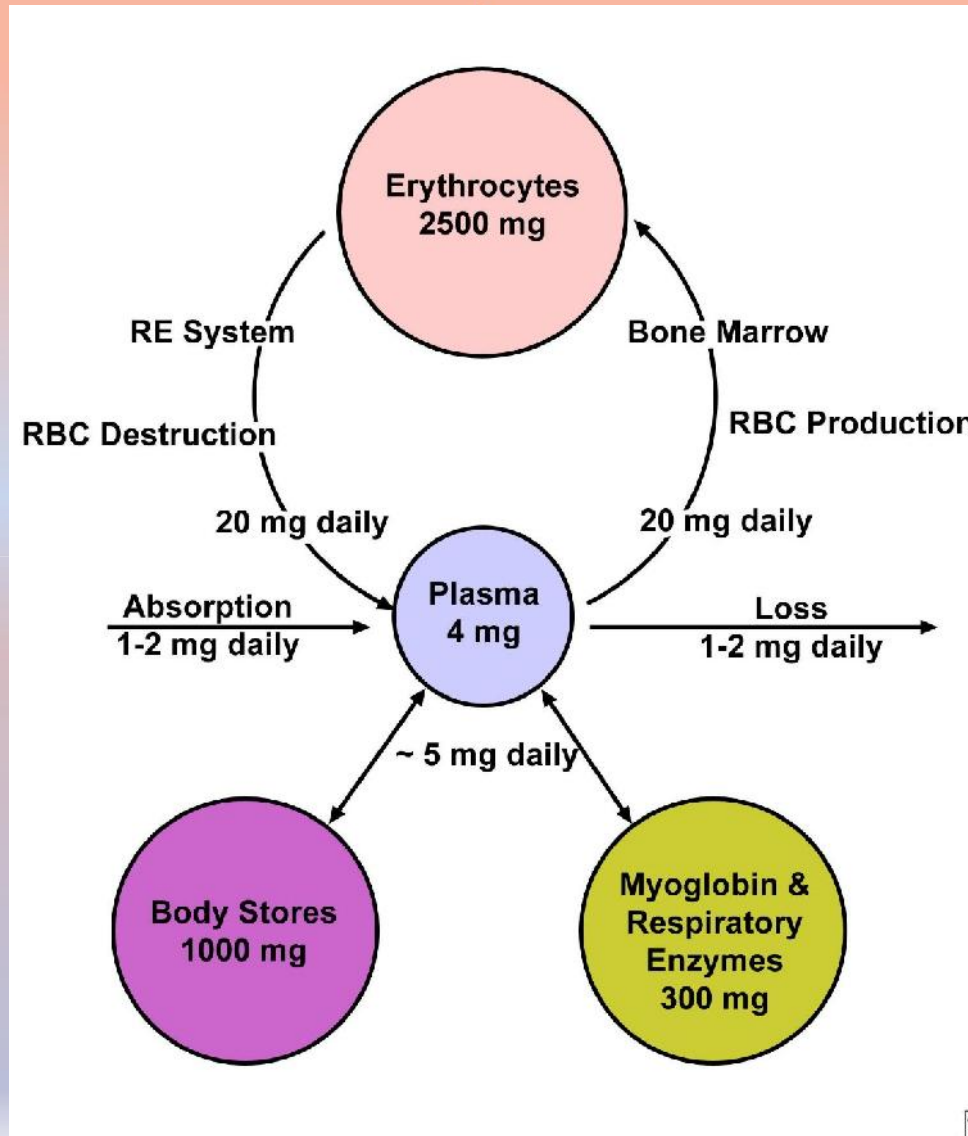


مروری بر دارو درمانی آنمی فقر آهن

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CAUSES OF IRON DEFICIENCY

Reduced iron intake

Insufficient intake, diet (e.g., vegetarian)

Reduced iron absorption:

- Celiac disease
- atrophic gastritis / H. pylori
- Bariatric surgery
- Inflammatory bowel disease
- Medications

Blood loss:

- Traumatic hemorrhage
- Hematemesis or melena or Hemoptysis
- Heavy menstrual bleeding
- Pregnancy and delivery
- Hematuria
- Frequent blood donation
- Excessive diagnostic blood testing
- Occult bleeding, typically gastrointestinal (eg, gastritis, malignancy, angiodysplasia) but may also include hemolysis with urinary losses
- Exercise-induced blood loss, often due to occult gastrointestinal bleeding

Risk Factors

You may have an increased risk for iron-deficiency anemia because of your age, unhealthy environments, family history and genetic, lifestyle habits, or sex.

- Age
- Unhealthy environments
- Family history and genetics
- Lifestyle habits
- Sex

CLINICAL MANIFESTATIONS

Symptoms of anemia

Chest pain

Coldness in the hands and feet

Difficulty concentrating

Dizziness

Fatigue, or feeling tired, is the most common symptom. This can make it hard to find the energy to do normal activities.

Headache

Irregular heartbeat. This is a sign of more serious iron-deficiency anemia.

Pica, which are unusual cravings for nonfood items, such as ice, dirt, paint, or starch.

Restless legs syndrome

Shortness of breath

Findings on examination

- Pallor
- Dry or rough skin
- Atrophic glossitis with loss of tongue papillae, which may be accompanied by tongue pain or dry mouth
- Cheilosis (also called angular cheilitis)
- Koilonychia (spoon nails)
- Alopecia (rare) in especially severe cases
- Swelling or soreness of the tongue

Complications

diagnosed or untreated iron-deficiency anemia may cause the following complications:

Depression

Heart problems. If you do not have enough hemoglobin-carrying red blood cells, your heart has to work harder to move oxygen-rich blood through your body. Cells in tissues need a steady supply of oxygen to work well. Normally, hemoglobin in red blood cells takes up oxygen in the lungs and carries it to all the tissues of the body. When your heart has to work harder, this can lead to several conditions: irregular heartbeats called [arrhythmias](#), a heart murmur, an enlarged heart, or even heart failure.

Increased risk of infections

Motor or cognitive development delays in children

Pregnancy complications, such as preterm delivery or giving birth to a baby with low birth weight

For people with chronic conditions, iron-deficiency anemia can make their condition worse or result in treatments not working as well.

Diagnosis

Iron-deficiency anemia may be detected during routine blood tests when you visit your doctor for a checkup. To diagnose iron-deficiency anemia, your doctor may ask you questions about your [risk factors](#), do a physical exam, or order blood tests or other diagnostic tests.

- Physical exam
- Blood tests
- Tests for gastrointestinal bleeding



Iron deficiency with mild anemia

Further loss of iron results in anemia, which is initially normocytic with a normal absolute reticulocyte count. Common laboratory findings at this stage include:

- Low levels of ferritin <20 ng/mL
- Low levels of serum iron (Fe) <60 mcg/dL
- Increased levels of transferrin
- Low percent saturation of transferrin

And Finally...

IDA

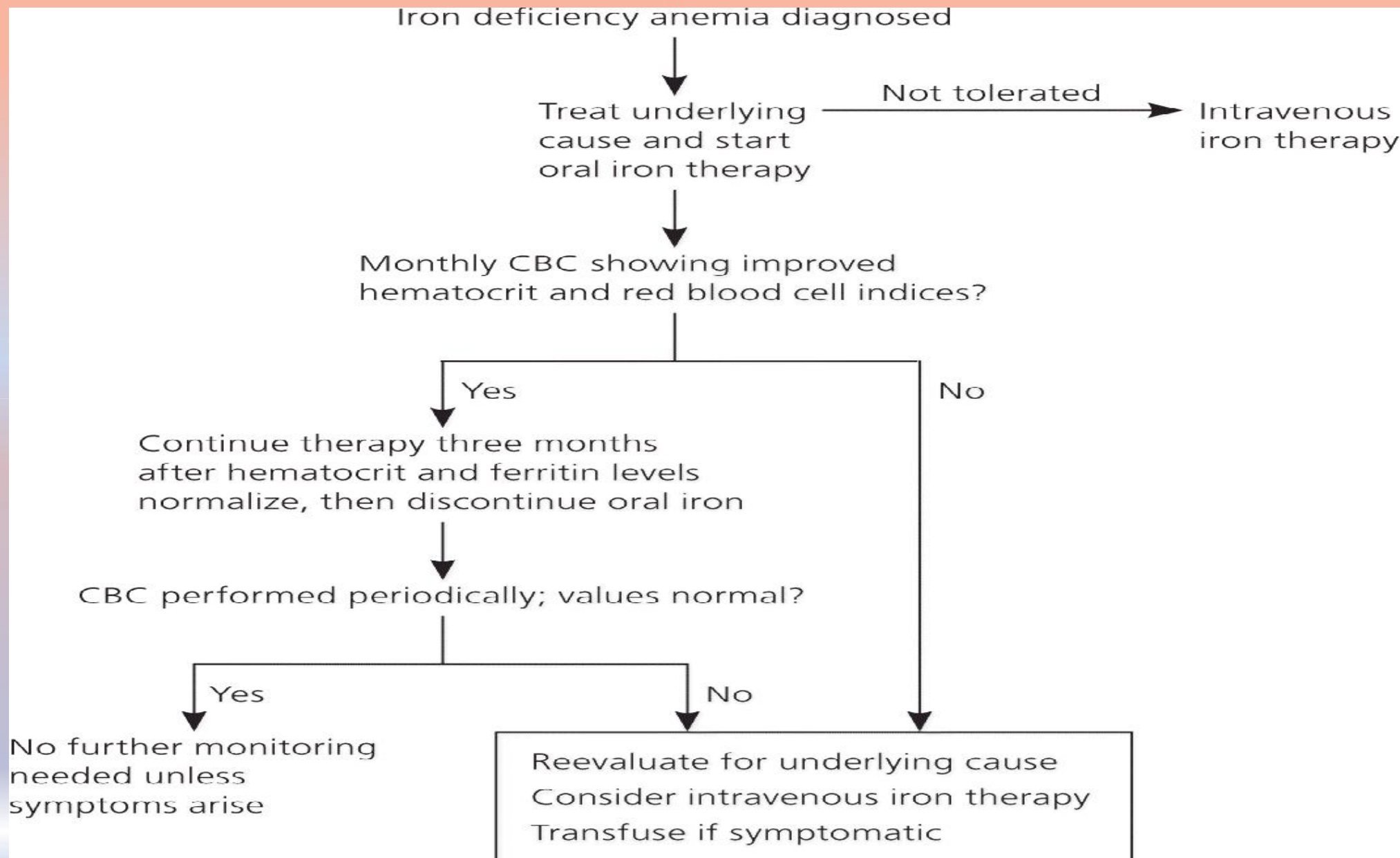


Severe iron deficiency with severe anemia

More profound deficiency results in the classical findings of anemia with RBCs that are hypochromic and microcytic. Reticulocyte production cannot be increased in the setting of iron deficiency, and the reticulocyte count becomes inappropriately low (despite being in the "normal" range in many cases)

| | Normal | Iron deficiency without anemia | Iron deficiency with mild anemia | Severe iron deficiency with severe anemia |
|---|--|---|--|---|
| Hemoglobin | Normal range* | Normal range* | 9 to 12 g/dL (90 to 120 g/L) | 6 to 7 g/dL (60 to 70 g/L) |
| Red blood cell size and hemoglobin content (MCV and MCHC) | Normal | Normal | Normal or slight hypochromia (slight decrease in MCHC) | Microcytosis (decrease in MCV) and hypochromia (decrease in MCHC) |
| Serum ferritin | 40 to 200 ng/mL (40 to 200 mcg/L; 89.9 to 449 picoM/L) | <40 ng/mL [¶] (<40 mcg/L; <89.9 picoM/L) | <20 ng/mL (<20 mcg/L; <45 picoM/L) | <10 ng/mL (<10 mcg/L; <22.5 picoM/L) |
| Serum transferrin | 60 to 150 mcg/dL (10.7 to 26.7 microM/L) | 60 to 150 mcg/dL (10.7 to 26.7 microM/L) | <60 mcg/dL (<10.7 microM/L) | <40 mcg/dL (<10.7 microM/L) |
| Serum transferrin receptor (sTfR; TfR index) | 300 to 360 mcg/dL (53.7 to 64.4 microM/L) | 300 to 390 mcg/dL (53.7 to 69.8 microM/L) | 350 to 400 mcg/dL (62.6 to 71.6 microM/L) | >410 mcg/dL (>71.6 microM/L) |
| Transferrin saturation (TSAT; TfR index/TIBC) | 20 to 50% | 20% | <15% | <10% |

Management of Iron Deficiency Anemia



Oral iron

INDICATIONs

- Treatment of iron deficiency anemia
- Treatment of iron deficiency without anemia
- Nutritional support to prevent deficiency



Dosing and administration (oral iron)

For many years, the recommended treatment of iron deficiency in adults used daily dosing, in the range of 150 to 200 mg of elemental iron per day . As an example, a 325 mg ferrous sulphate tablet contains 65 mg of elemental iron per tablet; three tablets per day will provide 195 mg of elemental iron, of which approximately 25 mg is absorbed and used in production of heme and other molecules

The dose of iron replacement therapy depends on the patient's ability to tolerate the administered iron.

**DAILY
DOSE**



**E V E R Y
O T H E R
D A Y**

We typically advise our patients to take their dose every other day as long as they can manage the schedule appropriately; a reasonable variation on the schedule that is easier to follow is to give the dose on Monday, Wednesday, and Friday.

Increasing evidence suggests that alternate-day dosing (taking the iron every other day rather than every day) appears to result in equivalent or better iron absorption than daily dosing, usually with fewer adverse effects

Number of doses per day

There is no reason to give more than one dose per day

- Single low doses of iron supplements (40–60 mg/day) are associated with less gastrointestinal side effects and lower hepcidin secretion, resulting in better treatment compliance and enhanced fractional absorption
- Twice daily supplementation seems to have limited additional effect compared with daily administration and may increase gastrointestinal side effects

Amount of iron per dose

The amount of iron in the every-other-day dose is also not well established and can be individualized (from 1 to 3 tablets [65 to 200 mg]) based on patient preference and tolerance.

A low single daily dose (40–60 mg) and/or single alternate day dose (80–100 mg) are preferred in order to reduce the side effects and maximize fractional absorption

strategies to improve tolerability

- Increasing the interval to every other day if not done already.
- Making dietary modifications (taking iron with food or milk), although this may reduce absorption.
- Switching to a formulation with a lower amount of elemental iron.
- Switching from a tablet to a liquid, for which it is easier to titrate the dose.
- Tolerance of iron salts improves with a small initial dose and gradual escalation to the full dose.

Indications for IV iron

Iron is appropriate for patients who are unable to tolerate gastrointestinal side effects of oral iron.

Iron may be needed for those with severe/ongoing blood loss or gastric surgery (bypass, resection) that reduces gastric acid may severely impair intestinal absorption of oral iron.

Malabsorption syndromes (celiac disease, Whipple's disease, bacterial overgrowth) may limit absorption of oral iron.

From the second trimester of pregnancy, if the Hb is less than 10.5 g, or any time in the third trimester, at which oral iron is unlikely to adequately supply adequate iron to the developing fetus.



Indications for IV iron

| | Examples/comments |
|---|---|
| <p>Failure of oral iron</p> <p>Intolerance of oral iron</p> <p>Chronic kidney disease (CKD)</p> <p>Inflammatory bowel diseases</p> <p>Severe iron deficiency anemia (IDA)</p> <p>Heart failure (HF)^a</p> | <p>Non-adherence, AEs</p> <p>Celiac disease, gastritis (atrophic, autoimmune, Hp +), surgery, genetic IRIDA</p> <p>Generally accepted threshold: Hb < 8 g/dl (+ Erythropoiesis Stimulating Agents-ESAs)</p> <p>IDA in active disease</p> <p>Severe IDA in II–III trimester</p> <p>Systolic HF (LVEF^b ≤ 45%)</p> |
| <p>(extended)</p> | <p>Examples/comments</p> |
| <p>In elderly</p> <p>Chronic liver disease</p> <p>Chronic kidney disease</p> <p>Chronic heart failure</p> <p>Chronic lung disease</p> <p>Chronic pain</p> <p>Chronic bleeding</p> | <p>If comorbidities/polypharmacy (including PPI) prevent adherence to (or effectiveness of) long-term oral iron</p> <p>Patient blood management strategies to prevent RBCs transfusion ± ESAs</p> <p>(Prevention)</p> |

RESPONSE TO IRON SUPPLEMENTATION

If pagophagia (pica for ice) is present, it often disappears almost as soon as oral or intravenous (IV) iron therapy is begun.

The patient will note an improved feeling of well-being within the first few days of treatment.

In patients with moderate to severe anemia, a modest reticulocytosis will be seen, peaking in approximately 7 to 10 days. Patients with mild anemia may have little or no reticulocytosis.

The hemoglobin concentration will rise slowly, usually beginning after approximately one to two weeks of treatment, and will rise approximately 2 g/dL over the ensuing three weeks. The hemoglobin deficit should be halved by approximately one month, and the hemoglobin level should return to normal by six to eight weeks.

- For oral iron, we often re-evaluate the patient two weeks after starting. We check the hemoglobin and reticulocyte count and review tolerability of the oral iron.
- For IV iron, we generally see patients four to eight weeks after the iron has been administered

BLOOD TRANSFUSION

Blood transfusion should **not** be used a treatment for iron deficiency unless the individual has severe anemia with hemodynamic instability.

- Patients with severe, severely symptomatic, or life-threatening anemia should be treated with red blood cell (RBC) transfusion because correction of iron deficiency anemia using iron replacement requires time for iron administration and incorporation into RBCs.
- RBC transfusion can be life saving for the patient who is hemodynamically unstable due to active bleeding, and/or when evidence of end-organ ischemia secondary to severe anemia is present. The following may be expected for each unit of packed RBCs transfused to an adult, as long as there is not ongoing bleeding:

Once the patient is stabilized with transfusion, the need for additional iron supplementation can be determined and evaluation for the cause can be pursued.

Anemia in pregnancy

Anemia in pregnancy is a global health problem. While some degree of dilutional anemia is part of normal pregnancy physiology, iron deficiency anemia can have serious adverse health consequences for the mother and child. Thus, it is critical to distinguish iron deficiency anemia from physiologic anemia, as well as to identify other less common causes of anemia that may require treatment.



DEFINITION OF ANEMIA in pregnancy

First trimester – Hemoglobin <11 g/dL (approximately equivalent to a hematocrit <33 percent)

Second trimester – Hemoglobin <10.5 g/dL (approximate hematocrit <31 or 32 percent)

Third trimester – Hemoglobin level <10.5 to 11 g/dL (approximate hematocrit <33 percent)

Postpartum – Hemoglobin level < 10 g/dL (approximate hematocrit <30 percent)

MANAGEMENT

The health of both the mother and the child can be affected by anemia during pregnancy. Thus, identifying, preventing, and treating anemia in pregnancy is likely beneficial, although not established by high-quality studies.

SCREENING of IDA DURING PREGNANCY

- We screen all pregnant women for anemia at the first prenatal visit
- We perform repeat screening at week 24 to 28

Prevention of iron deficiency

CDC recommends that all pregnant women begin a **30 mg/day** iron supplement at the first prenatal visit. This corresponds approximately to the amount of iron in most iron-containing prenatal vitamins.

For women who are intolerant of the iron in prenatal vitamins, it may be possible to take prenatal vitamins without iron and to supplement with oral iron supplements on an every-other-day basis (typical dose, 60 mg once every other day or 60 mg once daily).

Treatment of iron deficiency

Dosing(ORAL)

Recommended doses of oral iron range from 40 to 200 mg elemental iron per day .There has been a trend towards using doses on the **lower** end of this range as well as **alternate day dosing** due to recognition that higher and more frequent doses may increase adverse effects without improving iron uptake.

We agree with this dose range and often administer 60 mg of elemental iron.

Intravenous iron

For women with iron deficiency :

- who do not tolerate oral iron
- or those who do not have the expected increase in hemoglobin level with oral iron, which suggests impaired absorption and/or impaired adherence with therapy
- those with severe anemia, especially later in the pregnancy

intravenous iron is the optimal route of administration, as it can fully correct the deficiency in a single administration .**Intravenous iron is not given during the first trimester** but can be started after 13 to 14 weeks.

Choice of formulation – All intravenous iron products appear to have **equivalent safety** and **efficacy**, and the choice of products is based on the costs and burdens of administration .One exception is formulations that contain benzyl alcohol as a preservative (eg, the **ferric gluconate** preparation Ferrlecit); we avoid these formulations due to the potential risk to the fetus .

ing response to treatment

The expected response to iron repletion is improvement in RBC production, which typically begins with

- reticulocytosis after approximately one week
 - an increase in the hemoglobin level of at least 1 g/dL within two to three weeks
 - and an increase in serum ferritin into the normal range, typically within three weeks .
- For antepartum patients receiving oral iron, we typically check the hemoglobin level and reticulocyte count two to three weeks after starting therapy and review tolerability of the oral iron. If the expected response has occurred and the oral iron is well tolerated, it is continued throughout the pregnancy and into the postpartum period .If the oral iron is not well tolerated and/or the expected increase in hemoglobin level has not occurred, options include making changes to improve tolerability (appropriate if anemia is mild) or changing to intravenous iron.
 - For antepartum patients receiving intravenous iron, we generally obtain repeat iron parameters four to eight weeks after the iron has been administered. We wait a minimum of four weeks because intravenous iron interferes with most assays of iron status .
 - Patients also undergo repeat complete blood count (CBC) testing at 24 to 28 weeks.