.5

Since cereals are widely used as early complementary foods, they should be fortified during their commercial preparation, by extrusion, cooking, or mixing processes. Processed milk-based foods designed for infants and preschool children should also be fortified. Iron fortification is also used for infant cereals: small-particle-size metallic iron widely used in cereals.5

Iron supplementation

Another method of prevention is through supplementation of individuals or communities at risk of IDA. This tactic would be implemented for the treatment of individuals with anaemia or in situations where at-risk communities of infants and young children do not have ready access to targeted iron-fortified foods. However, adherence to long-term ingestion of oral iron drops is regularly poor because of the following:

- Unpleasant metallic taste of drops
- Drops can stain a baby’s teeth unless wiped off immediately after use;
- If the dose is high, the infant may complain of abdominal discomfort.

In studies in anemic infants, it has been demonstrated that the impact of iron drops on anaemia is similarly effective if the drops are provided once daily versus the
traditional 3 times daily, without additional “side effects.” Daily dosing may improve compliance with this intervention.¹

**Treatment of iron deficiency anaemia**

![Figure 1. Algorithm for treatment of iron deficiency anaemia. (CBC = complete blood count.)](algorithm)

**Oral Iron Therapy**

The dosage for children is 3 to 6 mg per kg per day, up to 60 mg per day. An increase in hemoglobin of 1 g per dL after one month of treatment shows an adequate response to treatment and confirms the diagnosis.⁷

Adherence to oral iron therapy can be a barrier to treatment because of gastrointestinal adverse effects such as epigastric discomfort, nausea, diarrhea, and constipation. These effects may be reduced when iron is taken with meals, but absorption may decrease by 40%. Medications such as proton pump inhibitors and factors that induce gastric acid hyposecretion (e.g., chronic atrophic gastritis,
recent gastrectomy or vagotomy) are associated with reduced absorption of dietary iron and iron tablets.\textsuperscript{7}

Current guidelines recommend empiric treatment in children up to two years of age with iron deficiency anaemia; however, if the hemoglobin level does not increase by 1 g per dL (10 g per L) after one month of therapy in children, further evaluation may be indicated.\textsuperscript{7}

Health professionals usually prescribe oral iron for 3 months (three times daily) to treat iron deficiency, depending on the severity of the anaemia and the patient’s tolerance up to 6 mg/kg of body weight for children.\textsuperscript{6}

With iron therapy the hemoglobin level will begin to increase by day 4. Iron therapy should be continued for 4 to 5 months, even after restoration of normal hemoglobin levels, to allow for repletion of body iron reserves.\textsuperscript{6}

**Iron– Protein complex (Peptonised iron)**

Bichile SK, reported in a study that peptonized iron (iron – protein complex) offered better efficacy in treating IDA. A liquid formulation (containing Peptonised iron) lead to significant rise in haemoglobin levels within 4 – 6 weeks and a rise continued up to 12 weeks. Peptonised iron appeared to restore ferritin levels with excellent tolerability as none of patients reported any adverse event. Thus, peptonised iron appears to be considered as iron therapy in children and adolescents.\textsuperscript{8}

**Dosage schedules for iron supplementation\textsuperscript{5}**

The recommended WHO regimen-based on daily supplementation as summarized in Table 3 - should be followed.

| Table 3: Dosage schedules for iron supplementation to prevent iron deficiency anaemia |
|---------------------------------|-----------------|-----------------|-----------------|
| Age groups                      | Indications for supplementation | Dosage schedule | Duration        |
| Low-birth-weight infants        | Universal supplementation        | Iron: 2 mg/kg body weight/day | From 2 months of age up to 23 months of age |
| Children from 6 to 23 months of age | Where the diet does not include foods fortified with iron or where anaemia prevalence is above 40% | Iron: 2 mg/kg body weight/day | From 6 months of age up to 23 months of age |
| Children from 24 to 59 months of age | Where anaemia prevalence is above 40% | Iron: 2 mg/kg body weight/day up to 30 mg | 3 months |
| School-aged children (above 60 months) | Where anaemia prevalence is above 40% | Iron: 30 mg/day Folic acid: 250 µg/day | 3 months |

**Monitoring**

No standard recommendations are for follow-up after initiating therapy for iron deficiency anaemia; however, one suggested course is to recheck complete blood
counts every three months for one year. If hemoglobin and red blood cell indices stay normal, one added complete blood count should be obtained 12 months later. A more practical approach is to recheck the patient periodically; no further follow-up is necessary if the patient is asymptomatic and the hematocrit level remains normal.7

**BLOOD TRANSFUSION**

No universally accepted threshold is for transfusing packed red blood cells in patients with iron deficiency anaemia. Guidelines often specify certain hemoglobin values as indications to transfuse, but the patient’s clinical condition and symptoms are an essential part of deciding whether to transfuse. If transfusion is performed, 15ml/kg of packed red blood cells should be given, then the clinical situation should be reviewed to guide further treatment.7

**Megaloblastic anaemias**

Megaloblastic anaemia is an uncommon problem in childhood. Megaloblastic anaemia reflects a disturbed synthesis of DNA, which results in morphologic and functional changes in erythrocytes, leukocytes, platelets, and their precursors in the blood and bone marrow. This anaemia is characterized by the presence of large, immature, abnormal, RBC progenitors in the bone marrow; 95% of cases are attributable to folic acid or vitamin B12 deficiency. Two disorders of cobalamin metabolism arise from mutations of the methionine synthase and methionine synthase reductase genes; these disorders feature both megaloblastic anaemia and neurologic manifestations. Both vitamins are essential to the synthesis of nucleoproteins. Hematologic changes are the same for both; however, the folic acid deficiency is the first to appear. Normal body folate stores are depleted within 2 to 4 months in individuals consuming folate-deficient diets. By contrast, vitamin B12 stores are depleted only after several years of a vitamin B12-deficient diet. In persons with vitamin B12 deficiency, folic acid supplementation can mask B12 deficiency. In correcting the anaemia, the vitamin B12 deficiency may remain undetected, leading to the irreversible neuropsychiatric damage that is only corrected with B12 supplementation.6,9

**Folic Acid Deficiency Anaemia**

**Etiology**

Folic acid deficiency anaemia is associated with tropical sprue, occurs in infants born to mothers with folic acid deficiency. Folic acid deficiency in early pregnancy can also result in an infant with a neural tube defect. Prolonged inadequate diets, faulty absorption and use of folic acid, and increased requirements resulting from growth are believed to be the most frequent causes. Other causes include gluten
induced enteropathy (childhood) idiopathic steatorrhea, non-tropical sprue and drugs (anti-convulsants, barbiturates, cycloserine, ethanol, sulfasalazine) and amino acid excess (glycine and methionine)\textsuperscript{6,10}

**Medical Nutrition Therapy**

Folate absorption takes place in the small intestine. Enzyme conjugates (e.g. pteroylopolyglutamate hydrolase, the folate conjugates), found in the brush border of the small intestine, hydrolyze the polyglutamates to monoglutamates and reduce them to dihydrofolate and tetrahydrofolic acid (THFA) in the small intestinal epithelial cells (enterocytes). From the enterocytes these forms are transported to the circulation, where they are bound to protein and transported as methyl THFA into the cells of the body\textsuperscript{6,11}

In the absence of vitamin B\textsubscript{12}, 5-methyl THFA, the major circulating and storage form of folic acid, is metabolically inactive. To be activated the 5-methyl group is removed, and THFA is cycled back into the folate pool, where it functions as the main 1-carbon unit acceptor in mammalian biochemical reactions. THFA may then be converted to the coenzyme form of folate required to convert deoxyuridylate to thymidylate, which is necessary for DNA synthesis\textsuperscript{12,13}

*Methylfolate Trap*. Vitamin B\textsubscript{12} deficiency can result in a folic acid deficiency by cause folate entrapment in the metabolically useless form of 5-methyl THFA. The lack of Vitamin B\textsubscript{12} to remove the 5-methyl unit means that metabolically inactive methyl THFA is trapped. It cannot release its I-carbon methyl group to become THFA, the basic I-carbon carrier that picks up I-carbon units from one molecule and delivers them to another. Hence a functional folic acid deficiency results\textsuperscript{6}.

**Medical Management**

Folate taken orally every day for 2 to 3 weeks replenishes folate stores. Maintaining repleted stores requires an absolute minimum oral intake of 50 to 100 mcg of folic acid daily. Symptomatic improvement, as evidenced by increased alertness, cooperation, and appetite, may be apparent within 24 to 48 hours, long before hematologic values revert to normal, a gradual process that takes approximately a month\textsuperscript{14,15}

**Medical nutrition therapy**

After the anaemia is corrected, the patient should be instructed to eat at least one fresh, uncooked fruit or vegetable or to drink a glass of fruit juice daily. One cup of orange juice supplies approximately 135 mcg of folic acid. Fresh, uncooked fruits and vegetables are good sources of folate because folate can easily be destroyed by heat\textsuperscript{6}. 

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Other Nutritional Anaemias

Anaemia of protein-energy malnutrition

Protein is essential for the proper production of hemoglobin and RBCs. Because of the reduction in cell mass and thus oxygen requirements in protein-energy malnutrition (PEM), fewer RBCs are required to oxygenate the tissue. Because blood volume remains the same, this reduced number of RBCs with a low hemoglobin level (hypochromic, normocytic anaemia), which can mimic an iron-deficiency anaemia, is actually a physiologic (non-harmful) rather than harmful anaemia. In acute PEM, the loss of active tissue mass may be greater than the reduction in the number of RBCs, leading to polycythemia. The body responds to this RBC production, which is not a reflection of protein and amino acid deficiency but of any oversupply of RBCs. Iron released from normal RBC destruction is not reused in RBC production but is stored, so that iron stores are often adequate. Iron-deficiency anaemia can reappear with rehabilitation when RBC mass expands rapidly. The anaemia of PEM may be complicated by deficiencies of iron and other nutrients and by associated infections, parasitic infestation, and malabsorption. A diet lacking in protein is usually deficient in iron, folic acid, and less frequently, vitamin B₁₂.

Copper-Deficiency Anaemia

Copper is essential for the proper formation of hemoglobin. Ceruloplasmin, a copper-containing protein, is required for normal mobilization of iron from its storage sites to the plasma. In a copper-deficient state, iron cannot be released; this leads to low serum iron and hemoglobin levels, even in the presence of normal iron stores. Other consequences of copper deficiency suggest that copper proteins are needed for use of iron by the developing erythrocyte and for optimal functions of the erythrocyte membrane. The amounts of copper needed for normal hemoglobin synthesis are so minute that they are usually amply supplied by an adequate diet; however, copper deficiency may occur in infants who are fed cow’s milk or a copper-deficient infant formula. It may also be seen in children who have a malabsorption syndrome or who are receiving long-term total parental nutrition that does not supply copper.

Sideroblastic (Pyridoxine-Responsive) Anaemia

Sideroblastic anaemia is characterized by a derangement in the final pathway of heme synthesis, leading to a buildup of iron-containing immature RBCs. It has four primary characteristics: (1) microcytic and hypochromic RBCs; (2) high serum and tissue iron levels (causing increased transferrin saturation); (3) the presence of an inherited defect in the formation of O-aminolevulinic acid synthetase, an enzyme involved in heme synthesis (pyridoxal-5-phosphate is necessary in this reaction);
and (4) a buildup of iron-containing immature RBCs (sideroblasts, for which the anaemia is named). The iron that cannot be used for heme synthesis is stored in the mitochondria of immature RBCs. These iron-laden mitochondria do not function normally, and the development and production of RBCs become ineffective. The symptoms are those of both anaemia and iron overload. The neurologic and cutaneous manifestations of vitamin B₆ deficiency are not observed. The anaemia responds to the administration of pharmacologic doses of pyridoxine and thus is referred to as vitamin B₆ (pyridoxine)-responsive anaemia, to distinguish it from anaemia caused by a dietary vitamin B₆ deficiency.¹⁶

Treatment consists of pyridoxine or pyridoxal phosphate supplementation. If the anaemia responds to one or the other, pyridoxine therapy is continued for life. However, the anaemia is only partially corrected; a normal hematocrit value is never regained. Patients respond to this treatment to varying degrees, and some may achieve near-normal hemoglobin levels.⁶

Acquired sideroblastic anaemias such as those attributable to drug therapy (isoniazid, chloramphenicol), copper deficiency, hypothermia and alcoholism are not responsive to vitamin B₆ (pyridoxine) administration.⁶

**Vitamin E-Responsive Hemolytic Anaemia**

Hemolytic anaemia occurs when defects in RBC membranes lead to oxidative damage and eventually to cell lysis.¹⁹

This anaemia is caused by shortened survival of mature RBCs. Vitamin E, an antioxidant, is involved in protecting the membrane against oxidative damage, and one of the few signs noted in vitamin E deficiency is early hemolysis of RBCs.⁶

**Non-nutritional Anaemias**

**Anaemia of Chronic Disease**

Anaemia of chronic disease occurs from inflammation, infection, or malignancy because there is decreased RBC production, possibly as a result of disordered iron metabolism. Ferritin levels are normal or increased, but serum iron levels and TIBC are low. It is important that this form of anaemia, which is mild and normocytic, not be mistaken for iron-deficiency anaemia; iron supplements should not be given. Recombinant erythropoietin therapy usually corrects this anaemia.²⁰

**Sickle Cell Anaemia**

**Pathophysiology**

Sickle cell anaemia (SCA), a chronic hemolytic anaemia also known as hemoglobin S disease. This results in defective hemoglobin synthesis, which produces sickle-
shaped RBCs that get caught in capillaries and do not carry oxygen well. The disease is usually diagnosed toward the end of the first year of life.

In addition to the usual symptoms of anaemia, SCA is characterized by episodes of pain resulting from the occlusion of small blood vessels by the abnormally shaped erythrocytes. The occlusions frequently occur in the abdomen, causing acute, severe abdominal pain. The hemolytic anaemia and vaso-occlusive disease result in impaired liver function, jaundice, gallstones, and deteriorating renal function. The constant hemolysis of erythrocytes increases iron stores in the liver; however, iron-deficiency anaemia and SCA can coexist. Iron overload is less common and is usually a problem only in those who have received multiple blood transfusions.

Typically serum homocysteine levels are elevated, which may be due to low concentrations of vitamin B₆. Children with SCA were found to have these lower vitamin B₆ levels despite B₆ intakes comparable to those of unaffected children.

Medical management

No specific treatment exists for SCA other than relieving pain during a crisis, keeping the body oxygenated, and possibly administering an exchange transfusion. It is important that SCA not be mistaken for iron-deficiency anaemia, which can be treated with iron supplements, because iron stores in the patient with SCA secondary to transfusions are frequently excessive.

Zinc can increase the oxygen affinity of both normal and sickle-shaped erythrocytes. Thus zinc supplements may be beneficial in managing sickle cell disease, especially because decreased plasma zinc is common in children with the SS genotype sickle cell disease and is associated with decreased linear and skeletal growth, muscle mass, and sexual maturation. Zinc supplementation (as little as 10 mg daily) may also prevent the deficit in growth that appears in these children. Because zinc competes with copper for binding sites on proteins, the use of high doses of zinc may precipitate copper deficiency.

Medical nutrition therapy

Children with SCA and their families should receive instruction about how they can develop a well-balanced food plan providing enough calories and protein for growth and development. Their dietary intake may be low because of the abdominal pain characteristic of the disease. They also have increased metabolic rates, leading to a need for a higher caloric intake. This hyper metabolism is probably due to a constant inflammation and oxidative stress. Therefore their diets must be high enough in calories to meet these needs and must provide foods high in folate and the trace minerals zinc and copper. In addition, they may be low in vitamins A, C, D and E, folate, calcium and fiber. The diet should be high in folate (400 to 600 mcg daily) because the increased production of erythrocytes needed to replace the cells being continuously destroyed also increased folic acid
requirements. When assessing the nutrition status of patient with SCA, the questions related to the use of vitamin and mineral supplements, and sources of protein (animal sources being high in both zinc and iron) in the diet must be given special attention. A multivitamin and mineral supplement containing 50% to 150% of the RDA for folate, zinc and copper (not iron) is recommended.

Dietary fluid and sodium intake influence the risk for vaso-occlusive events in SCA; increasing fluid intake and limiting high-sodium foods should be discussed. Intake of 2 to 3 quarts of water daily is recommended. Finally, it is important to remember that patients with sickle cell disease may require higher that RDA amounts of protein.

If it is necessary for the diet to be low in absorbable iron, the diet should emphasize vegetable proteins. Iron-rich foods, such as liver, iron fortified formula, iron-fortified cereals, and iron-fortified energy bars are excluded. Substances such as alcohol and ascorbic acid supplements, both of which enhance iron absorption should be avoided. However, it is important to remember that iron deficiency may be present in some patients with SCA owing to repeated phlebotomies, excessive transfusions, or hematuria secondary to renal papillary necrosis. This should be assessed, and the diet adjusted appropriately.

Thalassemia

Thalassemias (A and B) are severe inherited anaemias characterized by microcytic, hypochromic, and short-lived RBCs resulting from defective hemoglobin synthesis, which affects mostly persons in the Mediterranean region. The ineffective erythropoiesis leads to an increase in plasma volume, progressive splenomegaly, and bone marrow expansion with the result of facial deformities, osteomalacia, and bone changes. Ultimately there is increased iron absorption and progressive iron deposition in tissues, resulting in oxidative damage. The accumulation of iron causes dysfunction of the heart, liver, and endocrine glands. Because these patients require transfusions to stay alive, they must also have regular chelation therapy to prevent the damaging buildup of iron that can occur. Impaired growth in children accompanying thalassemia major can be partially corrected by increasing caloric intake.

Summary

Iron deficiency anaemia in childhood and adolescence is associated with serious adverse outcomes that may not be reversible. Infants born prematurely, infants who are exclusively breast-fed for a prolonged period and adolescent girls who are menstruating and restricting their food intake are particularly at risk of IDA. It can be prevented through the use of iron-containing or iron-fortified foods such as meat.
and fortified breakfast cereals. If anaemia is detected, it should be treated with appropriate doses of bioavailable iron, such as peptonized iron or ferrous sulfate or fumarate.

Anaemia in any form is harmful and the consequences that are discussed are applicable to all types of anaemia. However, all types of anaemia are not manageable in the same manner, and the genetic causes of anaemia, like thalassemia or sickle-cell anaemia need to be attended to differently and the expected results of the interventions will be different and relatively lesser and slower than iron-deficiency anaemia interventions.

References:

Dear Doctor,

Anemia in children is commonly encountered by the family physician and pediatricians. Its prevalence continues to remain over 70% in most parts of India. The irreparable damage that anemia in childhood can cause particularly to the development of a young child on one hand and the knowledge and mechanism available for its control on the other, makes this silent morbidity completely unacceptable in modern times.

It is indeed a pleasure to present to you this QMR issue by Dr. Sandipan Sabde, renowned pediatrician. In this issue, he is enlightening us on ‘Medical nutrition therapy in anaemic infants and children’.

With best regards,

Dr. Balaji More
Vice President - Medical

Feedback form: January - March 2017
Medical nutrition therapy in anaemic infants and children

1. Your comments on this issue of Q.M.R.

2. Please suggest medical topics for our QMR which could be printed in future.

3. Any other suggestions / comments:

4. Name: Dr. _____________________________ M ☐ F ☐
   Clinical Address: ___________________________
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Please mail this form to: Medical Director, RAPTAKOS, BRETT & CO. LTD.
21 A, Mittal Tower, 210, Nariman Point, Mumbai 400 021. India
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