### ANEMIA IN PREGNANCY

#### DEFINITION
Anemia is a significant problem; even in the US, it is seen in over 40% of pregnant adolescents. Anemia can result in small-for-gestational-age (SGA) infants. Routine testing in pregnancy includes a complete blood count (CBC) at intake and at 28 weeks to assess hemoglobin indices and platelet count. Severe anemia is a hemoglobin less than 8.0 g/dL. Mild anemia is defined differently in different trimesters of pregnancy because hemoglobin levels fall in the second trimester as a result of plasma volume expansion. The threshold for anemia in African American women is lower than for Caucasian women. Anemias can be categorized by the underlying causative mechanism, by red cell morphology or by being inherited or acquired. They also can be categorized as being due to suppressed blood cell production, increased hemolysis or blood loss. Decreased production is the most common cause of anemia in pregnancy, generally due to lack of iron, vitamin B₁₂ or folate. Iron requirements rise in pregnancy. The deficiency is generally due to dietary deficiency, but also may result from malabsorption or blood loss. Bone marrow disorders, chronic disease and hemolytic anemia also result in low hemoglobin. See Table 1 for a more complete list of causes. Iron supplementation in pregnant women with normal hemoglobin levels increases birth weight.

#### SUBJECTIVE
May include:
1. Asymptomatic.
2. Complaints of fatigue, weakness, pallor, palpitations, dyspnea, headache.
3. Dietary history revealing inadequate iron and/or folate.
4. History of prior anemia.
5. Tobacco addiction.
6. History of medical conditions: cardiac, respiratory, autoimmune, thyroid, cancer, hepatic, chemotherapy, radiation, etc.
7. Alcohol abuse.
8. Pica intake or inadequate nutrition.
9. Gastric or intestinal surgery or other causes of malabsorption.
10. Use of drugs that cause anemia (see Table 2).

#### OBJECTIVE
1. Pulse.
2. Blood pressure.
3. Exam for pallor (skin, conjunctiva).
4. Orthostatic vital signs if patient symptomatic but stable.

#### LABORATORY
Must include: CBC for hemoglobin and MCV at initial visit and at 28 week visit. See Tables 1 and 3 to interpret lab results.

#### ASSESSMENT
1. Mild anemia defined by ethnicity and trimester of gestational age: Hemoglobin by Trimester
   - 1st
   - 2nd
   - 3rd
   a. Hemoglobin (g/dL) in non-African American women: <11.0 <10.5 <11.0
   b. Hemoglobin (g/dL) in African American women: <10.2 <9.7 <10.2
2. Severe anemia (hemoglobin <8 g/dL).

#### PLAN
1. Severe anemia (hemoglobin <8 g/dL).
   a. If patient tachycardic, orthostatic or significantly symptomatic, refer to ER, especially if she is actively bleeding.
   b. If patient is not symptomatic, has normal vital signs, and is not currently bleeding, assess fetal well-being (if possible), order the following lab tests and consult with MD to develop management plans.
      1) If microcytic anemia (MCV less than 80 fL), order total iron, total iron binding capacity (TIBC), ferritin, reticulocyte count.
      2) If normocytic anemia (MCV 80-100 fL), rule out chronic diseases, order serum electrophoresis, peripheral smear, reticulocyte count.
### PLAN (Continued)

3) If macrocytic anemia (MCV greater than 100 fL), obtain drug history, order folate, vitamin B<sub>12</sub>, LFTs, reticulocyte count, TSH, peripheral smear.

2. Mild anemia: microcytic (MCV greater than 80 fL). Unless the patient provides another diagnosis (eg. Sickle cell trait or disease) from her history, assume she has iron deficiency anemia.
   a. Start therapy with iron supplementation in addition to prenatal vitamins. Table 4 displays content of elemental iron in various products. Start FeSO<sub>4</sub> 325 mg tablet once or twice daily 1 hour before or 2 hours after eating, if possible.
   b. Offer stool softener to use PRN constipation. If constipation or other side effects present, may offer intermittent iron (every other day).
   c. Try to avoid enteric coated iron tablets, unless woman suffers GI symptoms with uncoated tablets.
   d. If patient has nausea or vomiting of pregnancy and cannot tolerate oral iron, consult MD to determine if parenteral iron is needed.
   e. If patient does not have an appropriate rise in hemoglobin in 2-4 weeks of iron use, order serum electrophoresis, TIBC, serum ferritin and iron. Test stool for occult blood. Consider testing for parasites if history suggests exposure or GI pathology of occult “blood forms.” If ferritin >10-15 mcg/l, consider other etiology for microcytic anemia. (See Table 1 or consult MD).

3. Mild anemia: normocytic (MCV 80-100 fL).
   a. Start with iron supplementation.
   b. Order reticulocyte count, peripheral smear, serum electrophoresis.
   c. Screen for chronic diseases. Consult with MD for management.

4. Mild anemia: macrocytic (MCV greater 100 fL).
   a. Ask specifically about alcohol use, diet and medication use. Order serum folate, vitamin B<sub>12</sub>, LFTs, reticulocyte count.
   b. Prescribe folate 1mg orally daily, PNV and FeSO<sub>4</sub> 325 mg. 1 tablet orally daily pending lab values.
   c. Consult with MD.

5. Women with known sickle cell disease.
   a. Measure ferritin level.
   b. Give oral iron supplementation only if ferritin <30 mcg/L.
   c. See Protocol 7.2.11 Sickle Cell Hemoglobinopathies, Pregnancy.

### PATIENT EDUCATION

1. For women with iron deficiency anemia:
   a. Encourage intake of iron rich foods: clams, oysters, liver, beef, shrimp, turkey, enriched breakfast cereals, beans, lentils.
   b. Encourage that the following may enhance absorption of iron from the diet: orange juice, grapefruit, strawberries, broccoli, peppers.
   c. Suggest minimizing intake of foods that block iron uptake: dairy products, soy products, spinach, coffee, tea and pica.
   d. Caution against use of antacids at time of iron ingestion.
   e. Advise patient about side effects of iron, including constipation and nausea. If patient very uncomfortable with daily dosing, intermittent oral iron intake is also helpful.

2. For women with macrocytic anemia due to dietary deficiency, encourage increased intake of fresh leafy vegetables, legumes or animal protein.

3. Encourage consistent use of medicines.

4. Caution patient to store iron tablets in safe area out of the reach of children. As few as 6-12 tablets of FeSO<sub>4</sub> may be lethal to children (30% of drug poisoning of children in the past resulted from iron ingestion).

### REFER to MD/ER

1. Women with anemia who can not tolerate oral iron supplements.
2. Women unresponsive to treatment.
3. Women with unstable vital signs.
4. Women with severe anemia to interpret of lab results and plan therapy.
5. Women whose lab results are not consistent with diagnosis.
Table 1
Anemia by Mean Corpuscular Volume

<table>
<thead>
<tr>
<th>Microcytic anemia (MCV less than 80 fL)</th>
<th>Normocytic anemia (MCV 80-100 fL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency anemia</td>
<td>Hemorrhagic anemia</td>
</tr>
<tr>
<td>Thalassemia</td>
<td>Early iron deficiency anemia</td>
</tr>
<tr>
<td>Anemia of chronic disease</td>
<td>Anemia associated with bone marrow suppression</td>
</tr>
<tr>
<td>Sideroblastic anemia</td>
<td>Autoimmune hemolytic anemia</td>
</tr>
<tr>
<td>Anemia associated with copper deficiency</td>
<td>Hereditary spherocytosis</td>
</tr>
<tr>
<td>Anemia associated with lead poisoning</td>
<td>Hemolytic anemia with paroxysmal nocturnal hemoglobinuria</td>
</tr>
<tr>
<td>Malabsorption</td>
<td>Anemia of chronic disease (including renal insufficiency, hypothyroidism, other endocrine disorders, hypopituitarism dysfunction)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Macrocytic anemia (MCV greater than 100 fL)</th>
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</thead>
<tbody>
<tr>
<td>Folic acid or vitamin B12 deficiency</td>
</tr>
<tr>
<td>Anemia associated with reticulocytosis or acute anemia of alcohol abuse or liver disease</td>
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<tr>
<td>Drug-induced anemia</td>
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Table 2
Drug-Induced Hematologic Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Examples of associated drugs</th>
</tr>
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<tbody>
<tr>
<td>Immunohemolytic anemia</td>
<td>Penicillins, cephalorins, alpha-methyl-DOPA, oxaliplatin fludarabine, anti-RhD antiglobulin</td>
</tr>
<tr>
<td>Nonimmune hemolytic anemia</td>
<td>Ribavirin, phenazopyridine, chloroquine</td>
</tr>
<tr>
<td>Methemoglobinemia</td>
<td>Phenazopyridine, dapsone, benzocaine, prilocaine</td>
</tr>
<tr>
<td>Megaloblastic anemia</td>
<td>Primethoprim, pyrimethamine, diphenylhydantoin</td>
</tr>
<tr>
<td>Sideroblastic anemia</td>
<td>Isoniazid, chloramphenicol, linezolid</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>Chloramphenicol, gold, NSAIDs</td>
</tr>
<tr>
<td>Pure red cell aplasia</td>
<td>Chloramphenicol, gold, NSAIDs, diphenylhydantoin, azathioprine, chlorpropamide Isoniazid, erythrophoietin</td>
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</table>

Table 3
Diagnosis of Anemia

<table>
<thead>
<tr>
<th>Test</th>
<th>Iron Deficiency</th>
<th>Thalassemia</th>
<th>Chronic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>Decreased</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Total iron binding capacity</td>
<td>Increased</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Decreased</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>Iron/iron binding capacity</td>
<td>&lt;18%</td>
<td>Normal</td>
<td>&gt;18%</td>
</tr>
</tbody>
</table>

Table 4
Iron Supplements

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Ferrous sulfate</td>
<td>65 mg elemental iron per 300-325 mg tablet</td>
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<tr>
<td>Ferrous fumarate</td>
<td>106 mg elemental iron per 325 mg tablet</td>
</tr>
<tr>
<td>Ferrous gluconate</td>
<td>34 mg elemental iron per 300 mg tablet</td>
</tr>
<tr>
<td>Iron dextran</td>
<td>50 mg elemental iron per milliliters, IM or IV</td>
</tr>
<tr>
<td>Ferric gluconate</td>
<td>12.3 mg iron per milliliter, IV</td>
</tr>
<tr>
<td>Iron sucrose</td>
<td>20 mg iron per milliliter, IV</td>
</tr>
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