Management of Iron-deficiency Anemia during Pregnancy

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Abstract

Iron deficiency anemia (IDA) continues to be the commonest etiology of anemia in pregnancy. Untreated iron deficiency (ID) has significant adverse feto-maternal consequences. Plethora of investigations are available for diagnosis of IDA, each having specific advantages and disadvantages when used in the pregnancy setting. Therapy for ID includes dietary modification, oral iron supplementation, intravenous iron and blood transfusion. Newer parenteral iron preparations are safe and there is mounting evidence to suggest their use in frontline settings for pregnancy associated IDA in the second and third trimester.

Key Words: Iron-deficiency anemia, pregnancy, management.

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Introduction.

Medical care consists of establishing the diagnosis and reason for the iron deficiency. In most patients, the iron deficiency should be treated with oral iron therapy, and the underlying etiology should be corrected so the deficiency does not recur **(1).**

Surgical treatment consists of stopping hemorrhage and correcting the underlying defect so that it does not recur. This may involve surgery for treatment of either neoplastic or nonneoplastic disease of the gastrointestinal tract, the genitourinary tract, the uterus, and the lungs **(2).**

Consultations:

- Surgical consultation often is needed for the control of hemorrhage and treatment of the underlying disorder. In the investigation of a source of bleeding, consultation with certain medical specialties may be useful to identify the source of bleeding and to provide control.
- Gastroenterology consultation is the most frequently sought consult among the medical specialties. Endoscopy has become a highly effective tool in identifying and controlling gastrointestinal bleeding. If bleeding is brisk, angiographic techniques may be useful in identifying the bleeding site and controlling the hemorrhage. Radioactive technetium labeling of autologous erythrocytes also is used to identify the site of bleeding. Unfortunately, these radiographic techniques do not detect bleeding at rates less than 1 mL/min and may miss lesions with intermittent bleeding. **(2).**

Mineral supplementations:

These agents are used to provide adequate iron for hemoglobin synthesis and to replenish body stores of iron. Iron is administered prophylactically during pregnancy because of anticipated requirements of the fetus and losses that occur during delivery (table 1).

Table (1): Mineral supplementations:

Drug Name	**Ferrous sulfate (Feratab, Fer-Iron, Slow-FE)**
Description	Mainstay treatment for treating patients with iron deficiency anemia. They should be continued for about 2mo after correction of the anemia and its etiological cause in order to replenish body stores of iron. Ferrous sulfate is the most common and cheapest form of iron utilized. Tablets contain 50-60 mg of iron salt. Other ferrous salts are used and may cause less intestinal discomfort because they contain a smaller dose of iron (25-50 mg). Oral solutions of ferrous iron salts are available for use in pediatric populations.
Adult Dose	325 mg (60 mg iron) PO with each meal tid
Pediatric Dose	Administer weight-based dosing; 3-6 mg/kg/d PO divided tid suggested, depending on severity of anemia
Contraindications	Documented hypersensitivity; microcytic anemias without laboratory documentation of iron deficiency
Interactions	Calcium supplementation decreases bioavailability of iron when metals are ingested simultaneously; absorption is enhanced by ascorbic acid; interferes with tetracycline absorption; food and antacids impair absorption
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Iron poisoning is common in children; preferably, provide tablets containing <20 mg of iron to pregnant women without iron deficiency; adequate as dietary supplement to prevent iron deficiency and reduces risk if child ingests tablets; iron tablets should be dispensed in child-proof containers and stored away from young children; iron pills resemble a commonly available candy; children watch their mother consume iron tablets and then mimic her actions; children who consume multiple iron tablets should be taken to an ED immediately to prevent shock and death; in pregnant women with iron deficiency anemia, pregnancy vitamin and mineral tablets may not suffice to correct deficiency state; administer iron orally separate from the combination tablets.
Drug Name	**Carbonyl iron (Feosol)**
Description	Used as a substitute for ferrous sulfate. Has a slower release of iron and is more expensive than ferrous sulfate. Slower release affords the agent greater safety if ingested by children. On an mg basis, it is 70% as efficacious as ferrous sulfate. Claims are made that there is less gastrointestinal toxicity, prompting use when ferrous salts are producing intestinal symptoms and in patients with peptic ulcers and gastritis. Tablets are available containing 45 mg and 60 mg of iron.
Adult Dose	1 tab PO tid (usual dose recommended)
Pediatric Dose	Administer weight-based dosing; 3-6 mg/kg/d PO divided tid suggested, depending on severity of anemia.

Contraindications	Documented hypersensitivity; microcytic anemias without laboratory documentation of iron deficiency.
Interactions	Calcium supplementation decreases bioavailability of iron when metals are ingested simultaneously.
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Iron poisoning is common in children; preferably, provide tablets containing <20 mg of iron to pregnant women without iron deficiency; this is adequate as a dietary supplement to prevent iron deficiency and reduces risk if a child ingests tablets; iron tablets should be dispensed in child-proof containers and stored away from young children; iron pills resemble a commonly available candy; children watch their mother consume iron tablets and then mimic her actions; children who consume multiple iron tablets should be taken to an ED immediately to prevent shock and death.
Drug Name	**Dextran-iron (INFeD)**
Description	Replenishes depleted iron stores in the bone marrow where it is incorporated into hemoglobin. Parenteral use of iron-carbohydrate complexes has caused anaphylactic reactions, and its use should be restricted to patients with an established diagnosis of iron deficiency anemia whose anemia is not corrected with oral therapy. Required dose can be calculated (3.5 mg iron/g of hemoglobin) or obtained from tables in the PDR. For IV use, INFeD may be diluted in 0.9% sterile saline. Do not add to solutions containing medications or parenteral nutrition solutions.
Adult Dose	Test dose: 0.5 mL IV/IM (slowly over 1 min if IV); observe for 60 min before providing additional medication Usual adult dose: 2 mL/d (100 mg iron); may be given until amenia is corrected.
Pediatric Dose	<5 kg: Not established 5-10 kg: 50 mg iron (1 mL) IV/IM 10-50 kg: 100 mg iron (2 mL) IV/IM >50 kg: Administer as in adults
Contraindications	Documented hypersensitivity; microcytic anemias without laboratory documentation of iron deficiency; absence of iron deficiency anemia.
Interactions	Absorption is enhanced by ascorbic acid; interferes with tetracycline absorption; food and antacids impair absorption.
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Administer IM INFeD in upper outer quadrant of buttock using a Z-track technique to avoid tattooing; anaphylaxis, death, delayed serum sickness, fever, chest pain, respiratory arrest, wheezing and dyspnea, abdominal pain with nausea and vomiting, seizures, dizziness and disorientation, arthralgia, and back pain may occur; teratogenic effects are reported with high doses in some animals.

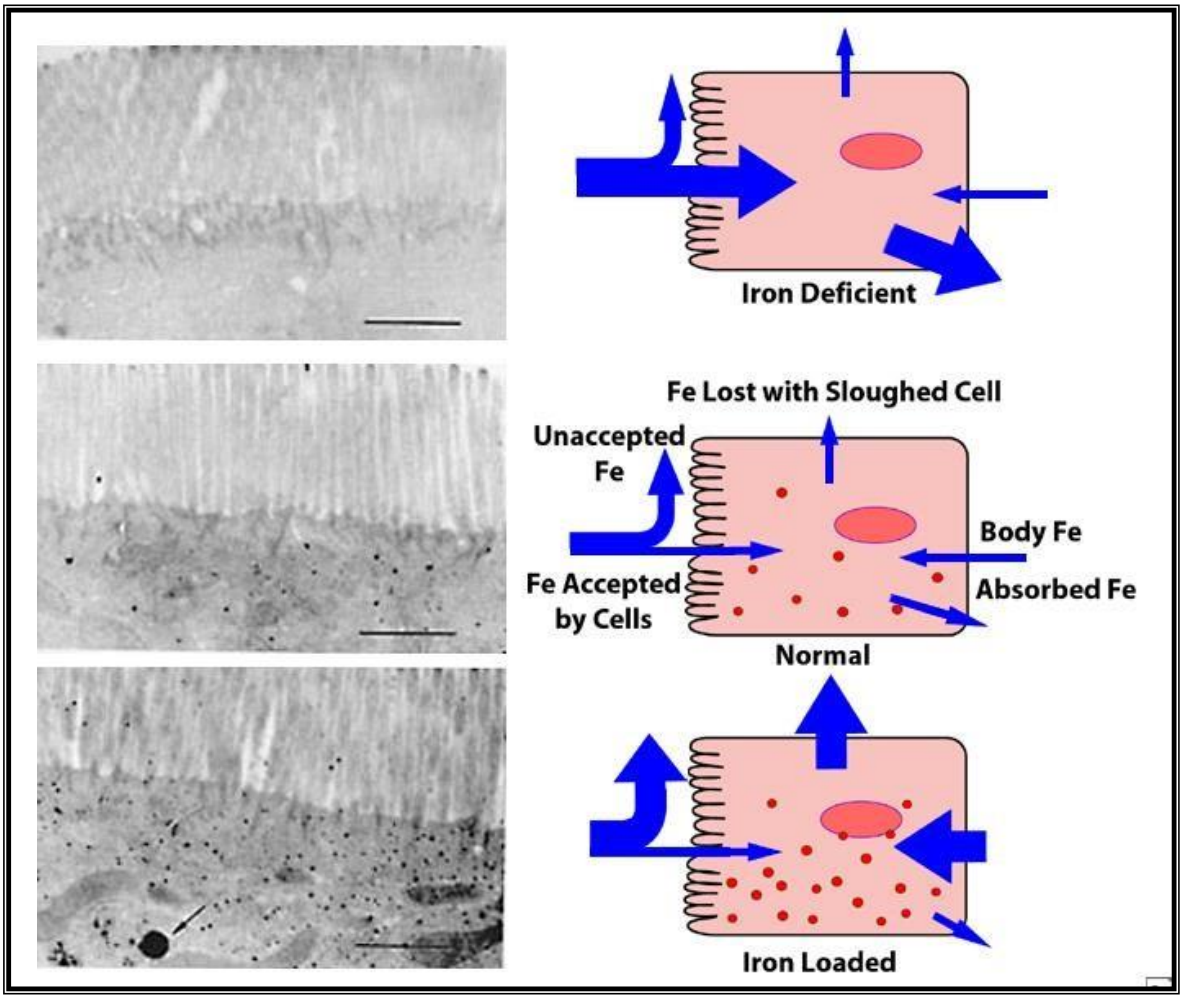

Fig. (1): Ultrastructural studies of the rat duodenum from iron-deficient (**top**), healthy (**middle**), and iron-loaded (**bottom**) animals are shown. They were stained with acid ferrocyanide for iron, which is seen as black dots in the specimens. No staining was seen with acid ferricyanide. This indicates that iron was in the ferric redox state. Respectively, the specimens showed no iron, moderate deposits, and increased deposits with ferritin (arrow). Incubation of the specimens with iron-nitrilotriacetic acid to satiate iron-binding proteins with iron provided specimens with equal iron staining, except that the iron-loaded specimens contained ferritin. The quantity of iron in the cell is derived from both the diet and body stores. It probably is important in the regulation of the quantity of iron accepted by the absorptive cell from the gut lumen. The authors postulate that the iron either satiates iron-binding proteins with iron, up-regulates iron regulatory protein, or does both to diminish iron uptake by the absorptive cell. The consequences of these findings are depicted in the flow charts.

Strategies to combat iron deficiency in pregnancy:

- **Daily supplementation:**

Iron supplementation regimens in pregnancy vary depending on the characteristics of the population. In developed countries most women enter pregnancy with normal hemoglobin concentrations and variable amounts of stored iron. In contrast, large numbers of women in developing countries are anemic at the onset of pregnancy **(3)**.

Prenatal iron supplementation is not compulsory in many industrialized countries and the recommended dose is often small (30 mg ferrous iron daily), but has been as high as 240 mg/d in developing countries **(4)**.

In 1989 the World Health Organization (WHO) recommended universal supplementation of all pregnant women with 60 mg ferrous iron twice daily in populations where gestational anemia is common and once daily in populations where overall iron nutrition is better. This

recommendation was subsequently modified to a single daily dose of 60 mg Fe for 6 mo in pregnancy or 120 mg Fe if 6 mo duration cannot be achieved. Keeping the dose as low as is compatible with unimpaired effectiveness is an important principle because the side effects of iron therapy, which can seriously limit compliance, are dose-dependent phenomena **(5)**.

Recommendations on the use of prenatal iron supplements need to be considered against the background of what is known about iron requirements and iron balance at the different stages of pregnancy. The iron requirement during pregnancy is between 800 and 1000 mg depending on the size of the woman (45–55 kg), with most of the extra requirements occurring in the second half of pregnancy. Iron absorption from a diet of very high iron bioavailability has been estimated to be 0.4, 1.9, and 5.0 mg/d during the first, second, and third trimesters, respectively. A diet with the above absorption rates would provide a total of 600 mg Fe during pregnancy, leaving a deficit of 200–400 mg Fe that would have to be met by mobilizing iron from stores, if they exist, and from the absorption of supplemental iron. In such circumstances, a daily dose of 30 mg ferrous iron during the second half of pregnancy would appear to be adequate because the daily absorption rate that would be required to make up the deficit would be at most <10%. This is, in fact, the iron dose widely used in developed countries, where it is given together with 250–400 mg folic acid **(6)**.

Although a low iron dose and a once-daily schedule are both positive factors in ensuring compliance, it is perhaps noteworthy that > 30% of low-income women in the United States are still anemic during the third trimester of pregnancy. The latter can probably be ascribed to both the consumption of a diet with relatively low iron bioavailability and poor compliance in taking iron supplements **(7)**.

Whether a dose larger than 30 mg of supplemental iron would reduce the prevalence of anemia is not clear, but note that in their classic study, **de Leeuw et al (8)** found that the mean hemoglobin mass at term was lower in women receiving 39 mg ferrous iron daily than in those receiving double that amount.

The problem of anemia during pregnancy in many developing countries is compounded by the fact that many women consume diets of low iron bioavailability and, therefore, enter pregnancy with no iron stores and less than optimal hemoglobin concentrations. In such circumstances, the iron deficit that must be met is correspondingly greater. During the latter part of pregnancy, between 200 and 400 mg Fe can be absorbed from diets with low to medium bioavailability; thus, a deficit of as much as 600–800 mg must be met from iron supplementation. The extra amounts of iron that would have to be absorbed to meet such a deficit would be 5.5–7 mg/d if supplementation was started at 20 wk of gestation, and double this concentration if it were started at 30 wk. These amounts could be met if 9–12% and 19–24% of a 60-mg ferrous iron tablet given in the fasting state at 20 and 30 wk of gestation, respectively, was absorbed. The above absorption ranges are not out of line with those obtained in radioiron studies using a 100-mg dose of ferrous iron (9.2% in the second trimester and 14.3% in the third trimester). For optimal results, the iron must be administered between meals because food reduces the absorption of iron substantially **(9)**.

It is apparent that a daily dose of 60 mg ferrous iron given to fasting pregnant women throughout the second half of pregnancy should be sufficient to combat iron deficiency in developing countries. A dose of 120 mg/d should be required only when iron deficiency is a

problem in women who are not pregnant or when supplementation therapy is not started the beginning of the second trimester **(10)**.

A daily dose of 60 mg Fe was associated with only a 2-g/L rise in the hemoglobin concentration compared with that of control subjects, whereas larger increases of 12 and 16 g/L were obtained with doses of 90 and 120 mg, respectively. These unexpected findings need to be confirmed because they appear to be at variance with the known relations between the dose of iron and the percentage absorbed **(11)**.

The etiology of anemia in developing countries is multifactorial and can be expected to vary by region and by season. In addition to the poor bioavailability of dietary iron, intestinal worm infections and particularly blood loss from hookworm infections compound the problem of anemia in many areas. Other important etiologic factors include folate deficiency; vitamin A deficiency; a variety of infections, including malaria and HIV infection; and hemoglobinopathies. HIV infection is particularly prevalent in sub-Saharan Africa and has been shown to be associated with a median hemoglobin decrease of 5.5 g/L in asymptomatic pregnant women **(12)**.

Programmatically, several factors can limit the effectiveness of iron supplement interventions, including problems related to costs and logistics that affect the supply of iron tablets, poor access to prenatal care, insufficient counseling on the need for and benefits of iron supplementation, and an unwillingness by pregnant women to take iron supplements **(13)**.

Galloway and McGuire (14) suggested that the most important reason for the failure of supplementation programs is a lack of supplies, but noncompliance on the part of pregnant women can also be a significant factor. Noncompliance is the result of both an aversion to the side effects of taking iron supplements and the failure of many primary health care systems to adequately motivate both health care providers to issue the iron tablets and pregnant women to take them.

The problem of noncompliance was highlighted in 2 studies. One study, in Tanzania, found only 42% of pregnant women adhered to a twice-daily schedule of 60 mg Fe as ferrous sulfate **(15)**. In the other study, in Indonesia, 36% of the women who had been receiving 60 mg ferrous iron daily had positive results on stool tests for iron **(16)**.

Various strategies have been adopted to reduce the gastrointestinal side effects associated with taking iron supplements, such as nausea and epigastric pain, which are important factors in noncompliance. Side effects are dose related; thus, a reduction in both the concentration and frequency of the oral iron dose has been advocated. The minimum effective dose of iron for a woman entering pregnancy with no iron stores is 60 mg/d and may be even greater for those who are already anemic at the onset of pregnancy. An alternative approach would be to administer the iron in a form that is both well absorbed and likely to produce fewer side effects. In this context, a formulation referred to as a gastric delivery system (GDS) has proved particularly promising **(17)**.

The GDS consists of ferrous sulfate incorporated into a hydrocolloid matrix that becomes buoyant on exposure to gastric secretions; thus, the GDS is retained for prolonged periods in a soluble form in the acidic environment of the stomach. Two trials have been conducted using the GDS and both showed that it is as effective as ferrous sulfate when given at half the dosage and that it is well tolerated **(17)**.

Its widespread application could, however, still be bedeviled by the operational problems that beset so many iron supplementation

programs. Indeed, these problems remain of such magnitude in parts of the Middle East that the United Nations Relief Works Agency recommended that routine universal prenatal iron supplementation be considered only in those countries where severe anemia is present and that most countries direct their attention to identifying and treating anemic subjects **(18)**.

♦ **Intermittent iron supplementation therapy:**

An alternative approach to daily iron supplementation therapy, be it for pregnant women or other individuals, is to give iron intermittently once or twice per week. The approach is based on experimental evidence that iron absorption is reduced in rats in the days immediately after the initial administration of a large dose of iron but is resumed after <3 d. It was therefore argued that the administration of iron weekly or twice weekly would be both more rational and cost-effective with fewer side effects**(19)**.

The rationale of the approach is, however, dubious, because the results of several double-isotope studies in human subjects have not confirmed the presence of a mucosal block when oral iron is given daily **(20)**, with the results of **Cook and Reddy (9)** showing a 6-fold greater absorption with daily as compared with weekly iron therapy.

Despite the spirited debate on both the rationale and efficacy of the approach, it has been widely applied in preschool children, schoolchildren, female adolescents, and pregnant women, and the results of several other trials have been reported at scientific meetings and in abstracts and preliminary reports. In addition, several developing countries seem to be in the process of changing their prenatal iron supplementation policy from daily to intermittent supplementation **(21)**.

In a study, which was carried out in West Java, hemoglobin concentrations rose significantly with both daily and weekly supplementation, but the increases were lower than reported in previous supplementation trials in which supervision was optimal. Compliance was poor in both groups. The final prevalence of anemia was greater with intermittent weekly therapy in each of the 4 trials conducted during pregnancy and it was concluded that weekly, instead of daily, iron administration is not recommended for pregnancy regardless of the degree of supervision that can be arranged. It was also noted that unless supplementation programs are tightly controlled they can be expected to have limited effectiveness **(22)**.

Further insight into problems attendant on iron supplementation in pregnancy was recently obtained in a study in Bangladesh in which weekly and daily supplementation were compared. Compliance was monitored with an electronic counting device that recorded the dates and times when the pill bottle was opened. Ordinary least-squares regression analysis showed a dose response between iron and hemoglobin that did not differ between the groups. It was concluded that iron absorption was not improved in the weekly group and that daily iron supplementation was more effective than weekly because of the higher dosage of iron that it provided **(23)**.

Intermittent iron supplementation therapy is also being applied to other iron-deficient groups, such as young children and women of childbearing age, with the aim of improving iron nutrition. The rationale for its use by women of reproductive age is for prevention, whereby the long-term application of intermittent therapy will ensure that women enter pregnancy with adequate iron reserves. Such a program of preventive supplementation is similar in aim to the WHO recommendation that supplemental iron be given

to adolescents and women in vulnerable populations for 2–4 mo/y **(5)**.

Beaton and McCabe (24), in a meta-analysis regarding daily versus intermittent iron supplementation in various populations, found that there was a higher final hemoglobin concentration associated with the daily administration of iron. **Gomber et al. (25)** studied daily versus weekly iron supplements in 80 pregnant women and concluded that weekly supplementation was as effective as daily. However, only 56 women could be followed up until the time of final analysis and the women were predominantly non-anemic at the time of recruitment.

In a study by **Bhargava et al. (26)** conducted under a similar setting, the prevalence of anemia in pregnancy was 30% in the urban area of Delhi. Mild anemia in pregnancy was not related to an increased incidence of preterm or low birth weight babies, although babies born to severely anemic mothers did have lower birth weights and shorter gestation. The level was 24.81 ng/mL in another study by **Iyer et al(27)**.

Goonewardene et al. (28) compared the effectiveness of weekly, thrice weekly and daily oral iron supplementation in the prevention of IDA of pregnancy. They recommended daily oral iron supplementation for pregnant women in communities at risk of IDA. Intermittent iron supplementation appears to be inappropriate.

Ziauddin Hyder et al. (29) investigated whether iron supplementation during pregnancy and puerperium has a dose effect on haemoglobin 6 weeks after delivery, and whether there is any differential effect between daily and weekly regimens at 6 weeks postpartum. They concluded that effects of iron supplementation in pregnancy and puerperium were observed at 6 weeks after delivery. The size of the effect was dependent on the number of tablets, not on daily or weekly regimen.

Mukhopadhyay et al. (30) compared the effect of weekly versus daily iron supplements on the hematological and the pregnancy outcomes. Weekly supplements as a prophylaxis are as good as daily in terms of hemoglobin rise or perinatal outcome. In fact, there were significantly fewer side-effects and patients were happier and more compliant with the weekly regimen. However, in anemic women, even those with mild anemia, daily supplementation appears to be superior to weekly.

Bouzari et al. (31) compared the effects of daily iron supplementation in three time frames-daily, weekly and three time weekly supplementation in preventing anemia in healthy pregnant women. They suggested that three times a week or weekly iron supplementation is as effective as daily supplementation for healthy pregnant women without anemia.

Two strategies that merit consideration are programs to modify dietary habits **(32)** and iron fortification of foods **(33)**. The second has the advantage that it can be applied to large population groups at low cost and the identification and cooperation of deficient or potentially deficient individuals is not a prerequisite, as it is with supplementation.

Although there are also problems associated with the implementation of iron fortification of foods, these are not insuperable and the results of 2 trials using iron-EDTA in developing countries have already indicated the potential impact of such programs. Although none of the strategies for combating iron deficiency are mutually exclusive, iron fortification programs adapted to the dietary habits of different populations hold the promise of yielding the most cost-effective benefits in the long term **(34)**.

***Further outpatient care*:**

- Monitor patients with iron deficiency anemia on an outpatient basis to ensure that there is an adequate response to iron therapy and that iron therapy is continued until after correction of the anemia to replenish body iron stores. Follow-up also may be important to treat any underlying cause of the iron deficiency.
- Response to iron therapy can be documented by an increase in reticulocytes 5-10 days after the initiation of iron therapy. The hemoglobin concentration increases about 1 g/dL weekly until normal values are restored. These responses are blunted in the presence of sustained blood loss or coexistent factors that impair hemoglobin synthesis**(35)**.

Transfer:

Transfer of a patient rarely is required for treatment of simple iron deficiency anemia; however, it may be necessary to identify the etiology of the anemia, such as occult blood loss undetected with chemical testing of stool specimens, for identification of a source of bleeding that requires endoscopic examinations or angiography or for treatment of an underlying major illness (eg, neoplasia, ulcerative colitis) **(35).**

Prevention*(36)*:

- Certain populations are at sufficiently high risk of iron deficiency to warrant consideration for prophylactic iron therapy. These include pregnant women, women with menorrhagia, consumers of a strict vegetarian diet, infants, adolescent females, and regular blood donors.
- Pregnant women have been given supplemental iron since World War II. Often, this is administered in all-purpose capsules containing vitamins, calcium, and iron. If the patient is anemic (hemoglobin <11 g/dL), administer the iron at a different time of day than calcium because calcium inhibits iron absorption. The practice of routinely administering iron to pregnant females in affluent societies has been challenged recently; however, provide prophylactic iron therapy during the last one half of pregnancy, except in settings where careful follow-up for anemia and methods for measurement of serum iron and ferritin are readily available.
- Iron supplementation of the diet of infants is advocated. Premature infants require more iron supplementation than term infants. Infants weaned early and fed bovine milk require more iron because the higher concentration of calcium in cow milk inhibits absorption of iron. Usually, infants receive iron from fortified cereal. Additional iron is present in commercial milk formulas.
- Iron supplementation in populations living on a largely vegetarian diet is advisable because of the lower bioavailability of inorganic iron than heme iron.

Complications:

- Iron deficiency anemia diminishes work performance by forcing muscles to depend, to a greater extent than in healthy individuals, upon anaerobic metabolism. This is believed to be due to deficiency in iron-containing respiratory enzymes rather than anemia **(37)**.
- Severe anemia due to any cause may produce hypoxemia and enhance the occurrence of coronary insufficiency and myocardial ischemia. Likewise, it can worsen the pulmonary status of patients with chronic pulmonary disease **(38)**.
- Defects in structure and function of epithelial tissues may be observed in iron deficiency. Fingernails may become brittle or longitudinally ridged with development of koilonychia (spoon-shaped nails). The tongue may show atrophy of the lingual papillae and develop a glossy appearance. Angular stomatitis may occur with fissures at the corners of the mouth. Dysphagia may occur with solid foods, with webbing of the mucosa at the junction of the hypopharynx and the esophagus (Plummer-Vinson syndrome); this has been associated with squamous cell carcinoma of the cricoid area. Atrophic gastritis occurs in iron

deficiency with progressive loss of acid secretion, pepsin, and intrinsic factor and development of an antibody to gastric parietal cells. Small intestinal villi become blunted.

- Cold intolerance develops in one fifth of patients with chronic iron deficiency anemia and is manifested by vasomotor disturbances, neurologic pain, or numbness and tingling **(39)**.
- Rarely, severe iron deficiency anemia is associated with papilledema, increased intracranial pressure, and the clinical picture of pseudotumor cerebri. These manifestations are corrected with iron therapy.
- Impaired immune function is reported in subjects who are iron deficient, and there are reports that these patients are prone to infection; however, evidence that this is directly due to iron deficiency is not convincing because of the presence of other factors **(40).**
- Children deficient in iron may exhibit behavioral disturbances. Neurologic development is impaired in infants and scholastic performance is reduced in children of school age. The IQ of school children deficient in iron is reported as significantly less than their nonanemic peers. Behavioral disturbances may manifest as an attention deficit disorder. Growth is impaired in infants with iron deficiency. All these manifestations improve following iron therapy **(38)**.

Prognosis:

Iron deficiency anemia is an easily treated disorder with an excellent outcome; however, it may be caused by an underlying condition with a poor prognosis, such as neoplasia. Similarly, the prognosis may be altered by a comorbid condition such as coronary artery disease.

Patient education:

- Physician education is needed to ensure a greater awareness of iron deficiency and the testing needed to establish the diagnosis properly. Physician education also is needed to investigate the etiology of the iron deficiency.
- Public health officials in geographic regions where iron deficiency is prevalent need to be aware of the significance of iron deficiency, its effect upon work performance, and the importance of providing iron during pregnancy and childhood. The addition of iron to basic foodstuffs is employed in these areas to diminish the problem **(41)**.
- For excellent patient education resources, visit eMedicine's Blood and Lymphatic System Center and Esophagus, Stomach, and Intestine Center. Also, see eMedicine's patient education articles Anemia and Celiac Sprue **(42).**

Medical/legal pitfalls*(42):*

- Failure to investigate the etiology of the iron deficiency anemia causing a delayed or missed diagnosis of neoplasm
- Giving iron to patients who have a microcytic iron-overloading disorder (eg, thalassemia, sideroblastic anemia).
- Failure to promptly and adequately treat a patient with iron deficiency anemia who is symptomatic with a comorbid condition such as coronary artery disease.
- Anaphylaxis pursuant to the use of parenteral iron therapy in patients who should be treated with oral iron.

Special concerns:

- Special effort should be made to identify and treat iron deficiency during pregnancy and early childhood because of the effects of severe iron deficiency upon learning capability, growth, and development.
- The addition of iron to basic foodstuffs in affluent nations where meat is an important part of the diet is of questionable value and may be harmful. The gene for familial hemochromatosis (*HFe* gene) is prevalent (8% of US white population). Excess body iron is postulated to be important in the etiology of coronary artery disease, strokes, certain carcinomas, and neurodegenerative disorders because iron is important in free radical formation **(43).**

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