SECTION 12

Hematology: Anemias and Blood Disorders

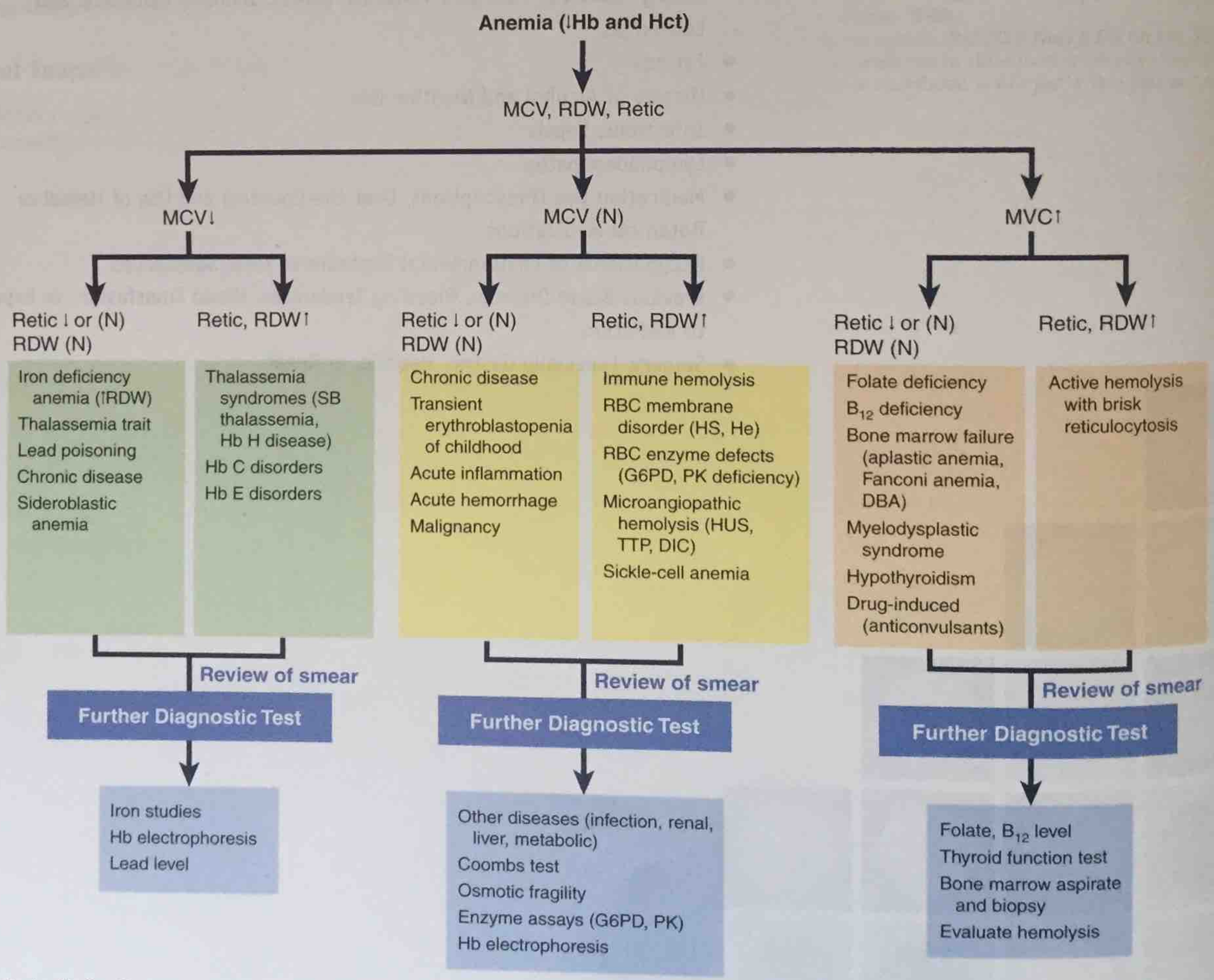
CHIEF ASSESSMENT FACTORS

- Anorexia
- Beefy, Red Tongue or Magenta Tongue; Other Signs of Nutrient Deficiencies
- Blood Type
- Bruising
- Concurrent Asthma, Cancer, Cerebrovascular Disease, Hemorrhage, Myocardial Infarction, Renal Disease
- Dietary Habits: Use of Heme and Nonheme Iron, Vitamin and Mineral Deficiencies, Protein Intake, Vegan Lifestyle
- Exposure to Lead Paint, Other Toxins
- Family History of Allergies, Anemias, Cancer, Immune Disorders, and Leukemias
- Fatigue
- History of Alcohol and Nicotine Use
- Infections, Sepsis
- Lymphadenopathy
- Medication Use (Prescriptions, Over-the-Counter) and Use of Herbal or Botanical Medications
- Occupational or Environmental Exposure to Toxic Substances
- Previous Blood Disorder, Bleeding Tendencies, Blood Transfusion, or Exposure to Radiation
- Surgery, Especially Gastric, Hepatic, or Renal

GENERAL INFORMATION ABOUT ANEMIAS

Blood contains plasma and cells. Plasma is clear and yellow and makes up 55% of blood. It contains proteins, nutrients, hormones, and electrolytes. White cells, red blood cells (RBCs), and platelets make up the remaining 45% of blood. The white cells fight infection, platelets are necessary for blood clotting, and RBCs carry oxygen throughout the body. Hepcidin, the main iron regulatory hormone, is made primarily in hepatocytes in response to liver iron levels, inflammation, hypoxia, and anemia (Munoz et al, 2009). Erythropoietin is the hormone that stimulates RBC production. The erythrocyte life span is 120 days, after which the cells are destroyed by the spleen. Anemias are a set of hematological disorders with a reduced number of RBCs, reduced amount of hemoglobin (Hgb), or reduced number of volume-packed RBCs (hematocrit [Hct]). Excessive bleeding, decreased RBC production, and increased RBC destruction may lead to anemias. The main consequences of these disorders include hypoxia and decreased oxygen-carrying capacity. Overall, anemias affect over 3.4 million people in the United States. Chronic disease and iron deficiency are the most common causes. Other causes of anemias include peptic ulcers, inflammation, infection, cancers, gastritis, liver disease, renal disease, hypothyroidism, history of blood transfusions, blood coagulation disorders, and poor diet. Generally, Hgb, serum iron, TIBC or UIBC, and serum ferritin will establish iron status. In conditions due to blood cell production or cancers, other tests or procedures are needed to determine the cause for abnormal iron levels. These may include a complete blood count (CBC) with differential, zinc protoporphyrin (ZPP) immunological tests, hormone tests, reticulocyte count, C-reactive protein (CRP), sedimentation rate (SED rate), B_{12} or folate levels, genetic testing, tissue biopsy, MRI, ultrasound, bone marrow aspiration, blood smears, urine or fecal sampling, scopes (endoscope or colonoscopy), and tests associated with specific diseases or conditions that can have anemia or iron overload.

Anemias can be encountered with generalized or specific nutritional deficiencies (Table 12-1). The nutritional anemias are caused by deficits, but not all anemias require nutritional intervention. Use caution when evaluating single laboratory results; most anemias have a specific profile. For example, iron and copper participate in one-electron exchange reactions; the same property that makes them essential also generates free radicals that can be seriously deleterious to cells (Arredondo and Nunez, 2005). Table 12-2 provides some key definitions that are used to describe anemias.



Red cell distribution width (RDW), a measure of heterogeneity in the size of circulating erythrocytes, is associated with some chronic diseases and predicts mortality.

TABLE 12-1 Nutritional Factors in Blood Formation

Protein
Iron
Vitamin C
Vitamin E
Folic acid
Vitamin B_6
Vitamin B_{12}
Vitamin K
Copper
Riboflavin (minute amounts)

Inadequate intakes of many nutrients are now known to contribute to several chronic diseases. Folic acid and vitamin B_{12} are among the key nutrients involved. Vitamin B_{12} deficiency, iron or folate deficiency, chronic gastrointestinal (GI) bleeding, and myelodysplastic syndrome are causes of anemia in the elderly. Anemias are more common in the hospitalized elderly than among those who live independently.

Iron is an essential micronutrient as it is required for adequate erythropoietic function, oxidative metabolism, and cellular immune responses (Munoz et al, 2009). Yet it is one of the most frequently lacking nutrients in both developing and developed countries. Iron-deficiency anemia (IDA) affects about 25% of infants worldwide. Adults, especially menstruating women, are also susceptible. Laboratory tests provide evidence of iron depletion in the body, or reflect iron-deficient red cell production; the appropriate combination of these laboratory tests help establish a correct diagnosis of ID status and anemia (Munoz et al, 2009). Table 12-3 lists some relevant tests and Table 12-4 lists common signs and symptoms of anemias.

Up to 10% of young women in developed countries are iron deficient. The problem is not easily resolved by adopting

TABLE 12-2 Definitions

Acute anemia	Precipitous drop in the RBC population due to hemolysis or acute hemorrhage
Anemia	Reduction in the number of circulating RBCs, the amount of hemoglobin, or the volume of packed RBCs (Hct)
Chronic anemia	Anemia that lasts 2 months or longer
Hypochromia	Blood condition in which there is a low level of hemoglobin and color
Hyperchromia	Blood that is excessively pigmented
Microcytic anemia	Usually caused by or resulting in iron deficiency; RBCs are small in size
Macrocytic anemia	Folic acid or vitamin B_{12} insufficiency; RBCs are larger than usual
Megaloblastic anemia	Anemias in which there are large, nucleated abnormal RBCs that are irregular in shape, from pernicious anemia or use of certain immunosuppressive or antitumor drugs
Normocytic anemias	Inhibition of marrow by infection or chronic disease; RBCs are of usual size
Normochromia	Blood with a normal color and level of hemoglobin

TABLE 12-3 Iron Tests

Hemoglobin	Reflects the level of functional iron. Low levels can indicate iron-deficiency anemia or ACD. Hemoglobin values help determine if anemia is present and if a blood donation can be done
Serum ferritin	Measures the amount of iron in storage. One ferritin molecule can hold as many as 4500 iron atoms. Ferritin can be elevated when a person has an infection or inflammatory condition
Serum iron (Fe)	Free or unbound iron in serum. Ideal range is 40–180 µg/dL. Measurement is best done fasting because serum iron is sensitive to foods or supplements recently consumed, time of day, and menstruation
Transferrin	Iron-binding and transport protein that can bind to and transport two molecules of iron. Transferrin carries iron through the bloodstream to the bone marrow, the liver, and ferritin. Transferrin is no longer measured directly by most physicians, instead TIBC is used
TIBC	Demonstrates the iron-binding ability of transferrin. Serum iron divided by TIBC × 100% provides the transferrin-iron saturation percentage (Tsat%), which is also called iron saturation. Normally, Tsat% is 25–35%. Higher numbers are suggestive of iron loading. Lower numbers are suggestive of iron-deficiency anemia

From: Iron Overload Disease Association, http://www.irondisorders.org/Forms/irontests.pdf, accessed December 21, 2009.

TABLE 12-4 General Signs and Symptoms of Anemia

- Anorexia
- Ascites
- Bowel irregularity
- Chest pain, palpitations
- Coldness of extremities
- Dizziness, especially postural
- Dyspnea, especially exercise intolerance
- Decreased libido or impotence
- Decreased urine output
- Difficulty sleeping or concentrating
- Fatigue, weakness, irritability
- Headache
- Mental status changes
- Pale conjunctiva
- Tachycardia
- Thirst
- Tinnitus
- Vertigo, syncope

Comparing Disorders of Iron

IRON PANEL TESTS	Serum Iron	Serum Ferritin	Transferrin Iron Saturation Percentage	Total Iron Binding Capacity (TIBC)	Transferrin	Hemoglobin
Hemochromatosis	↑	↑	↑	↓	↓	NORMAL
Iron Deficiency Anemia	↓	↓	↓	↑	↑	↓
Sideroblastic Anemia	↑	↑	↑	↓	↓	↓
Thalassemia	↑	↑	↑	↓	↓	↓
Porphyria Cutanea Tarda (PCT)	↑	↑	↑	↓	↓	NORMAL
Anemia of Chronic Disease (ACD)	↓	↑ OR NORMAL	↓	↓	↓	↓
African Siderosis (AS)	↑	↑	↑	↓	↓	NORMAL
Vitamin B_{12} Deficiency (pernicious anemia)	↑ OR NORMAL	↑ OR NORMAL	↑ OR NORMAL	↓ OR NORMAL	↓ OR NORMAL	↓

an iron-rich diet because absorption varies greatly. Although the absorption of dietary iron (1–2 mg/d) is regulated tightly, it is balanced with losses (Munoz et al, 2009). Dietary heme iron is important and more readily absorbed than nonheme iron derived from vegetables and grains. Most heme is absorbed in the proximal intestine.

Inherited Hgb disorders, such as sickle cell anemia and thalassemia, can be attributed to the effects of natural selection. In environments in which malaria was common, carriers were protected and survived to have more children.

For More Information

- National Anemia Action Center
  http://www.anemia.org/
- National Heart, Lung, and Blood Institute Information Center
  http://www.nhlbi.nih.gov/about/dbdr/

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ANEMIAS

ANEMIA OF CHRONIC DISEASE

NUTRITIONAL ACUITY RANKING: LEVEL 2

DEFINITIONS AND BACKGROUND

Anemia of chronic disease (ACD) is the condition of impaired iron utilization where functional iron (Hgb) is low, but tissue iron (such as in storage) is normal or high. ACD is known as anemia of inflammation (AI). Low Hgb, low total iron-binding capacity (TIBC), and low transferrin with elevated ferritin are identified. ACD is the second most common type of anemia after anemia of iron deficiency; it results in increased morbidity and mortality of the underlying disease (Agarwal and Prchl, 2009). ACD is seen in a wide range of chronic autoimmune, cancerous or leukemic

inflammatory, and infectious disease conditions. In rheumatoid arthritis, ACD and iron-deficiency anemia coexist, resulting from GI bleeding due to the use of many drugs. ACD is also found in approximately 50% of patients with lupus (Giannouli et al, 2006). In aging and heart failure, chronic anemia is common.

Hepcidin is the iron regulatory peptide that is synthesized in the liver to suppress iron absorption and utilization. Synthesis is suppressed by anemia, hypoxia, and erythropoiesis, and induced by inflammatory cytokines such as interleukin-6 (Matsumoto et al, 2009). ACD is characterized by macrophage iron retention induced by cytokines and hepcidin. Excess hepcidin causes proteolysis of the cellular iron exporter, ferroportin, trapping iron in macrophages, and iron-absorbing enterocytes (Ganz and Nemeth, 2009). Because circulating hepcidin levels affect iron traffic, its determination may aid to differentiate between ACD and iron-deficiency anemia to select an appropriate therapy (Theurl et al, 2009).

Hgb improvement is an independent predictor of quality of life improvement in anemic patients, yet supplementation with iron for those with ACD can be harmful and even result in death. Levels of erythropoietin are reduced in ACD. The genetically engineered form (epoetin) can correct anemia caused by cancer in about 50–60% of patients and may improve survival in HIV infection.

Epoetin can eliminate the need for transfusions but is very expensive.

Successful treatment of the underlying disease improves ACD, but if not possible, treatment with erythropoietic agents (ESAs), supplemented with iron if necessary, is helpful in many cases (Agarwal and Prchl, 2009). ESAs are safe and may forestall some of the target-organ damage (Nurko, 2006).

SAMPLE NUTRITION CARE PROCESS STEPS

Abnormal Nutritional Laboratory Values

Assessment Data: Weight, BMI normal. Hgb is low at 10; ferritin is normal. GI bleeding and pain.

Nutrition Diagnoses (PES): Abnormal nutritional laboratory values related to chronic anemia and high doses of medications for lupus as evidenced by low Hgb, normal serum ferritin, and GI bleeding.

Interventions: Food-nutrient delivery—encourage nutrient-dense foods and frequent snacks; avoid fasting. Education about low-calorie, nutrient-dense foods and timing with medications. Counseling about timing of medications with food to reduce GI bleeding. Coordinate care with medical and nursing teams to review medications and determine which, if any, could be changed to reduce impact on GI tract.

Monitoring and Evaluation: No additional GI bleeding or distress. Resolution or improvement of anemia. Hgb closer to normal.

INTERVENTION

OBJECTIVES

- Prevent infections or sepsis.
- Reduce fever and excessive inflammation.
- Lessen bleeding tendencies and hemorrhages.
- Ensure adequate periods of rest. Simplify meal planning if needed.
- Prepare for bone marrow transplantation, if needed.
- Prevent further complications and decline in organ functioning.

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Modifications of hepcidin gene expression suggest a key role for hepcidin in iron homeostasis. HAMP is the gene that encodes hepcidin.

Clinical/History

Height
Weight
Body mass index (BMI)
Diet history
Intake and output (I & O)
Blood pressure (BP)
Fatigue and weakness
Headache, irritability

Lab Work

Complete blood count (CBC)
RBC count
Serum hepcidin level
Total iron-binding capacity (TIBC) (low)
Hgb and Hct (H & H) (high)
Serum ferritin (high)
Serum Fe
Glucose (Gluc)
Transferrin (low)
Albumin (Alb)
C-reactive protein (CRP)

FOOD AND NUTRITION

- Provide a balanced diet that is easily prepared, with six small feedings.
- Provide extra fluid unless contraindicated.
- If steroids are used, limiting sodium intake may be needed.
- Correct iron overload where present.

Common Drugs Used and Potential Side Effects

- Genetically engineered erythropoietin (epoetin) is often used; given weekly, it can improve quality of life and levels of energy.
- Avoid iron supplements in this condition; they can be harmful and even result in death.
- Corticosteroids may be used. Watch side effects of chronic use such as elevated serum sodium levels, decreased potassium and calcium levels, and negative nitrogen balance. Hyperglycemia may occur; alter diet accordingly.
- Antibiotics may be required when infections are present. Monitor for GI distress and other effects.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.
- Alpha tocopherol and *N*-acetylcysteine have been recommended, but more controlled studies are needed.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Discuss needs of the patient, which are specific for signs, symptoms, and side effects of any medications.
- Discuss nutritious meal planning. If patient has diabetes, heart failure, or cirrhosis, counsel specifically for those issues.
- Correcting anemia in heart failure patients improves quality of life and exercise capacity in both men and women (Fox and Jorde, 2005). Once improvement is noted, activity levels can be increased.
- Counsel about reduction of iron overload if present. For example, iron-fortified cereals and oral supplements containing iron should be avoided. Increase grains, fruits, vegetables, cheese, and dairy foods; use fewer heme iron sources.
- Being female is often independently associated with lower Hgb, so assess using sex-specific laboratory values (Fox and Jorde, 2005).

Patient Education—Food Safety

If tube feeding or central parenteral nutrition (CPN) is needed, careful handwashing procedures should be followed.

For More Information

- Anemia of Chronic Disease
  http://www.emedicine.com/emerg/topic734.htm

ANEMIA OF CHRONIC DISEASE—CITED REFERENCES

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ANEMIAS IN NEONATES

NUTRITIONAL ACUITY RANKING: LEVEL 2

DEFINITIONS AND BACKGROUND

Anemia of prematurity (AOP) is a normocytic, normochromic anemia that presents with very low Hgb and low erythropoietin level. Inadequate RBC production may occur, and the average life span of these cells is about 35–50 days (compared with 120 days for adults). Three causes of AOP include inadequate RBC production, shortened RBC life span, or blood loss. AOP is very common among those born prematurely, where prevalence may be as high as 50% in those born before 32 weeks of gestation. It is also especially common in those born with weight below 1500 g (Haiden et al, 2006).

Hemolytic disease of the newborn (erythroblastosis fetalis) is a condition in which RBCs are broken down or destroyed more rapidly than normal, causing hyperbilirubinemia, anemia, or death; hemolytic disease of the newborn may occur in Rh-positive babies born to Rh-negative mothers (Merck Manual, 2009). Critically ill, extremely premature infants develop anemia because of intensive laboratory blood testing and undergo multiple RBC transfusions in the early weeks of life (Widness et al, 2005). Poor weight gain, apnea and tachypnea, lethargy, tachycardia, and pallor are symptoms.

Reducing anemia in infants may be a preventive measure to lower disease burden from infectious disease in this vulnerable population (Levy et al, 2005). Nutritional deficiencies of vitamin E, vitamin B_{12}, and folate exaggerate the degree of anemia. Vitamin E supplementation, however, when given to preterm infants, does not reduce the severity of this anemia. Administration of vitamin B_{12} and folate with erythropoietin and iron may enhance erythropoietin-induced erythropoiesis more than erythropoietin alone (Haiden et al, 2006).

When detected early in pregnancy, iron-deficiency anemia is associated with a greater risk of preterm delivery (Scholl, 2005). However, it is important not to overdo iron intake. High levels of Hgb, Hct, and ferritin are associated with an increased risk of fetal growth restriction, preterm delivery, and preeclampsia (Scholl, 2005).

Diamond-Blackfan anemia (DBA) (erythrogenesis imperfecta or congenital hypoplastic anemia) is a rare blood disorder characterized by deficiency of RBCs at birth. Other symptoms including slow growth, abnormal weakness, fatigue, pallor, characteristic facial abnormalities, protruding shoulder blades, abnormal shortening of the neck due to fusion of cervical vertebrae, hand deformities, and congenital heart defects. DBA may be inherited as either an autosomal dominant or recessive genetic trait, where the body's bone marrow produces little or no RBCs. A genetic error on chromosome

19 is associated with about 25% of cases, and there is a family history of the disorder in 10–20% of cases.

DBA affects approximately 600–700 million people worldwide but can be difficult to identify. The symptoms may also vary greatly, from very mild to severe and life threatening. DBA is usually diagnosed within the first 2 years of life, sometimes even at birth, on the basis of symptoms. The diagnosis of this anemia might not be recognized right away, however, because it is rare.

The first line of treatment for DBA is prednisone. About 70% of children with DBA will respond to this long treatment, where the medication stimulates the production of more RBCs. If steroids do not work, the next treatment is blood transfusions. Regular blood transfusions will provide RBCs but can lead to iron overloading. Normally, the body uses iron when making new RBCs, but since the person with DBA is not making many cells, the iron builds up. The person then needs to take medication that takes the excess iron out of the body. The only cure available for DBA is bone marrow transplantation. Stem-cell transplantation with human leukocyte antigen (HLA)-matched stem cells has been used for DBA (Kuliev et al, 2005).

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Anemia in a newborn may be caused by a genetic condition such as congenital hypoplastic anemia. In DBA, a genetic alteration on chromosome 19 has been noted.

Clinical/History

Height
Weight
BMI
Diet history
Slow growth in child (low height–weight percentiles)
BP
Weakness
Fatigue and pallor
I & O

Lab Work

CBC
RBC count
H & H (>2 standard deviations below mean for age)
Serum Fe and ferritin
Gluc
Alb
CRP
Serum folic acid and B_{12}
K^+, Na^+
Calcium

INTERVENTION

OBJECTIVES

- Provide improved oxygenation for tissues.
- Prevent infections or sepsis. Reduce fevers or excessive inflammation.
- Control hyperglycemia or other side effects of treatments.

SAMPLE NUTRITION CARE PROCESS STEPS

Inadequate Vitamin-Mineral Intake

Assessment Data: Low birth weight (1450 g), poor suck. Lab work shows low Hgb and serum B_{12}; diagnosis of anemia. Pallor, listlessness, and tachycardia.

Nutrition Diagnoses (PES): Inadequate vitamin and mineral intake related to poor suck and low birth weight as evidenced by lab work with low Hgb and serum B_{12}. Inadequate weight gain.

Interventions: Nutrient delivery—specialized infant formula with added calories and administration of vitamin B_{12}, folate, erythropoietin and iron.

Monitoring and Evaluation: Improvement in heart rate, growth, and pallor. Resolution of anemia.

- Prevent further complications.
- Support growth.

FOOD AND NUTRITION

- Provide an appropriate formula that is easily prepared, with small feedings given frequently.
- Provide extra fluid unless contraindicated.

Common Drugs Used and Potential Side Effects

- If corticosteroids are used, watch side effects of chronic use such as elevated serum sodium levels, decreased potassium and calcium levels, and negative nitrogen balance. Hyperglycemia may occur; alter diet accordingly. Besides diabetes, glaucoma, bone weakening, and high blood pressure can occur, and the medication may suddenly stop working for that person at any point in time.
- Antibiotics may be required when infections are present. Monitor for gastrointestinal distress and other side effects.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Discuss needs of the patient, which are specific for signs and symptoms and for side effects of any medications.
- Discuss nutritious meal planning.
- If patient has diabetes, counsel specifically for nutritional management.
- Activity levels must be restricted to avoid accidents or falls that could promote bleeding.
- Referral to the Women, Infants, and Children (WIC) Program can be beneficial. WIC programs are helpful in

improving Hgb concentration among young children (Altucher et al, 2005). Age-specific values should be used to assess progress:

Age-Specific Values for Hemoglobin and Hematocrit

Age	Hb (g/dL)	Hct (%)
28-week gestation	14.5	45
32-week gestation	15	47
Term	16.5	51
1–3 days	18.5	56
2 weeks	16.6	53

Source: Merck Manual, http://www.merck.com/mmpe/print/sec19/ch273/ch273b.html, accessed December 22, 2009.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- Anemia of Prematurity
  http://www.emedicine.com/ped/topic2629.htm
- Diamond Blackfan Anemia
  http://www.diamondblackfan.org.uk/
- Perinatal Anemia
  http://www.merck.com/mmpe/sec19/ch273/ch273b.html

ANEMIAS IN NEONATES—CITED REFERENCES

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ANEMIA OF RENAL DISEASES

NUTRITIONAL ACUITY RANKING: LEVEL 2

DEFINITIONS AND BACKGROUND

Anemia of renal disease occurs in both acute and chronic renal disease. This type of anemia is often normochromic, normocytic, and sometimes microcytic. When the kidneys become diseased, scar tissue forms and prevents the cells that make erythropoietin from functioning. The buildup of uremic toxins and decreased erythropoietin production adversely affects erythropoiesis. The accumulation of toxic metabolites, which are normally excreted by the kidneys, shortens the life span of circulating RBCs. Management is complicated by a vicious circle of cardiorenal anemia syndrome in which CKD, heart failure, and anemia exacerbate each other (Besarab et al, 2009).

There is an inverse relationship between blood urea nitrogen (BUN) levels and RBC life span, but there is also diminished renal production of erythropoietin. If no cause for anemia other than chronic kidney disease is detected on the basis of the workup and the serum creatinine is ≥2 mg/dL, anemia is most likely due to erythropoietin deficiency; measurement of serum erythropoietin levels is not needed.

Anemia usually starts during the third stage of renal disease, when glomerular filtration rate (GFR) is below 60 cc/minute but before dialysis has started. Short daily hemodialysis and daily home nocturnal hemodialysis can control blood pressure and manage anemia in this population (Pierratos, 2005). Correction of anemia appears to improve cardiac function and quality of life without a greater risk for adverse events (Besarab et al, 2009).

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: In disorders such as type-2 diabetes, chronic kidney disease is common. Anemia may be present and cause fatigue and difficulty with daily activities such as climbing stairs.

Clinical/History	Lab Work	
Height	CBC and RBC count	[a]Transferrin saturation (serum iron × 100 ÷ TIBC) <20%?
Weight	Serum Fe	[b]Reticulocyte hemoglobin content (CHr)
BMI	Hgb (may be <12 g/dL)	Serum soluble transferrin receptor (sTfR)—elevated?
Diet history	Hct (often <33%)	
BP	Serum ferritin: (100 absolute deficiency; overload >800 ng/dL	
I & O	TIBC	
Weakness		
Fatigue and pallor		
Dizziness		
Difficulty concentrating		
Shortness of breath		

Gluc	Test for occult blood	Creatinine (Creat)
Alb	Blood urea nitrogen (BUN)	
CRP		
Serum folic acid and B_{12}		

[a]The best indicator for iron availability for erythropoiesis.
[b]Half-life of reticulocytes is 1 day; it represents immediate availability of bone marrow iron.

INTERVENTION

OBJECTIVES

- Prevent infections or sepsis. Reduce fever and excessive inflammation.
- Prevent further complications such as heart failure. Fluid may accumulate and build up in the lungs and liver.
- Support growth in children.
- Improve energy level and decrease fatigue, irritability, and infections.

FOOD AND NUTRITION

- Provide a balanced diet that is easily prepared, with small feedings given frequently.
- Provide extra fluid unless contraindicated.
- Provide sufficient foods rich in iron and B-vitamins, as appropriate (depending on laboratory values, current status, predialysis, or dialysis).

Common Drugs Used and Potential Side Effects

- Iron therapy is effective in 30–50% of patients with CKD. A serum ferritin concentration of 100–500 ng/mL is the target during oral and IV iron therapy for predialysis and peritoneal dialysis patients. IV administration and a target serum ferritin concentration of 200–500 ng/mL is recommended for hemodialysis patients (Besarab et al, 2009; Grabe, 2007).
- Erythropoietin Stimulating Agents (ESAs) are given when Hgb falls below 10 g/dL. Epoetin (EPO) is used when oral iron therapy fails (Nurko, 2006). This can be given every week, or every 2 weeks, or monthly. The two formulations of EPO, epoetin alpha (ProCrit) and darbepoetin (Aranesp, DPO), are effective. Longer half-life of darbepoetin alpha permits administration on a once-monthly basis in patients with CKD and anemia (Grabe, 2007). A recent addition is methoxypolyethylene glycol-epoetin beta (Mircera) that has a longer half-life and can be given every 2 weeks.
- Iron deficiency and inflammation are possible causes of inadequate response to ESAs (Grabe, 2007). In the iron-replete patient with an inadequate response to epoetin, the following conditions should be evaluated and treated, if reversible: infection or inflammation (AIDS, lupus); chronic blood loss; aluminum toxicity; hemoglobinopathies (thalassemias, sickle cell anemia); folate or vitamin B_{12} deficiency; multiple myeloma; malnutrition; or hemolysis.
- Ferric gluconate maintains Hgb and allows lower epoetin doses in anemic hemodialysis patients with low TSAT and ferritin levels up to 1200 ng/mL (Kapoian et al, 2008).
- Parenteral iron is reserved for dialysis patients or those who are intolerant of oral iron. Iron dextran (In-FeD, Dexferrum), sodium ferric gluconate (Ferrlecit), and iron sucrose (Venofer) are available. Ferumoxytol is a new IV iron preparation for CKD (Schwenk, 2010). Iron dextran may cause serious allergic reactions.
- Vitamin C helps increase absorption. Dairy and antacids decrease absorption.
- Docusate helps alleviate constipation. Iron supplements can darken stools.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician. Because the use of CAM is increasing among children and adults with chronic illnesses, efforts should be made to identify those therapies that are beneficial, harmless, and cheap for possible integration with conventional therapy (Oshikoya et al, 2008). Adverse side effects are possible.

SAMPLE NUTRITION CARE PROCESS STEPS

Inadequate Vitamin Intake

Assessment Data: CKD with low erythropoietin production; Hgb >12 and Hct >33% with EPO. Serum folic acid and vitamin B_{12} levels remain low. Physical signs of vitamin deficiency.

Nutrition Diagnoses (PES): Inadequate vitamin intake related to poor oral intake as evidenced by diet history, recent anorexia, low serum levels of B_{12} and folate, and minimal use of prescribed water-soluble vitamins.

Interventions: Food-Nutrient Delivery—In addition to EPO and iron, use vitamin B_{12} and folic acid supplements. Educate about the need to use the supplements daily and to retest lab work every 3–6 months. Counseling about good food sources of folic acid and vitamin B_{12}.

Monitoring and Evaluation: Lab work showing normal B_{12} and folic acid levels. Fewer complaints of fatigue; no physical signs of vitamin deficiency.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Discuss needs of the patient that are specific for signs and symptoms and side effects of any medications.
- Discuss simplified, but nutritious, meal planning.
- If patient has diabetes, heart failure, or cirrhosis, counsel specifically for nutritional management.
- Activity levels must be restricted to avoid accidents or falls that could promote bleeding.

- People who take EPO shots should have regular tests to monitor their Hgb. If it climbs above 12 g/dL, their doctor should prescribe a lower dose of EPO.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- American Association of Kidney Patients
  http://www.aakp.org/aakp-library/Anemia-in-Chronic-Kidney-Disease/
- National Institute of Diabetes and Digestive and Kidney Diseases–Anemia
  http://kidney.niddk.nih.gov/kudiseases/pubs/anemia/
- National Kidney Foundation – Anemia
  http://www.kidney.org/Atoz/pdf/anemia.pdf

ANEMIA OF RENAL DISEASES—CITED REFERENCES

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APLASTIC ANEMIA AND FANCONI'S ANEMIA

NUTRITIONAL ACUITY RANKING: LEVEL 1

DEFINITIONS AND BACKGROUND

Aplastic anemia is a rare bone marrow disorder with normocytic, normochromic anemia in which normal marrow is replaced with fat. Aplastic anemia, myelodysplastic syndromes, and paroxysmal nocturnal hemoglobinuria (PNH) occur when the bone marrow stops making healthy blood-forming stem cells that produce RBCs, white blood cells, and platelets. Telomeres, repeat sequences at the ends of chromosomes, are protective chromosomal structures that shorten with every cell cycle; aplastic anemia is associated with inherited mutations in telomere repair or protection genes (Calado, 2009).

In about 50% of cases, the cause may be inherited or due to autoimmunity. In other cases, exposure to toxic agents (e.g., radiation, heavy metals, inorganic arsenic) or use of drugs (e.g., phenylbutazone, chloramphenicol, anticonvulsants) may be the cause. Use of interferon-gamma (IFN-γ) may be responsible for certain aspects of the pathology seen in bone marrow failure syndromes, including aplastic anemia (Zeng et al, 2006). Signs and symptoms are listed in Table 12-5.

Treatment includes blood transfusion, preventive antibiotics, careful handwashing, hormone therapy, immunosuppressive therapy, and medications to enhance bone marrow cell production. Severe aplastic anemia (SAA) is life threatening and can be treated with bone marrow transplantation, immunosuppressive therapy, and high-dose cyclophosphamide (Brodsky et al, 2009). Resolution of iron overload (such as serum ferritin >1000 ng/mL) should be addressed before transplant because it may lead to lethal infections (Storey et al, 2009).

Fanconi's anemia (FA) is a rare, genetic disorder characterized by multiple congenital anomalies, progressive bone marrow failure, and an increased prevalence of leukemia or liver cancer (Fagerlie and Bagby, 2006). FA is characterized by delayed bone marrow failure with progression to aplastic anemia. It may be apparent at birth or between ages 2 and 15 and is characterized by deficiency of all bone marrow elements including RBCs, white blood cells, and platelets (pancytopenia). FA is associated with cardiac, kidney, or skeletal abnormalities as well as vitiligo or patchy, brown discolorations (pigmentation changes) of the skin. There are

TABLE 12-5 Signs and Symptoms of Aplastic or Fanconi's Anemias

Blood in stool
Bronzing of skin (café au lait spots)
Dizziness
Headache, irritability
Hemorrhagic diathesis (gums, nose, GI tract, urinary tract, vagina)
Hemosiderosis with resulting cirrhosis, diabetes, heart failure
Increasing fatigue and weakness
Increasing or persistent infections
Irritability
Missing or horseshoe kidney (FA)
Missing or misshapen thumbs (FA)
Nausea
Oral thrush or lesions
Petechiae, ecchymosis
Scoliosis
Skeletal anomalies of spine, hips, ribs (FA)
Slow thought processes, headache
Small head, low birth weight (FA)
Tachycardia, tachypnea, dyspnea
Waxlike pallor

several different subtypes, each of which results from abnormal mutations of different genes. Prognosis is poor among those individuals with low blood counts. Treatment of FA involves transfusions, bone marrow transplantation, or gene therapy. FA patients do not tolerate radiation well and are prone to cancers, even after transplantation. Currently, life span is not long; many children do not survive to adulthood.

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: In Caucasians, genetic variations in IFNG may be found. Mutations TERC and TERT genes are also seen in aplastic anemia. The FANCM or FNACJ gene mutations are responsible for some forms of Fanconi's anemia.

Clinical/History	Lab Work	
Height	RBC count (decreased)	White blood cell (WBC) count (<1500)
Weight	Prothombin time (PT)	Alb, transthyretin
BMI	Serum Fe	CRP
Diet history	Gluc	Alanine amino-transferase (ALT)
BP	Granulocytes (decreased)	Aspartate aminotrans-ferase (AST)
GI problems	Transferrin	Bilirubin
See Table 12-5 also	H & H	
Bone marrow biopsy	Platelets (decreased)	
Ultrasound		
Hand x-ray or CT scan		

SAMPLE NUTRITION CARE PROCESS STEPS

Self-Feeding Difficulty

Assessment Data: Low BMI, medical hx with diagnosis of Fanconi's anemia, misshapen thumbs with difficulty holding utensils.

Nutrition Diagnoses (PES): Self-feeding difficulty (NB-2.6) related to hand deformity as evidenced by low BMI and difficulty consuming enough at mealtimes.

Interventions: Food-nutrient delivery—add extra kilocalories to foods and recipes, such as extra fats and carbohydrates. Include extra protein-rich foods as tolerated between meals. Serve finger foods and beverages that can be taken through a straw (milkshake, eggnog). Educate parents about changes in menus and foods for greater intake of nutrient and energy-dense foods. Counsel for ways to enhance self-feeding with use of adaptive feeding equipment.

Monitoring and Evaluation: Improvement in BMI over time and better intake from nutrient and energy-dense foods. Enhanced skills using adaptive feeding tools.

INTERVENTION

OBJECTIVES

- Prevent infections or sepsis. Reduce fevers.
- Reduce bleeding tendencies and hemorrhages.
- Ensure adequate periods of rest.
- Prepare for splenectomy or bone marrow transplantation.
- Prevent further complications, where possible, and decline in cardiovascular and hepatic functions.

FOOD AND NUTRITION

- Replenish nutrient stores.
- Provide a balanced diet that is easily prepared, with six small feedings.
- Provide extra fluid unless contraindicated (35 cc/kg or more).
- If patient has mouth lesions, avoid excesses of hot or cold foods, spicy or acidic foods, or foods with rough textures.
- If steroids are used, limit sodium intake.

Common Drugs Used and Potential Side Effects

- Growth factors (erythropoietin, G-CSF, and GM-CSF) may help to improve blood counts.
  - Corticosteroids may be used. Side effects of chronic use include elevated serum glucose and sodium levels, decreased potassium and calcium levels, and negative nitrogen balance.
  - High-dose cyclophosphamide is highly effective therapy for SAA, but large randomized controlled trials are necessary to compare with either bone marrow transplantation or use of antithymocyte globulin and cyclosporine (Brodsky et al, 2009).
  - Antibiotics may be required for infections; monitor for GI distress and other side effects.
  - Aspirin should be avoided because it may aggravate blood losses. Other drugs that may aggravate the condition include chloramphenicol, phenylbutazone, sulfa drugs, and ibuprofen. Each of these has specific GI side effects that should be monitored (see index for more information).
  - A list of drugs that can cause acquired aplastic anemia is found at http://www.wrongdiagnosis.com/a/aplastic_anemia/medic.htm#medication_causes_list

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

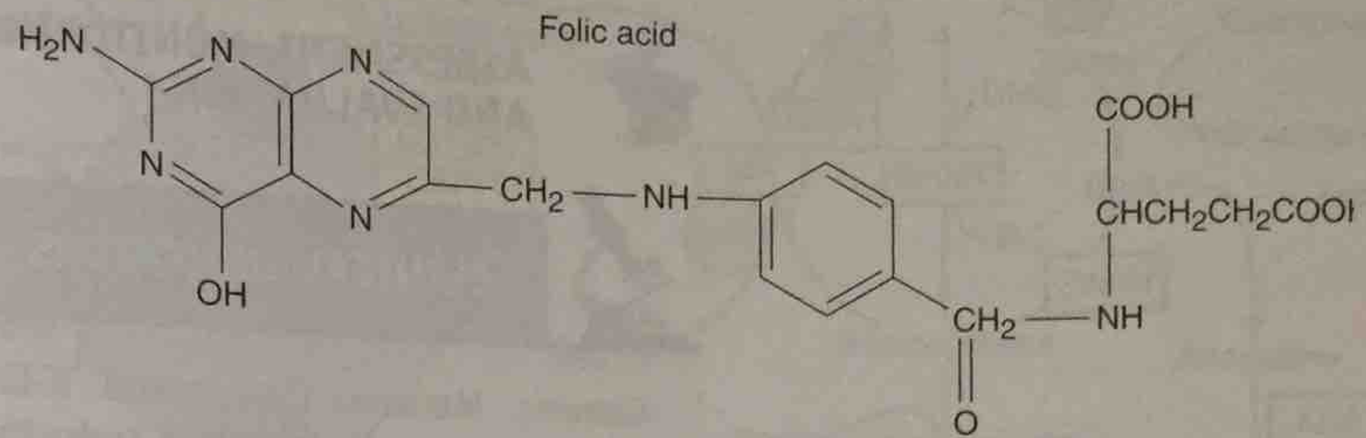
NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Discuss needs of the patient, which are specific for signs and symptoms and for side effects of any medications.
- Discuss simplified, but nutritious, meal planning.

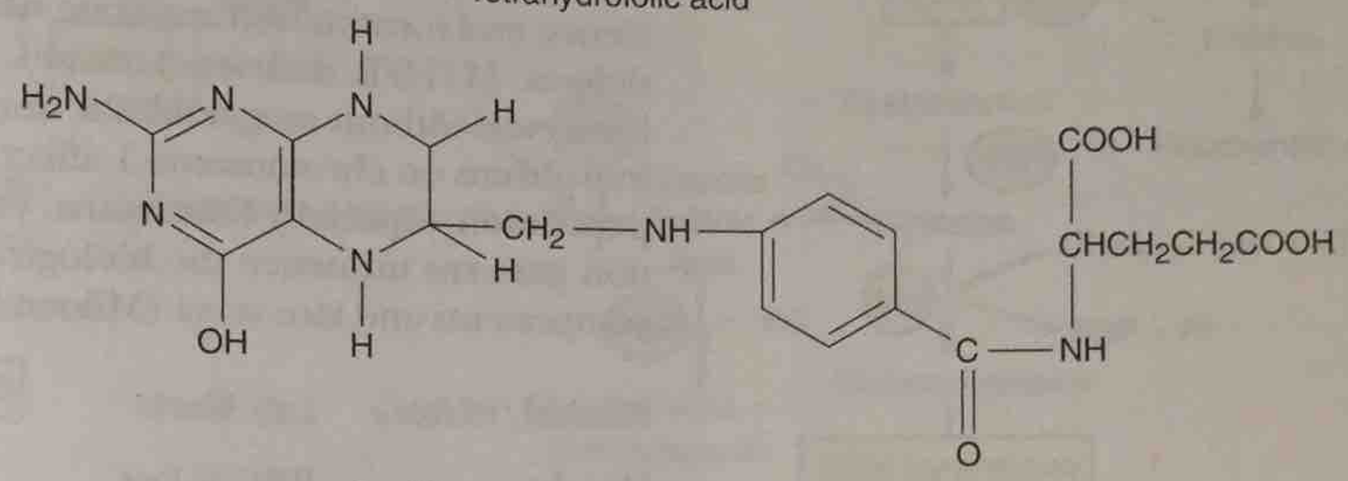
FOLIC ACID DEFICIENCY ANEMIA

NUTRITIONAL ACUITY RANKING: LEVEL 2

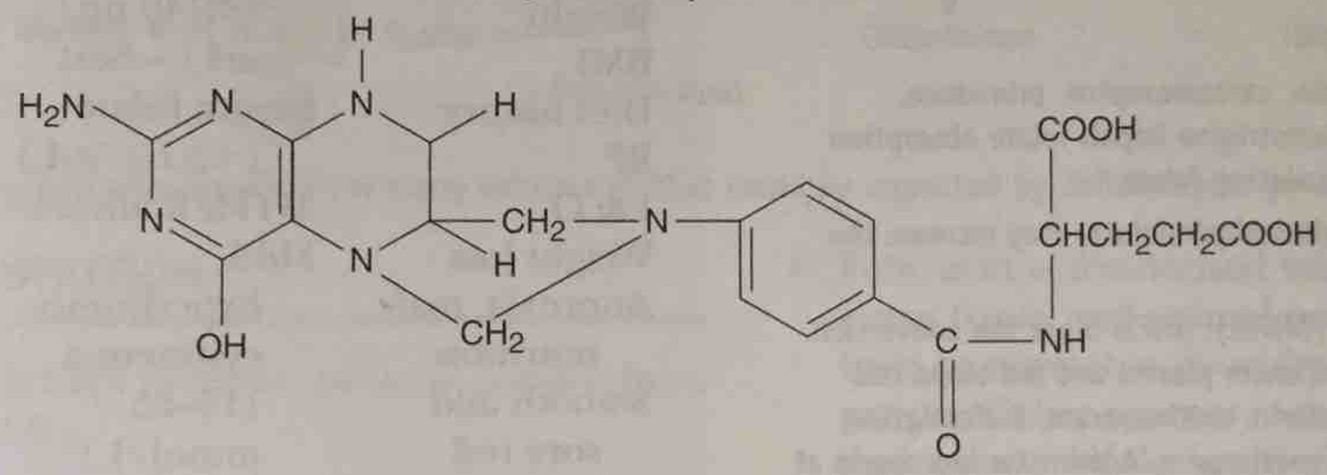
Folic acid



Tetrahydrofolic acid



N^5, N^{10}-methylenetetrahydrofolic acid



Three steps for metabolism of dietary folic acid to the bioavailable form.

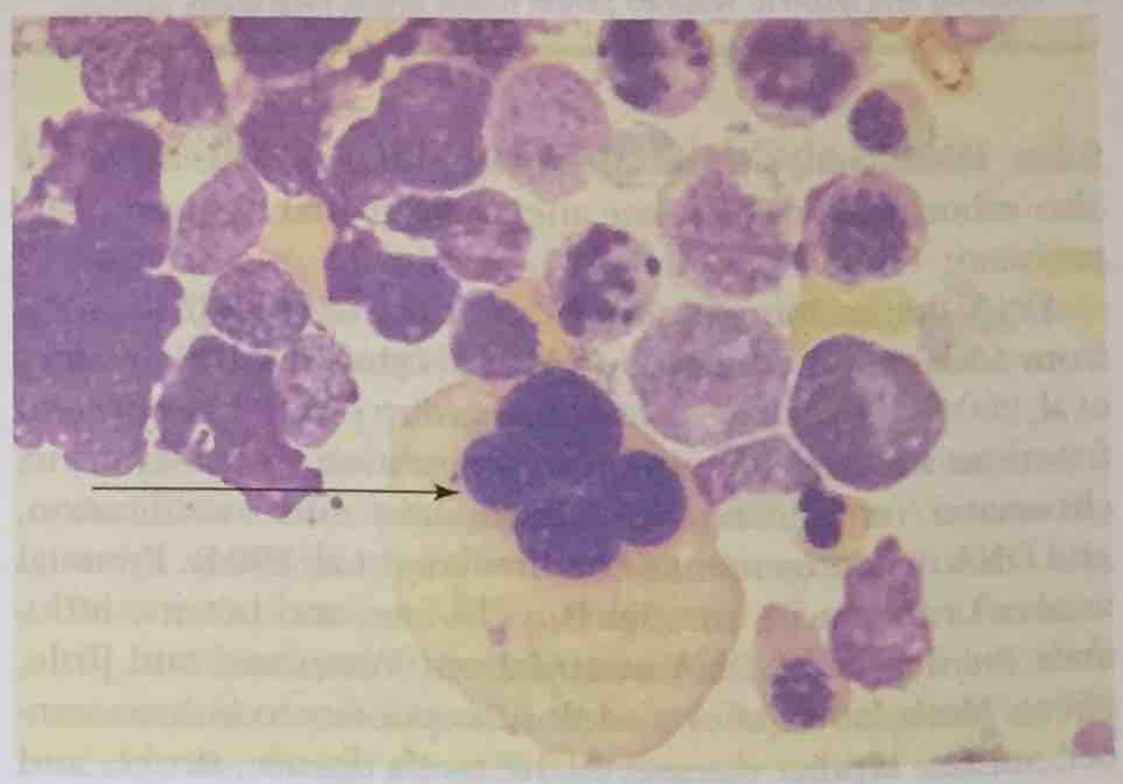
DEFINITIONS AND BACKGROUND

Folic acid is composed of a pterin ring connected to *p*-aminobenzoic acid (PABA). Humans do not generate folate because they cannot synthesize PABA. The amino acid histidine is metabolized to glutamic acid. Formiminoglutamic acid (FIGLU) is an intermediary in this reaction, and tetrahydrofolic acid is the coenzyme that converts it to glutamic acid. Under normal conditions, sufficient intake of dietary histidine can prevent anemia. When dietary intake of histidine is diminished or urinary excretion is greatly increased, anemia results. Folate deficiency depletes histidine through increased urinary excretion.

Folic acid is needed for the synthesis of DNA and maturation of RBCs. Deficiency of folate can lead to many clinical abnormalities, including macrocytic anemia, cardiovascular diseases, birth defects, and carcinogenesis (including colorectal cancer). Folic acid-deficiency anemia generally is caused by inadequate diet, intestinal malabsorption, alcoholism, or pregnancy (Table 12-8).

Folic acid deficiency yields a hyperchromic, macrocytic, megaloblastic anemia. Because similar hematological changes occur with vitamin B_{12} deficiency, it is important to check the serum levels of vitamin B_{12} along with folate tests. Folate is best measured by RBC folate because serum levels are misleading and reflect more recent intake.

Homocysteine elevation is a risk factor for vascular and thrombotic disease. Genetic and acquired influences have been evaluated. While neural tube defects result from maternal



Folic acid anemic cells are hypochromic and macrocytic. Adapted from: *Anderson's Atlas of Hematology;* Anderson, Shauna C., PhD. Copyright 2003, Wolters Kluwer Health/Lippincott Williams & Wilkins.

TABLE 12-8 Conditions and Medications That Deplete Folic Acid

Aging
Alcoholism
Blind-loop syndrome
Burns
Cancers
Celiac disease
Crohn's disease
Dialysis
Elevated homocysteine levels
Hemolytic anemias
Hepatitis
Infection
Inflammatory diseases
Malabsorption
Megacolon
Pregnancy and lactation
Smoking
Stress
Surgery
Medications that interact with folic acid:

- Antiepileptic drugs (AED): phenytoin, carbamazepine, primidone, valproic acid, phenobarbital, and lamotrigine impair folate absorption and increase the metabolism of circulating folate
- Capecitabine: Folinic acid (5-formyltetrahydrofolate) may increase the toxicity of Capecitabine
- Dihydrofolate reductase inhibitors (DHFRI): DHFIs block the conversion of folic acid to its active forms, and lower plasma and red blood cell folate levels. DHFIs include aminopterin, methotrexate, sulfasalazine, pyrimethamine, triamterene, and trimethoprim. Administer leucovorin at the same time
- Nonsteroidal anti-inflammatory drugs (NSAIDs): NSAIDs inhibit some folate dependent enzymes. NSAIDs include ibuprofen, naproxen, indomethacin, and sulindac
- Cholestyramine, Colestipol, Cycloserine, Isotretinoin, oral contraceptives, Methylprednisolone, pancreatic enzymes, Pentamidine, Sulfasalazine either decrease folic acid absorption or increase excretion
- Smoking and alcohol: reduced serum folate levels may occur

folate insufficiency in the periconceptual period, there are also inborn errors of folate metabolism that aggravate the problem.

DNA methylation occurs by transfer of a methyl group from *S*-adenosylmethionine (SAM) to cytosine (Abdolmaleky et al, 2004). SAM serves as a methyl group donor in important functions such as changing norepinephrine to epinephrine, chromatin remodeling, RNA inhibition and modification, and DNA rearrangement (Abdolmaleky et al, 2004). Prenatal intakes of folic acid, vitamin B_{12}, choline, and betaine influence the degree of DNA methylation (Waterland and Jirtle, 2004). Methylation affects adult susceptibility to asthma, cancer, autism, bipolar disease, Alzheimer's disease, stroke, and schizophrenia.

Folate deficiency can result in congenital neural tube defects and megaloblastic anemia; inadequacy is associated with high blood levels of the amino acid homocysteine, which has been linked with the risk of arterial disease, dementia, and Alzheimer's disease (Malouf et al, 2008). Decreasing or low levels of folic acid may also be associated with depression in older adults.

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

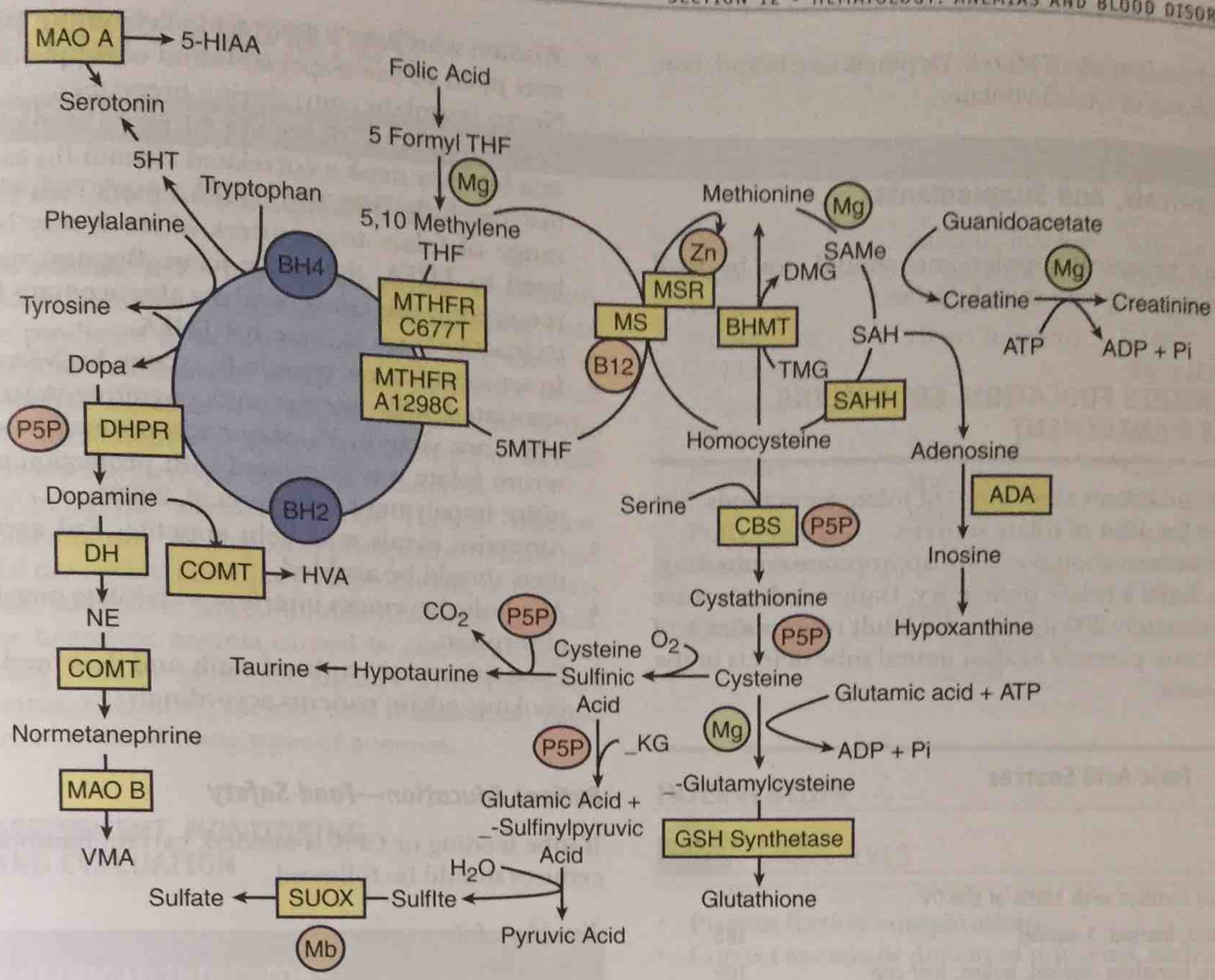
Genetic Markers: Congenital folate malabsorption, methylenetetrahydrofolate reductase (MTHFR) deficiency, and formiminotransferase deficiency are genetic defects. MTHFR deficiency causes neurological problems even without megaloblastic anemia. MTHFR polymorphisms on chromosome 1 affect 10% of the world's population, especially Caucasians. Varied DNA methylation patterns influence the biological response to food components and vice versa (Milner, 2006).

Clinical/History	Lab Work	
Height	RBC folate (<140 ng/mL) – best	Serum Fe (increased)
Weight	Serum folate (<3 ng/mL)	Mean cell volume (MCV)
BMI	MTHFR alleles?	Leukopenia, WBC
Diet history	Mild hyperhomocystinemia (15–25 mmol/L)	Urinary formiminoglutamic acid (FIGLU) after histidine load
BP	Moderate hyperhomocystinemia (26–50 mmol/L)	Serologic testing for parietal cell and intrinsic factor (IF) antibodies (vs. Schilling test)
I & O	Low RBC	
Weight loss	H & H	
Anorexia, malnutrition	CBC (macrocytic cells)	
Smooth and sore red tongue	Transferrin	
Diarrhea	Serum B_{12}	
Fatigue, lethargy		
Poor wound healing		
Coldness of extremities		
History of alcohol abuse?		

INTERVENTION

OBJECTIVES

- Increase folate in diet and supplemental folic acid to alleviate anemia.
- Improve diet to provide nutrients needed to make RBCs: folate and other B-complex vitamins, iron, and protein. Instruct patient to correct faulty diet habits if relevant.
- Check for malabsorption syndromes (celiac disease, blind-loop syndrome, congenital or acquired megacolon, Crohn's disease) and correct these as far as possible through use of medications and other treatments.
- Monitor serum folic acid status regularly.



Folic acid-B_{12} pathway, showing the many substances that could be impacted by deficiency or genetic alterations.

FOOD AND NUTRITION

- Provide a diet that is high in folate, protein, copper, iron, and vitamins C and B_{12}.

SAMPLE NUTRITION CARE PROCESS STEPS

Inadequate Vitamin Intake and Food- and Nutrition–Related Knowledge Deficit

Assessment Data: Hx of MTHFR (C>T) allele and spina bifida in two infants. Diet Hx shows poor intake of folate from diet and no use of supplemental sources. Dislikes fruits and vegetables.

Nutrition Diagnoses (PES): Inadequate vitamin intake of folate (NI 5.9.1.9) related to lack of folic acid food sources in daily diet as evidenced by headache, fatigue, decreased serum and RBC folate, and giving birth to two infants with spina bifida in the past 5 years. Food and nutrition-related knowledge deficit (NB 1.1) related to lack of prior exposure and interest in accurate nutrition-related information as evidenced by daily intake lacking sources of folate, especially from fruits and vegetables.

Interventions: ND 3.2.1, 3.2.3.9—multivitamin/mineral supplement, folic acid supplement of additional 400 mcg/d. E 1.2—priority modifications to diet including addition of food sources rich in folic acid, basic information concerning food pyramid, and balanced meal planning.

Monitoring and Evaluation: One month follow-up visit acceptance of supplements, dietary recall for daily use of folic acid sources, and efficacy of personal meal planning for meeting basic nutrition needs/food pyramid servings.

- Folic acid is distributed widely in green leafy vegetables, citrus fruits, and animal products. Ingestion of one fresh fruit or vegetable provides sufficient folic acid for most people. Other sources include fish, legumes (dried beans and peas), whole grains, leafy dark green vegetables, broccoli, citrus juices, berries, and meats.
- Food manufacturers in the United States have fortified grains with folic acid since 1998. These fortified foods include most enriched breads, flours, corn meal, rice, noodles, macaroni, and other grain products.
- Diets that provide bland, liquid, or soft foods may be needed for patients with a sore mouth; six to eight small meals may be helpful.

Common Drugs Used and Potential Side Effects

- Supplements of folic acid (Folvite) are better than diet alone to alleviate the anemia. Folate deficiency is generally treated with 800–1000 μg of folic acid daily. Leucovorin is an active reduced form.
- Be aware of the interdependence between vitamin B_{12} and folic acid, especially in older individuals. Vitamin B_{12} helps methylate folic acid so that it can travel into cells. The transport form is 5-methyltetrahydrofolate. Because B_{12} deficiency can produce anemia similar to folate deficiency, there is a risk that folate supplementation can delay the diagnosis of B_{12} deficiency, which can lead to irreversible neurological damage (Malouf, 2009).
- 5-methyltetrahydrofolate is an option for supplementation and fortification without masking the anemia of vitamin B_{12} deficiency (Pentieva et al, 2004). Metafolin is a

registered trademark of Merck; Deplin is one brand, containing 7.5 mg of L-methylfolate.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Vitamin C promotes absorption of folate from foods. See Table 12-9 for a list of folate sources.
- Pregnant women should receive appropriate counseling; 30% may have a folate deficiency. Daily needs increase by approximately 200 μg over the adult requirements of 400 μg. Folate protects against neural tube defects in the first trimester.

TABLE 12-9 Folic Acid Sources

Source	Folic Acid (μg)
Breakfast cereals fortified with 100% of the DV	400
Beef liver, cooked, braised, 3 ounces	185
Black-eyed peas, immature, cooked, boiled, half cup	105
Spinach, frozen, cooked, boiled, half cup	100
Great Northern beans, boiled, half cup	90
Asparagus, cooked, four spears	85
Broccoli, cooked, half cup	84
Rice, white, long-grain, parboiled, enriched, cooked, half cup	65
Vegetarian baked beans, canned, one cup	60
Spinach, raw, one cup	60
Green peas, frozen, boiled, half cup	50
Broccoli, chopped, frozen, cooked, half cup	50
Egg noodles, cooked, enriched, half cup	50
Avocado, raw, all varieties, sliced, half cup sliced	45
Peanuts, all types, dry roasted, 1 ounce	40
Lettuce, Romaine, shredded, half cup	40
Wheat germ, crude, two tablespoons	40
Tomato Juice, canned, 6 ounces	35
Orange juice, chilled, includes concentrate, three-fourth cup	35

Derived from: NIH Fact Sheet, http://ods.od.nih.gov/factsheets/folate.asp, accessed December 27, 2009.

- Women who have a folic acid allele in the MTHFR gene may need to use a special brand of supplement, such as Neevo (pamlabs.com) during pregnancy.
- Large intakes of folic acid (>1 mg/d) can cure the anemia but may mask a correlated vitamin B_{12} anemia; monitor carefully. 5-methyl THFA enters cells via a diverse range of folate transporters where it may be demethylated to THFA, the active form. Because vitamin B_{12} is required in this conversion, its absence traps folic acid in its inactive form as 5-methyl THFA.
- In seniors with low vitamin B_{12} status, high-serum folate is associated with anemia and cognitive impairment but when not vitamin B_{12} status was normal; however, high-serum folate was associated with protection against cognitive impairment (Morris et al, 2009).
- Attractive meals may help appetite. Fad and restrictive diets should be avoided.
- Alcoholic beverages interfere with folate metabolism and absorption.
- Food folates are oxidized easily and destroyed by lengthy cooking; advise patients accordingly.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- E-medicine
  http://www.emedicine.com/med/topic802.htm
- Folic Acid Supplements
  http://ods.od.nih.gov/factsheets/folate.asp
- March of Dimes–Folic Acid Deficiency
  http://www.marchofdimes.com/professionals/19695_1151.asp

FOLIC ACID DEFICIENCY ANEMIA—CITED REFERENCES

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Milner JA. Diet and cancer: facts and controversies. *Nutr Cancer.* 56:216, 2006.

Morris MS, et al. Folate and vitamin B-12 status in relation to anemia, macrocytosis, and cognitive impairment in older Americans in the age of folic acid fortification. *Am J Clin Nutr.* 85:193, 2007.

Ng TP, et al. Folate, vitamin B12, homocysteine, and depressive symptoms in a population sample of older Chinese adults. *J Am Geriatr Soc.* 57:871, 2009.

Pentieva K, et al. The short-term bioavailabilities of [6S]-5-methyltetrahydrofolate and folic acid are equivalent in men. *J Nutr.* 134:580, 2004.

Waterland RA, Jirtle RL. Early nutrition, epigenetic changes at transposons and imprinted genes, and enhanced susceptibility to adult chronic diseases. *Nutrition.* 20:63, 2004.

HEMOLYTIC ANEMIAS

NUTRITIONAL ACUITY RANKING: LEVELS 2–3

DEFINITIONS AND BACKGROUND

In **hemolytic anemia,** RBCs have an abnormal membrane, which results in hemolysis. RBCs are destroyed faster than they can be produced in bone marrow. In severe cases in infancy, encephalomalacia can result. The incidence of all types of hemolytic anemias is 4 in 100,000 persons in the United States. Treatment may involve splenectomy or steroid use. Most are not affected specifically by vitamin E.

Types of hemolytic anemias include Hgb-SC disease, hemolytic anemia due to glucose-6-phosphate dehydrogenase (G6PD) deficiency, hereditary elliptocytosis, hereditary spherocytosis, idiopathic autoimmune hemolytic anemia, nonimmune hemolytic anemia caused by chemical agents, and secondary immune hemolytic anemia. This text covers aplastic anemia, sickle cell anemia, and thalassemia. Table 12-10 describes some of these types of anemias.

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Some types of hemolytic anemia have genetic links.

Clinical/History		
Height	BMI	BP
Weight	Diet history	Tachycardia
	Growth percentile	Shortness of breath
Dizziness	Fatigue, intolerance for exercise	Hgb in urine
Edema	Heart murmur	Hemosiderin in urine
Pallor		TIBC
Nosebleeds, bleeding gums	**Lab Work**	Bilirubin (elevated)
Dark urine	RBC (low)	Transferrin
Jaundice, splenomegaly	Hgb (low)	Gluc
Puffy eyelids	Reticulocyte count (increased)	AST (increased)
Weakness, confusion	Serum alpha-tocopherol levels	Blood test for G6PD
Chills		CRP

INTERVENTION

OBJECTIVES

- Prevent further complications.
- Correct anemia or deficits of nutrients, such as vitamin E.

FOOD AND NUTRITION

- Provide diet as usual for age and sex.
- Avoid excesses of iron.
- Ensure adequate intake of vitamin E and zinc, which may become deficient. Good sources of vitamin E include wheat germ, almonds, sunflower seeds, sunflower or safflower oil, peanut butter, peanuts, corn oil, spinach, broccoli, and

TABLE 12-10 Types of Hemolytic Anemia

Type	Description
Acquired autoimmune hemolytic anemia	A rare autoimmune disorder characterized by the premature destruction of RBCs. Normally, RBCs have a life span of 120 days before the spleen removes them, but in this condition, RBCs are destroyed prematurely. Bone marrow production of new cells can no longer compensate. This anemia occurs in individuals who previously had a normal RBC system. Patients with autoimmune hemolytic anemia usually are associated with thrombosis
Familial hemolytic jaundice (spherocytic anemia)	A hereditary anemia in which RBCs are shaped like spheres rather than their normal, donut-like shape. Jaundice and anemia occur from destruction of the abnormal cells by the spleen. Surgical removal of the spleen usually is indicated. There is no permanent cure
Glucose-6-phosphate dehydrogenase (G6PD) deficiency anemia	This anemia is seen in about 10% of African–American males in the United States and is also common in persons from the Mediterranean area or Asia. The severity differs among different populations. In the most common form in the African–American population, the deficiency is mild, and the hemolysis affects primarily older RBCs. In Caucasians, G6PD deficiency tends to be more serious because even young red blood cells are affected. It affects millions of people worldwide, especially in malaria-prone areas
Hereditary nonspherocytic hemolytic anemia	A group of rare genetic blood disorders characterized by defective RBCs (erythrocytes) that are not abnormally "sphere shaped" (spherocytes). Membranes of RBCs, abnormal metabolism of a chemical contained in hemoglobin (porphyrin), and deficiencies in certain enzymes such as G6PD or pyruvate kinase are thought to be the cause of these disorders
Vitamin E–sensitive hemolytic anemia	This condition may occur in infants who receive polyunsaturated fatty acids (PUFAs) without adequate vitamin E. Children with cystic fibrosis should be screened for vitamin E–deficient hemolytic anemia

SAMPLE NUTRITION CARE PROCESS STEPS

Unintentional Weight Loss

Assessment Data: BMI 20, recent weight loss 10#. GI distress and pallor noted. Diagnosis of hemolytic anemia with splenectomy planned.

Nutrition Diagnoses (PES): Unintentional weight loss related to GI distress and loss of appetite as evidenced by recent weight loss of 10# in 6 weeks.

Interventions: Prepare for splenectomy; use nutrient-dense and energy-rich foods as tolerated, such as milkshakes or eggnogs with or between meals. Educate patient about ways to enhance food intake while not feeling well.

Monitoring and Evaluation: Postoperative evaluations; return of appetite and improved intake. No further weight loss; eventual weight regained.

soybean oil. Good sources of zinc include oysters, beef shank, crab, pork, chicken, lobster, baked beans, cashews, and yogurt.

Common Drugs Used and Potential Side Effects

- For hemolytic anemia that is sensitive to vitamin E deficiency, water-soluble vitamin E (alpha-tocopherol) is likely to be given daily. Avoid taking with an iron supplement, which could interfere with utilization.
- Persons with G6PD deficiency need to avoid exposing themselves to certain medicines such as aspirin (acetylsalicylic acid), certain antibiotics used to treat infections, fava beans, and mothballs.
- Medicines can improve autoimmune hemolytic anemia (AIHA). Where prednisone is used, monitor for side effects. Monoclonal antibody therapy such as rituximab is used in difficult cases; it appears to be a safe and effective option (Hoffman, 2009).

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.
- Flavonoid preparations, marketed for a variety of effects and generally safe, should be evaluated carefully because there have been reports of toxic flavonoid–drug interactions, hemolytic anemia, and other problems (Galati and O'Brien, 2004).

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- For hemolytic anemia that is sensitive to vitamin E deficiency, discuss, in layman's terms, the role of vitamin E in lipid oxidation and utilization. Discuss sources of polyunsaturated fatty acids (PUFAs) and why excesses should be controlled. Discuss sources of vitamin E in the diet; natural sources are more bioavailable than synthetic sources.
- Discuss exercise tolerance and ability to eat sufficient amounts of food as related to fatigue.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- American Autoimmune Related Diseases Association, Inc. http://www.aarda.org
- Medline http://www.nlm.nih.gov/medlineplus/ency/article/000571.htm
- NIH – Hemolytic Anemias http://www.nhlbi.nih.gov/health/dci/Diseases/ha/ha_whatis.html

HEMOLYTIC ANEMIAS—CITED REFERENCES

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IRON-DEFICIENCY ANEMIA

NUTRITIONAL ACUITY RANKING: LEVEL 2

DEFINITIONS AND BACKGROUND

Hgb transports oxygen to the tissues and carbon dioxide back to the lungs where it is exhaled. Hgb levels are influenced by sex, age, altitude, and smoking. In the adult male and the elderly, iron deficiency is usually caused by chronic blood loss. In children and women, low intake of iron may be a problem. The nutrient most commonly deficient in the world is iron. Iron deficiency affects two billion people, mostly in developing countries (Lynch, 2005).

IDA results from inadequate intake, impaired erythropoiesis or absorption of iron, blood loss, or demands from closely repeated pregnancies (Table 12-11). Serious systemic consequences include impaired cognitive function, koilonychia, and impaired exercise tolerance. Hct is the measure of RBCs in a given volume of blood, packed by centrifuge. Transferrin is the carrier protein that picks up iron from the intestines.

Absorption of iron occurs in the ferrous form; storage is in the liver, spleen, and bone marrow. See Table 12-12 for

TABLE 12-11 Stages of Iron Deficiency

Stages of Iron Deficiency	Indicator	Diagnostic Range
Stage 1 Depletion of iron stores	Stainable bone marrow iron Total iron binding capacity Serum ferritin concentration	Absent >400 µg/dL <12 µg/L <20 µg/L + low Hb or Hct indicates iron deficiency
Stage 2 Early functional iron deficiency	Transferrin saturation Free erythrocyte protoporphyrin Serum transferrin receptor	<16% >70 µg/dL erythrocyte >8.5 mg/L
Stage 3 Iron deficiency anemia	Hemoglobin concentration Mean cell volume	<12 g/dL <80 fL

Adapted from: Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2002), Iron, p. 302 Food and Nutrition Board (FNB), Institute of Medicine (IOM).

content of iron in various body sources. Approximately 90% of the body's store of iron is reused. Diet replaces iron lost through sweat, feces, and urine. The duodenum (upper small intestine) is where iron is best absorbed. Damage or surgery of the duodenum can greatly inhibit total iron absorption, thus leading to greater risk of deficiency. Table 12-13 describes factors that can modify iron absorption.

IDA is the final stage of a long period of deprivation. Serum ferritin (storage form) is the most useful test to differentiate IDA from ACD. Iron deficiency is relatively common in toddlers, adolescent girls, and women of childbearing age. Ingestion of cow's milk causes occult intestinal blood loss in young infants. The Hgb content of reticulocytes (young RBCs) is a good indicator of iron deficiency and IDA in children. Risk of iron deficiency may be underestimated in high-risk populations.

Postpartum anemia is associated with breathlessness, tiredness, palpitations, and maternal infections, and blood transfusions and iron supplementation have been used in the treatment of IDA. Erythropoietin may be useful.

TABLE 12-12 Normal Iron Distribution in the Body

Forms	Men (mg iron/kg BW)	Women (mg iron/kg BW)
Storage—ferritin	9	4
Storage—hemosiderin	4	1
Transport protein: transferrin	<1	<1
Functional hemoglobin	31	31
Functional myoglobin	4	4
Enzymes	2	2
TOTAL	50	42

Based on data from: Insel P, Turner R, Ross D. *Nutrition*. Sudbury, MA: Jones & Bartlett Publishers, 2001.

TABLE 12-13 Factors That Modify Iron Absorption

Factor	Description
Physical state (bioavailability)	Heme > Fe^{2+} > Fe^{3+}
High gastric Ph	Hemigastrectomy, vagotomy, pernicious anemia, histamine H_2-receptor blockers, calcium-based antacids
Disruption of intestinal structure	Crohn's disease, celiac disease (nontropical sprue)
Inhibitors	Phylates, tannins, soil clay, laundry starch, iron overload
Competitors	Cobalt, lead, strontium
Facilitators	Ascorbate, citrate, amino acids, iron deficiency

From: Information Center for Sickle Cell and Thalassemic Disorders. Iron deficiency. Available at http://sickle.bwh.harvard.edu/fe-def.html.

Celiac disease may be present in children and is associated with IDA (Goel et al, 2005). In persistent IDA, screening for celiac disease (anti-tissue transglutaminase antibodies), autoimmune gastritis (gastric, anti-parietal, or anti-IF antibodies), and *Helicobacter pylori* (IgG antibodies and urease breath test) is recommended (Hershko and Ronson, 2009).

Because menstruation increases iron losses each month, women of childbearing age tend to become iron deficient. When there is not enough Hgb, free erythrocyte protoporphyrin (FEP) accumulates. Athletes are also at risk for iron deficiency. Recreational athletes should be screened for iron deficiency using serum ferritin, serum transferrin receptor, and Hgb (Sinclair and Hinton, 2005).

As many as 25% of children and 20% of those seen in mental health clinics have pica, which is characterized by persistent and compulsive cravings to eat nonfood items. Pica can occur in pregnant women, in autism, and in persons with brain injuries. Pica is seen in about half of patients with iron deficiency; it is a consequence of iron deficiency and is relieved by iron supplementation.

Exposure to lead also has a significant effect on Hgb and Hct levels. Serum levels above 50 mcg/dL are a problem. Lead poisoning reduces Hgb production, causes iron deficiency, and elevates FEP as the precursor.

Poor intake of vitamins A, B_{12}, C, and E, folic acid, and riboflavin is also linked to the development and control of IDA. Multiple micronutrient (MMN) supplementation during pregnancy reduces the risk of low birth weight, small-for-gestational age, and anemia; MMN supplementation improves CD4 counts and HIV-related morbidity and mortality in adults (Allen et al, 2009).

When Hgb levels are seriously low, the heart is particularly vulnerable. Anemia in heart failure patients is associated with reduced exercise tolerance, increased heart failure hospitalizations, and increased all-cause mortality (Stamos and Silver, 2009). Whole-blood transfusion or IV iron may be needed. Iron fortification of food is also a cost-effective method for reducing the prevalence of nutritional iron deficiency. In populations where young children are routinely fed cooked rice daily, fortifying it with iron helps improve iron status (Beinner et al, 2010).

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Mutations in a type-II serine protease, matriptase-2/TMPRSS6, are associated with severe iron deficiency caused by inappropriately high levels of hepcidin expression; hemojuvelin is a cell surface protein that regulates hepcidin expression (Lee, 2009).

Clinical/History

Weight
BMI
Diet history
BP
I & O
Pallor
Brittle, spoon-shaped fingernails (koilonychia)
Stool examination for occult blood
Impaired cognitive function
Blue sclerae
Impaired exercise tolerance
Weakness, fatigue
Vertigo
Headache, irritability
Heartburn
Dysphagia
Flatulence, vague abdominal pains
Anorexia
Diarrhea
Glossitis, stomatitis
Ankle edema
Tingling in extremities
Palpitations
Alopecia

Lab Work

Ferritin (decreased stores in liver, spleen, bone marrow; levels are <20 g/L)
Serum iron (low)
H & H (Hgb is more sensitive)
Mean cell Hgb (MCH) (decreased)
Mean cell Hct (MCHC) (decreased)
CBC (every 3–6 months after initial)
Transferrin (increased)
MCV (<80)
RBC (small, microcytic, hypochromic)
WBC/differential (increased)
TIBC (increased >350 μg/dL)
Reticulocyte count
Serum copper
Cholesterol (Chol)
Test for *H. pylori*

SAMPLE NUTRITION CARE PROCESS STEPS

Harmful Beliefs About Food

Assessment Data: Diet hx indicates pica during this pregnancy. Mom states that "the starch is good for my baby." Eats starch after each meal. Twenty-weeks pregnant; age 19. Low H & H.

Nutrition Diagnoses (PES): Harmful beliefs/attitudes (NB-1.2) about food or nutrition-related topics.

Interventions: Initial/Brief nutrition education (N.I.2.2) to provide basic nutrition-related educational about food and foods rich in iron; reasons to discontinue eating starch and to begin taking a prenatal vitamin. Counseling—work with client to set goals for a healthier pregnancy.

Monitoring and Evaluation: Improvement in H & H. Discontinuation of pica. Positive pregnancy outcome.

INTERVENTION

OBJECTIVES

- Alleviate cause of the anemia and associated anorexia.
- Provide adequate oral iron to replace losses or deficits, especially heme sources of protein (liver, beef, oysters, lamb, pork, ham, tuna, shellfish, fish, and poultry).
- Provide an acid medium to favor better absorption. Enhancers include gastric juice and ascorbic acid. Food sources of vitamin C should be included daily.
- Monitor and correct pica, including geophagia (clay eating), amylophagia (starch eating), ice eating, or any lead exposure.
- Avoid or correct constipation.
- Screen for IDA or sports anemia in athletes (Sinclair and Hinton, 2005).
- Reduce iron inhibitors, such as excessive fiber (as in whole grains), phytic acid (as in spinach, bran, legumes, and soy products), tannins in tea, and polyphenols in coffee or red wine. In many developing countries, cereal and legume-based diets contain low amounts of bioavailable iron, which may increase the risk of iron deficiency (Zimmermann et al, 2005).

FOOD AND NUTRITION

- If IDA is related to inadequate iron in diet, usually adding three portions of lean red meat (heme iron sources) per week, along with all other essential vitamins and minerals, will correct the anemia. The average mixed diet contains approximately 6 mg of iron per 1000 kcal. Iron absorption increases as stores become depleted. Good sources of iron include liver, dried beans, egg yolks, kidney, lean beef, dark meat of chicken, salmon, tuna, dried fruits, enriched whole-grain cereals, molasses, and oysters.
- Heme iron is found readily in beef, pork, and lamb; consume with fruit or fruit juice. Heme iron is absorbed well, regardless of other foods in the diet.
- Nonheme iron absorption is greatly affected by other foods. Absorption of nonheme iron is best in the presence of foods rich in vitamin C or with heme-containing sources. Increase intake of vitamin C (oranges, grapefruit, tomatoes, broccoli, cabbage, baked potatoes, strawberries, cantaloupe, and green peppers), especially with an iron supplement.
- Detect pica and discuss with patient. Pica substance may displace other important foods, leading to nutrient malnutrition. The ingested substance may also be toxic.
- Tea, coffee, wheat brans, and soy products tend to inhibit absorption of nonheme iron. Monitor use carefully; avoid excesses.

Common Drugs Used and Potential Side Effects (Table 12-14)

- If anemia is caused by an increased demand for iron such as a growth spurt (toddlers, adolescents) or pregnancy, oral supplementation may be necessary: inorganic

TABLE 12-14 Medications to Correct Iron-Deficiency Anemia

Medication	Description
Ferrous salts (Feosol, Fer-In-Sol, Mol-Iron) or tablets (Feostat, Fergon, Feosol)	Prolonged-release ferrous sulfate (Slow Fe) improves iron absorption with fewer side effects than standard ferrous sulfate pills. Other forms include ferrous fumarate (Femiron, Feostat, Fumerin, Hemocyte, Ircon) and ferrous gluconate (Fergon, Ferralet, Simron). These may cause gastric irritation and constipation.
Enteric-coated or sustained-release iron	More expensive and often carry the iron past maximal absorption site in the upper intestine.
Heme iron (Proferrin Forte)	This is a medical food that contains heme iron plus folic acid. It is absorbed regardless of achlorhydria, and has fewer GI side effects than IV or ferrous iron sources. It can be taken with or without meals.
Parenteral or IV iron	Can be administered by injection or infusion. This therapy is reserved for cases of trauma where blood loss is life threatening and is not used for insufficiency due to inadequate dietary iron intake. Imferon can be given intramuscularly, if oral iron is not tolerated; pain and skin discoloration may result.

iron in ferrous form (50–200 mg/d for adults; 6 mg/kg for children) combined with increased consumption of heme-rich sources of iron. This is best absorbed on an empty stomach, but with food if there are GI side effects.

- Iron pills should be taken 2 hours before or after other medications. Iron can inhibit the effectiveness of thyroid medications, antibiotics, and some antidepressant drugs. Once ingested, it is imperative that the stomach contains acid to dissolve the iron salt; if taking antacids or H2 blockers such as cimetidine (Tagamet), the iron salt will not dissolve.
- The amount of elemental iron contained in iron pills will vary. A 325-mg supplement is probably made of ferrous fumarate or gluconate, with only 100 mg of elemental iron per pill.
- Heme iron supplements (such as Proferrin) can be taken with meals, unlike ionic iron preparations, which must be taken on an empty stomach between meals. However, individuals with allergies to beef, milk, or other dairy products should not be given Proferrin.
- It takes 4–30 days to note improvements after iron therapy, especially in Hgb levels. Hgb should rise 0.1–0.2 g/dL/day after the fifth day of treatment; then should rise 2.0 g/dL/week for 3 weeks. Iron therapy should be continued for at least 2 months after the Hgb has returned to normal to replenish the iron stores.
- Iron stores are replaced after 1–3 months of treatment. Increased supplementation in normal individuals can cause additional, unnecessary iron to go into storage, reflected by ferritin elevation.
- Aspirin or corticosteroids can cause GI bleeding or peptic ulceration. Vitamin C and nutrient levels may be decreased.
- Some medications, including antacids, can reduce iron absorption. Iron tablets may also reduce the effectiveness of other drugs, including the antibiotics tetracycline, penicillamine, and ciprofloxacin and the anti-Parkinson's drugs methyldopa, levodopa, and carbidopa. Wait 2 hours between doses of these drugs and iron supplements.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Hgb is made from protein, iron, and copper. RBCs are made from vitamin B_{12}, folacin, and amino acids. Explain which foods are good sources of iron, protein, vitamin C, and related nutrients.
- Temporary changes in stool color (green or tarry and black) are common with supplements; this is not cause for alarm. To avoid side effects of supplements, take them with meals or milk; food iron has fewer side effects.
- Foods and substances that can interfere with the absorption of iron include calcium, tannins, which are found in coffee, tea, grapes, red wine, purple or red rice, and bran fiber or chocolate. Avoid excesses of oxalates, alkalis, and antacids; discuss sources. Iron supplementation is best taken 2 hours after consuming these substances.
- The average American diet contains 10–20 mg of iron daily, roughly 10% of which is absorbed. Avoid overdosing with iron supplements. The body can only synthesize 5–10 mg of Hgb per day, and excesses may work against the immune system.
- Local or systemic infections interfere with iron absorption and transport.
- In children under age 2, limit milk intake to no more than 500 mL/d for better iron status.
- Explain nonfood pica—clay, starch, plaster, paint chips—and the relationship with nutrition. In food pica in which singular foods are eaten instead of balanced meals, the foods chosen are often crunchy or brittle. Excessive consumption of lettuce, ice, celery, snack chips, and chocolate has been noted; after iron supplementation, cravings often subside.
- Iron deficiency may be partly induced by plant-based diets containing low levels of poorly bioavailable iron (Kesa and Oldewage-Theron, 2005). Young people who follow a vegan diet should have their iron status monitored closely.
- Use culturally appropriate nutrition counseling. In some cultures, boys may be fed iron-rich foods preferentially over girls; counseling should be designed to improve intake by girls (Shell-Duncan and McDade, 2005).

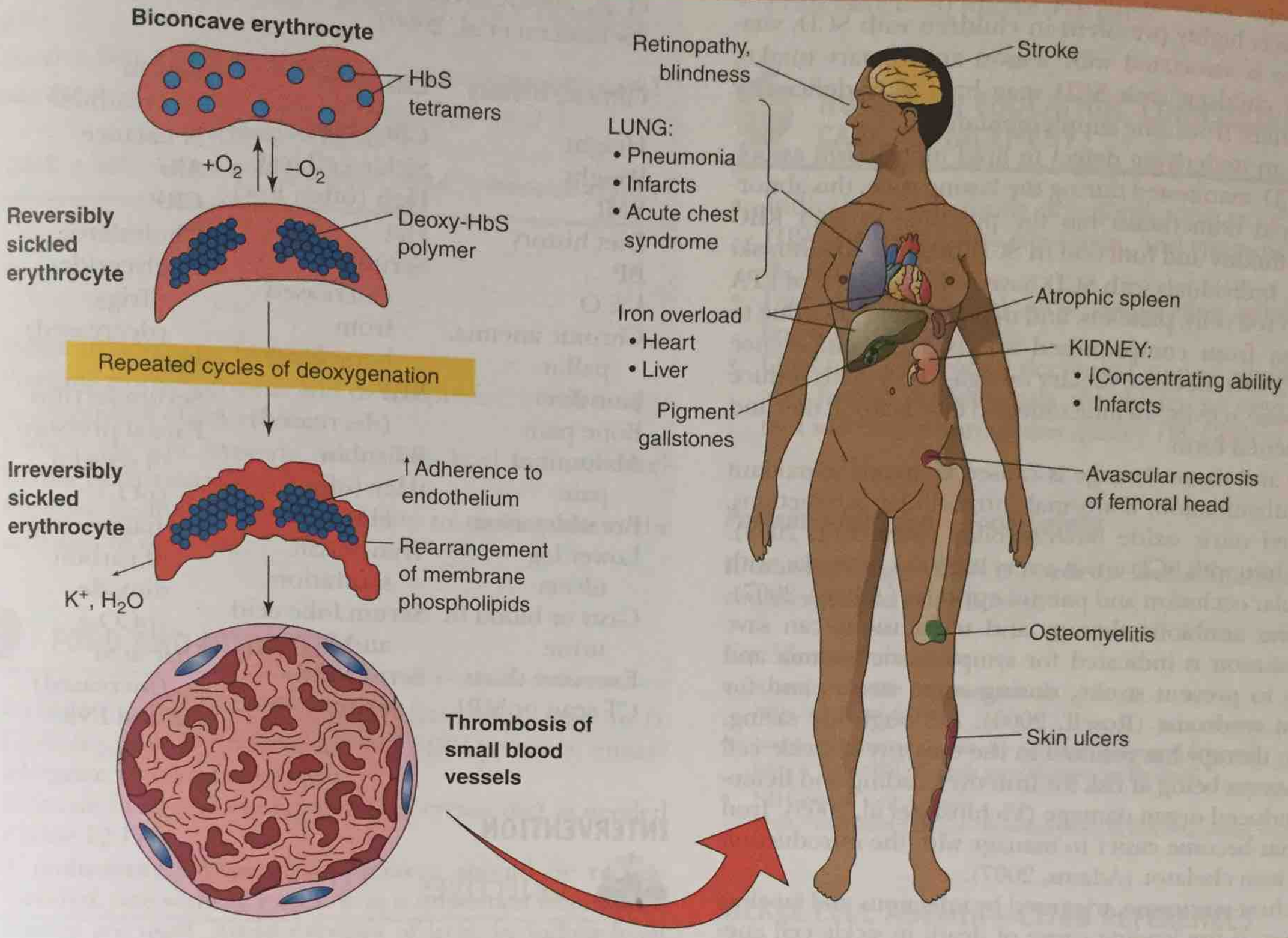
Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

HEMOGLOBINOPATHIES

SICKLE CELL ANEMIA

NUTRITIONAL ACUITY RANKING: LEVEL 1



Adapted from: Raphael Rubin, David S. Strayer, *Rubin's Pathology: Clinicopathologic Foundations of Medicine*, 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2008.

DEFINITIONS AND BACKGROUND

Sickle cell disease (SCD) is the most common genetic disorder of the blood. SCD involves anemia that is hereditary and hemolytic. Cells in SCD are crescent shaped and become rigid; they lodge themselves in the capillaries of the peripheral-blood system outside the heart. The sickling of RBCs occurs when partially or totally deoxygenated Hgb molecules distort their normal disk shape, producing stiff, sticky, sickle-shaped cells that obstruct small blood vessels; this causes vaso-occlusion as well as deprivation of oxygen to body tissues (Edwards et al, 2005). Everyone with SCD has chronic hemolytic anemia, vasculopathy, vaso-occlusive disease, acute and chronic organ damage, and shortened life span (Steinberg, 2008).

SCD has several forms including sickle cell anemia, sickle cell Hgb C disease, and sickle cell thalassemia disease. It is usually detected within the first year of life. Routine use of daily antibiotics until 5 years of age, immunization of children with pneumococcal vaccine, annual influenza vaccination after 6 months of age, and meningococcal vaccination after 2 years of age are important preventive measures (Mehta et al, 2006).

The largest population in the world with sickle cell anemia is in Africa. While this condition most commonly affects blacks of African descent, it is also found in people of Middle Eastern, East Indian, and Mediterranean origin. About 100,000 Americans have SCD (~1 in every 400–500 African–Americans). Carrier frequency varies, with high rates associated with zones of high malaria incidence. Carriers are often protected against malaria.

Patients with SCD are at risk for delayed growth and sexual maturation; acute and chronic pulmonary dysfunction; stroke; aseptic necrosis of the hip, shoulders, or both; sickle cell retinopathy; dermal ulcers; and severe chronic pain (Edwards et al, 2005). The homozygous state (SS) is associated with complications and a reduced life expectancy.

Chronic anemia, pallor, and jaundice result because sickled cells do not last as long as normal blood cells. Bone marrow functions at six times the normal rate. Because there are fewer cells, the blood is thinner or anemic. When RBCs are destroyed, bilirubin is released into the blood and turns the whites of the eyes to a shade of yellow.

Inadequate dietary intakes of folate are common, whereas vitamin B_{12} intakes are usually adequate. Low RBC folate levels may occur. Serum total homocysteine (tHcy) levels may be elevated in this population; greater intakes than normal of folate may be needed. Elevated tHcy levels contribute to

thrombosis, a frequent event in this population. Children with sickle cell anemia have lower vitamin B_6 concentrations.

Infants and children who have SCD are at risk for nutritional deficiencies and loss of body mass during acute illness. Suboptimal vitamin A intake is common, with more frequent hospitalizations and poor growth. Low serum vitamin D status is highly prevalent in children with SCD; vitamin D status is associated with season and dietary intake. Prepubertal children with SCD may have zinc deficiency and may benefit from zinc supplementation.

There is an underlying defect in lipid metabolism associated with SCD, manifested during the fasting state; this abnormality in lipid homeostasis has the potential to alter RBC membrane fluidity and function in SCD patients (Buchowski et al, 2007). Individuals with SCD have reduced levels of EPA and DHA in red cells, platelets, and mononuclear cells due to peroxidation from compromised antioxidant competence (Ren et al, 2008). Because dietary omega-3 fatty acids reduce prothrombotic activity, include omega-3 fatty acids in diet and in supplemental form.

Cellular and tissue damage is caused by hypoxia, oxidant damage, inflammation, abnormal intracellular interactions, and reduced nitric oxide bioavailability (Steinberg, 2008). Young children with SCD are at a very high risk of stroke, with microvascular occlusion and painful episodes (Adams, 2007).

Aggressive antibiotic therapy and transfusions can save lives. Transfusion is indicated for symptomatic anemia and specifically to prevent stroke, during acute stroke, and for acute chest syndrome (Roseff, 2009). Although life saving, transfusion therapy has resulted in the majority of sickle cell anemia patients being at risk for iron overloading and hemosiderosis-induced organ damage (Vichinsky et al, 2005). Iron overload has become easier to manage with the introduction of an oral iron chelator (Adams, 2007).

Acute chest syndrome, triggered by infections and fat clots in the lungs, is the leading cause of death in sickle cell anemia. Treatment includes hydroxyurea therapy to decrease the frequency of painful episodes and hematopoietic cell transplantation (Mehta et al, 2006). Bone marrow transplantation requires a perfect match from a sibling. Because patients with SCD have problems with surgery, including prolonged bleeding, vitamin K should be given preoperatively (Raffini et al, 2006). Use of transcranial Doppler ultrasonography helps identify asymptomatic, at-risk children who should be considered for chronic blood transfusions (Mehta et al, 2006).

Studies of gene expression are bringing new solutions. Human progenitor cell (from bone marrow, peripheral blood stem cells, or umbilical blood) transplant can cure the disease and is used for patients with severe disease for whom conventional therapy may not be effective (Roseff, 2009).

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Sickle cell anemia is an autosomal recessive disease caused by a mutation in the *hemoglobin beta gene* (*HBB*) found on chromosome 11p15.5. Genetic studies have identified regions on chromosome 6q23 and BCL11 A on chromosome 2p16 that account for 20–50% of the common variation in fetal Hgb levels in patients with sickle cell anemia (Thein et al, 2009). SNPs have also been found in KCNK6 (Sebastiani et al, 2009).

Clinical/History	Lab Work	
Height	CBC, WBC	Serum creatinine
Weight	Sickle cell test	N balance
BMI	Hgb (often low)	Alb
Diet history	Hct	CRP
BP	Serum Fe (increased from hemolysis)	Cholesterol
I & O		Triglycerides (Trig) (decreased)
Chronic anemia, pallor	RBP (decreased)	MCV
Jaundice	Bilirubin	Serum ferritin
Bone pain	tHcy (often elevated)	Partial pressure of oxygen (pO_2)
Abdominal pain	Transferrin saturation	Partial pressure of carbon dioxide (pCO_2)
Breathlessness	Serum folic acid and B_{12}	Uric acid (increased)
Lower leg ulcers	Serum and urinary zinc	PT and INR
Casts or blood in urine		
Excessive thirst		
CT scan or MRI		

INTERVENTION

OBJECTIVES

- Supplement diet with missing nutrients. Correct any malnutrition.
- Reduce oxygen debt and hemolytic crises.
- Reduce painful cramps, liver dysfunction, cholelithiasis, jaundice, and hepatitis.
- Lessen likelihood of pressure ulcers, infections, and renal failure. Infections may include pneumonia, cholecystitis, osteomyelitis, or urinary tract infections.

SAMPLE NUTRITION CARE PROCESS STEPS

Involuntary Weight Loss

Assessment Data: Weight pattern, percent desirable body weight, diet history, problems with meal planning or shopping, financial challenges.

Nutrition Diagnosis (PES): Involuntary weight loss related to sick cell anemia with inadequate caloric intake as evidenced by 10% loss of usual body weight in the last 2 months.

Intervention: Nutrition counseling, encouraging energy-dense foods and favorites. Coordination of care with referral to social service agencies for help with meal preparation and delivery.

Monitoring and Evaluation: Weight records, improvements in appetite and intake.

TABLE 12-17 Equation to Predict Energy Needs in Adolescents with Sickle Cell Disease

Basal energy requirements are higher in adolescents with sickle cell anemia than in healthy control subjects (Buchowski et al, 2002)

Males: REE (kcal/d) = 1305 + 18.6 × weight (kg) − 55.7. hemoglobin (g/dL)

REE (kJ/d) = 5461 + 77.7 × weight (kg) − 233.2 × hemoglobin (g/dL)

Females: REE (kcal/d) = 1100 + 13.3 × weight (kg) − 30.2 × hemoglobin (g/dL)

REE (kJ/d) = 4603 + 55.6 × weight (kg) − 126.2 × hemoglobin (g/dL)

- Maintain adequate hydration.
- Promote normal growth and development, which tend to be stunted in children.
- Prevent chronic hypoxia, which can lead to lower intellectual performance.
- Improve quality of life and ability to participate in the activities of daily life.

FOOD AND NUTRITION

- Include food sources of omega-3 fatty acids; vitamins D, C, A, B_{12}, and B_6; folic acid; and HBV proteins; ensure adequate zinc and riboflavin.
- Estimate fluid and energy needs; increase diet as needed (Table 12-17).
- A multivitamin–mineral supplement should be recommended; one without excess iron is important when transfusions are used. Avoid excesses of iron, including from tube feedings or parenteral nutrition.
- Energy deficits are common in this population. Nightly tube feeding can help to improve nutritional status. While supplementation with arginine has been suggested, more studies are needed.

Common Drugs Used and Potential Side Effects

- Pain medicines (such as ibuprofen) may be used. Monitor for all side effects and GI distress.
- Hydroxyurea therapy (Droxia, Hydrea) can be used to increase Hgb production.
- Rofecoxib is a cyclo-oxygenase-2 (COX-2) inhibitor approved for pain and has been tested in children with no adverse effects.
- Rituximab may be used to prevent delayed hemolytic transfusion reaction disorder in SCD.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.
- A phytomedicine, Niprisan, may reduce episodes of SCD crisis associated with severe pain.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Indicate which foods are good sources of folic acid, HBV proteins, zinc, riboflavin, and vitamins A, C, D, E, B_6, and B_{12}.
- Discuss ways for easy meal preparation because fatigue tends to be a problem.
- Quality of life is often decreased among adults with SCD, and health professionals should try to offer assistance that will help improve this quality (McClish et al, 2005).

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- American Sickle Cell Association
  http://www.ascaa.org/
- National Institutes of Health (NIH)–Genes and Disease
  http://www.ncbi.nlm.nih.gov/disease/sickle.html
- NIH–Sickle Cell Anemia
  http://www.nlm.nih.gov/medlineplus/sicklecellanemia.html

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OTHER BLOOD DISORDERS

BLEEDING DISORDERS: HEMORRHAGE AND HEMOPHILIA

NUTRITIONAL ACUITY RANKING: LEVEL 2

DEFINITIONS AND BACKGROUND

The circulatory system is a closed system, with low volume and high pressure. It provides efficient delivery of nutrients to all tissues. When there is volume loss, a large decrease in nutrient delivery occurs.

Hemorrhage is the excessive discharge of blood from a ruptured vessel. Bleeding (bright red in spurts from an artery; dark red and steady flow from a vein) can be external, internal, or into skin or other tissue. When massive, a hemorrhage can cause such symptoms as rapid, shallow breathing; cold, clammy skin; thirst; visual disturbances; and extreme weakness. Loss of more than 20% of blood volume causes hypotension and tachycardia; loss of more than 1 quart of blood may lead to shock. Peptic ulcer, hemophilia, spontaneous liver rupture, or stroke may lead to a hemorrhage. In some cases, surgery may be necessary. In chronic myelogenous leukemia (CML), a slowly progressive disease, platelets are increased in number and easy bleeding occurs.

To stop a hemorrhage, blood must clot properly. Blood clots when its fibrinogen is converted to fibrin by action of thrombin. Vitamin K works as a coenzyme that converts glutamic acid to gamma-carboxyglutamic acid; this helps to bind calcium and is required for the activation of the seven vitamin K–dependent clotting factors in the coagulation cascade (Table 12-18).

Hemophilia is an inherited bleeding disorder. Diagnosis may be early in life, or later after surgery or trauma. In severe cases, serious bleeding may occur without any cause. While internal bleeding may occur anywhere, bleeding into joints is common. Standard treatment involves replacing the missing clotting factor. In pregnant women who carry the trait, a C-section is often recommended. **Von Willebrand disease** is the most common hereditary bleeding disorder, where bleeding gums, abnormal menstrual bleeding, nose bleeds, and bruising are the symptoms. Desamino-8-arginine vasopressin (DDAVP) is given to raise the levels of von Willebrand factor, which reduces the bleeding tendency.

The immune response to coagulation factors VIII or IX with formation of inhibitory antibodies complicates the treatment of hemophilia; regulatory T cells (Treg) are an important component of the mechanism by which tolerance is maintained (Cao et al, 2009). New gene therapy and immune tolerance protocols are under study.

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Hemophilia A, which affects 80–90% of cases, shows a mutation in the FVIII gene. People with Hemophilia B have low or missing levels of clotting factor IX. Hemophilia affects mostly males, although women carry the trait.

Clinical/History		
Height	Temperature	Excessive or easy bleeding
Weight	I & O	Excessive bruising
BMI	Blood in urine or stool?	Nose bleeds
Diet history	Petechiae	Abnormal menstrual bleeding
BP	Hemophiliac arthropathy	
Pulse		

TABLE 12-18 Blood Clotting Factors That Involve Nutrition

The coagulation cascade involves a series of steps that stop bleeding through clot formation. Vitamin K–dependent coagulation factors are synthesized in the liver. Consequently, severe liver disease results in lower blood levels of vitamin K–dependent clotting factors and an increased risk of uncontrolled bleeding (hemorrhage). The following factors involve nutrition:

I. Fibrinogen
II. Prothrombin
III. Thromboplastin
IV. Calcium

In hemostatic (bleeding) disorders, it is important to evaluate for bleeding problems in the family history, history of heavy menses or easy bruising, and prior blood transfusions. Bleeding disorders include a number of conditions in which people tend to bleed longer. Clotting involves about 20 different plasma proteins (clotting factors). Normally, clotting factors form fibrin that stops bleeding. In bleeding disorders, the process does not occur normally

Some bleeding disorders are present at birth (hemophilia and von Willebrand's disease), or they can be acquired (such as vitamin K deficiency, severe liver disease, use of anticoagulant drugs or prolonged use of antibiotics, bone marrow problems, leukemia, pregnancy-associated eclampsia, or snake bite). In these disorders, vision loss can occur from bleeding into the eye, or anemia may result, or there may be neurological problems or even death. Gene therapy may one day be available to treat the bleeding disorders.

Lab Work		
Coagulation testing	Thrombin time (thrombin added to plasma, and time to clot measured)	Transferrin
PT, International normalized ratio (INR)—prolonged?	Fibrinogen	RBC
Activated partial thromboplastin time (aPTT)	Platelet count (may be normal)	Alb
	Von Willebrand factor level (reduced?)	BUN
		CBC
		H & H
		Serum Fe
		Serum folic acid and B_{12}
		TIBC (increased)
		Creatinine
		CRP

INTERVENTION

OBJECTIVES

- Medical management is designed to control bleeding, take care of the underlying cause of the bleeding, and replace lost blood. Transfusions may be needed. Less severe hemorrhages may require iron, vitamin B_{12}, and folic acid to help replace RBCs.
- Support erythropoiesis.
- Control intestinal impact of gastrointestinal bleeding, which can cause a protein overload.
- Prevent hypovolemic shock (low cardiac output, decreased blood pressure, and decreased urinary output) from uncontrolled bleeding.

FOOD AND NUTRITION

- Ensure that diet is rich in proteins, iron, folic acid, vitamin B_{12}, and copper.
- Check need for vitamin K. Patients with intestinal or liver disease may become deficient. If medications to replace vitamin K are used, diet should provide a balance without excess. Monitor content of meals or enteral feedings and multivitamin supplements carefully to ensure that all RDAs are met without excesses (Table 12-19).

TABLE 12-19 Food Sources of Vitamin K

Food	Serving	Vitamin K (μg)
Kale, raw	One cup (chopped)	547
Broccoli, cooked	One cup (chopped)	420
Parsley, raw	One cup (chopped)	324
Swiss chard, raw	One cup (chopped)	299
Spinach, raw	One cup (chopped)	120
Leaf lettuce, raw	One cup (shredded)	118
Watercress, raw	One cup (chopped)	85
Soybean oil	One tbsp	26
Canola oil	One tbsp	20
Mayonnaise	One tbsp	12
Olive oil	One tbsp	7

Source: U.S. Department of Agriculture. USDA national nutrient database for standard reference, release 16. Available at http://www.nal.usda.gov/fnic/foodcomp/Data/SR16/wtrank/wt_rank.html.

SAMPLE NUTRITION CARE PROCESS STEPS

Inadequate Vitamin Intake

Assessment Data: Bleeding disorder (Hemophilia A) with easy bruising and blood in urine and stool. Currently taking Alphanate; scheduled for dental surgery in 2 weeks. Serum vitamin K levels low. Diet hx shows little intake of any vitamin K–rich foods.

Nutrition Diagnoses (PES): Inadequate vitamin K intake related to hereditary bleeding disorder and minimal dietary intake as evidenced by low serum vitamin K levels, easy bruising and blood in urine and stool even while taking Alphanate.

Interventions: Food–nutrient delivery: identify foods that could be included and tolerated. Educate about the sources of vitamin K from diet. Counsel about multivitamin–mineral supplements that contain a desired dose of vitamin K (10–120 μg per dose).

Monitoring and Evaluation: Fewer episodes of blood in urine and stool; less easy bruising. Tolerance for multivitamin–mineral supplement and foods. Improved serum levels of vitamin K. No difficulty with dental surgery and excessive bleeding.

Common Drugs Used and Potential Side Effects

- Avoid aspirin, NSAIDs, and other blood thinners. Oral anticoagulants, such as Warfarin, inhibit coagulation through antagonism of the action of vitamin K. Inadequate gamma-carboxylation of vitamin K–dependent proteins will inhibit clot formation. Patients taking these drugs are cautioned against consuming very large or highly variable quantities of vitamin K in their diets; they need a reasonably constant dietary intake.
- If vitamin K is needed, it is available in multivitamins and other supplements in doses that range from 10 to 120 μg per dose.
- Alphanate (antihemophilic factor) is approved to decrease bleeding in patients with bleeding diseases who must have surgery or other invasive procedures. People with hemophilia and their families can be taught to give factor VIII concentrates at home at the first signs of bleeding. XYNTHA is a new recombinant factor VIII product for both the control and prevention of bleeding episodes and surgical prophylaxis.
- FEIBA therapy, consisting of activated prothrombin complex concentrate (aPCC) and recombinant activated factor VII (rFVIIa), is effective and safe for reducing bleeding in hemophilia A (Valentino, 2009).

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.
- Potential adverse effects of high vitamin E intakes in humans, such as bleeding, are not clear (Hathcock et al. 2005).

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Blood donors should be alerted to the need to replace daily iron intake by 0.7 mg for a year. Every pint is equivalent to 250 mg of iron lost.
- Discuss adequate dietary replacement for lost nutrients. A multivitamin–mineral supplement may be indicated.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- All About Bleeding
  http://www.allaboutbleeding.com/
- Anemia from Excessive Bleeding
  http://www.merck.com/mmhe/sec14/ch172/ch172b.html
- Blood Line
  http://www.bloodline.net/
- International Society on Thrombosis and Haemostasis
  http://www.isth.org/
- National Hemophilia Foundation
  http://www.hemophilia.org/about/programs.htm
- World Federation of Hemophilia
  http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/Gudelines_Mng_Hemophilia.pdf

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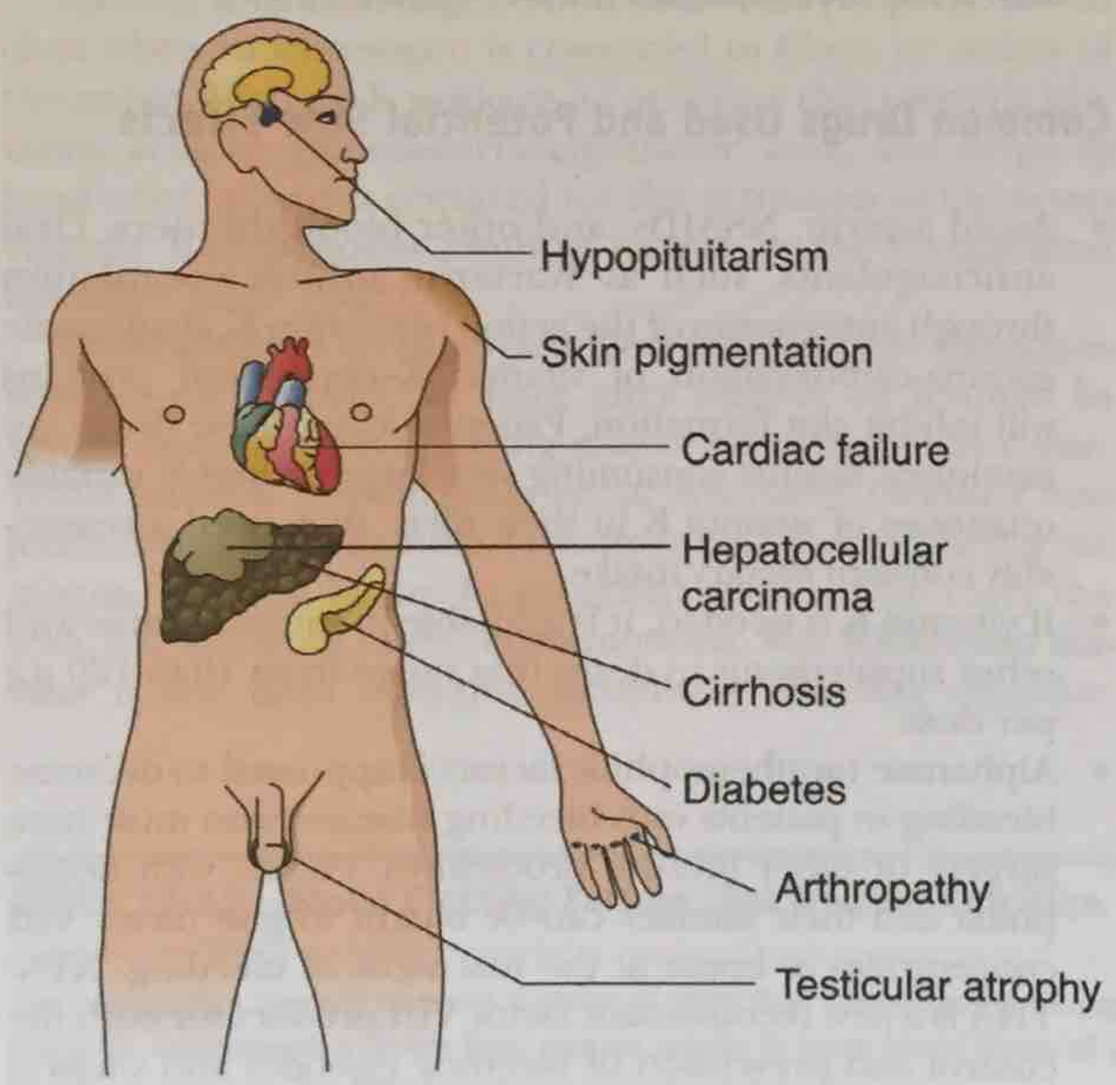
Hathcock JN, et al. Vitamins E and C are safe across a broad range of intakes. *Am J Clin Nutr.* 81:736, 2005.

Valentino LA. Assessing the benefits of FEIBA prophylaxis in haemophilia patients with inhibitors. Haemophilia. 2009 Dec 16. [Epub ahead of print]

HEMOCHROMATOSIS AND IRON OVERLOAD

NUTRITIONAL ACUITY RANKING: LEVEL 2



Adapted from: Rubin E MD and Farber JL MD. *Pathology*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.

DEFINITIONS AND BACKGROUND

Hereditary hemochromatosis (HH) is one of the most common autosomal recessive disorders among Caucasians. One in 200–400 individuals of Northern European ancestry is at risk for hemochromatosis (Camaschella and Merlini, 2005). It is also common in Hispanics or people of Mediterranean descent and is 10 times more common in males than females. Irish Americans and African–Americans have double the usual frequency. Tragically, hemochromatosis remains underdiagnosed.

In hemochromatosis, iron stores are deposited in excess, often from excess intake or liver/pancreatic diseases, renal dialysis, or frequent and long-term transfusions. Healthy people may accumulate up to 1 g of iron, but people with this condition accumulate 15–30 g. Increased iron absorption leads to excessive accumulation of iron deposits within cells of the liver, heart, pituitary gland, pancreas, and other organs, gradually causing tissue damage.

Because hemochromatosis has many possible symptoms, it often goes undiagnosed. However, early detection is important and may prevent organ failure that can occur if it is left untreated. Long-term complications include liver cirrhosis, diabetes, cardiomyopathy, hypogonadism, arthropathy, skin pigmentation, and susceptibility to liver cancer (Camaschella and Merlini, 2005) (Table 12-20).

Iron overload patients may have diagnoses other than HH: non-alcoholic fatty liver disease (NAFLD), chronic hepatitis C, and chronic alcohol use are most common (Dever et al, 2009). Iron toxicity can also occur in aplastic anemia, chronic hemolytic anemia, porphyria cutanea tarda, sideroblastic anemia, thalassemias, diabetes, rheumatoid arthritis, or transfusional iron overload. Sometimes, individuals with Alzheimer's or Parkinson's disease may have heavy metal toxicities that contribute to an iron overload. Free iron is destructive to cells, and too much iron can be a carcinogen because cancer cells need it for their DNA synthesis. With chronic kidney disease, keep serum ferritin levels below 500 ng/dL.

Porphyrias are rare disorders caused by lack of the enzymes necessary for production of heme; this causes heme precursors, porphyrins, to accumulate in the bone marrow, liver, and bloodstream (MedlinePlus, 2009). The porphyrins may also

TABLE 12-20 Facts About Hemochromatosis

1. Undetected or untreated excess iron kills after inflicting injury to a variety of body organs. The physician's concern must be to detect any excess iron instead of establishing the diagnosis
2. Some literature suggests treatment when ferritin alone is elevated. Giving blood does no harm and, instead, is beneficial to health. About one fourth of patients have low hemoglobin; treatment is the same unless the anemia is so severe that blood transfusions are required. Severely anemic patients require iron removal by an iron chelator, Desferal
3. Iron overloading is preventable. When diagnosis is in doubt, the patient should begin a trial of weekly phlebotomies at the blood bank. Four to 6 weeks will usually provide the answer, and getting rid of a little excess iron will improve health
4. The patient should be taken to the blood bank upon the physician's order for weekly phlebotomies
5. A liver biopsy is not always necessary, and waiting can delay important treatment. DNA testing is not useful because it cannot detect all of the known mutations
6. When iron levels test low, the cause must be found. It is dangerous to medicate with iron without testing first and then finding the reason for any deficiency
7. Symptoms vary. Chronic fatigue, arthritis, anemia (iron-loading anemia is one symptom), and elevated liver enzymes must not be ignored. Hemoglobin level does not indicate iron status. A disorder of thyroid or any part of the body can be a symptom of iron overload
8. Excess iron lowers immunity. Many diseases (such as cancer, hepatitis, and AIDS) will show a poor outcome unless any excess iron is removed. Excess iron stored in the brain exacerbates severity in Alzheimer's, multiple sclerosis, Lou Gehrig's disease, Parkinson's disease, psychological problems, autism, and other diseases

Adapted from: Iron Overload Diseases Association, http://www.ironoverload.org/, accessed December 23, 2009.

be excreted in the urine or stool. Most porphyrias are hereditary, but attacks may also be triggered by drugs, alcohol, hormones, or infections.

Acute, hepatic porphyrias affect the nervous system. Symptoms include nerve damage with pain or paralysis, abdominal pain and liver damage, red or brown urine, anxiety and delirium, muscle pain or weakness, numbness or tingling, tachycardia, loss of deep tendon reflexes, low blood pressure, and electrolyte imbalances. Constipation or diarrhea may occur. A diet high in carbohydrate (55–60% of total kilocalories) and beta carotene may be beneficial (MedlinePlus, 2009).

Porphyria cutanea tarda (PCT) can occur without an inherited enzyme deficiency. The porphyrins accumulate in the liver and skin, causing photosensitivity, skin damage, and cirrhosis. Phlebotomy removes excess iron, and chloroquine or hydroxychloroquine removes the excess porphyrins from the liver (Anderson, 2007).

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: HH is recessive, requiring the gene from two carrier parents. There are several types of genetic hemochromatosis: type I or classic (HHC); type II a, b, or juvenile (JHC); type III or transferrin receptor mutation; and type IV or ferroportin mutation. Iron overload can also occur in individuals with the HFE C2824 gene in 1 out of 200 people.

Clinical/History		I & O
	BMI	Bronzing of the skin
Height	Diet history	
Weight	BP	
Profound fatigue (in HH)	Enlarged spleen	Serum Cu (increased)
Arthralgia (in HH)	Hypothyroidism	Alb
Loss of body hair	Depression	Serum Fe
Loss of libido	Liver biopsy	Ferritin (increased >1000 ng/mL?)
Lack of menstruation or early menopause	Bone marrow studies	Hgb (desirable = 10 g/dL)
Abdominal pain	**Lab Work**	Hct (desirable = 30–35%)
Chronic intermittent diarrhea	Transferrin-Iron Saturation Percentage[a] (normal 25–35%)—best test	Gluc
Irregular heartbeat	TIBC (normal, 12–45%)	Serum B_6
Cardiomegaly with congestive failure	Transferrin (increased)	Serum B_{12}
Hepatomegaly		Serum folic acid
		Thyroid tests
		Liver function tests
		CRP

[a]Divide total serum iron by TIBC for percentage of tissue saturation (TS). Divide the serum iron level by TIBC for percentage of transferrin saturation.

INTERVENTION

OBJECTIVES

- Remove excess iron from body (usually with phlebotomies of 500 mL weekly, performed by the physician over several months). Then therapy is repeated several times annually for rest of the life.
- Prevent liver cancer, heart attack, or stroke by unloading storage iron as fast as possible; keep serum ferritin at low normal range.
- If excess iron intake is a chronic problem, discontinue use in supplements and fortified foods (such as iron-fortified cereals). Read labels carefully.

SAMPLE NUTRITION CARE PROCESS STEPS

Excessive Mineral Intake

Assessment Data: Male with transferrin-iron saturation percentage (46%), ferritin (160 ng/mL), elevated H & H. Diagnosis of iron overloading. Diet hx reveals high intake of animal proteins and heme iron (about 20 g/day).

Nutrition Diagnoses (PES): Excessive iron intake related to diet high in animal proteins and heme iron as evidenced by transferrin-iron saturation percentage (46%), ferritin (160 ng/mL), elevated H & H.

Interventions: Food–nutrient delivery—encourage more vegetarian meals and fewer ounces of meats at mealtime. Educate about the role of heme iron intake in iron overloading disorders. Counsel and provide meal planning tips and portion guides for intake of meats.

Monitoring and Evaluation: Improvement in serum laboratories (transferrin-iron saturation percentage, ferritin, and H & H) with levels closer to normal. Diet hx reveals improved intake of 8–10 g/day.

- Teach principles of nutrition and menu planning to incorporate adequate intake of other nutrients that may be depleted with excessive phlebotomies (e.g., folate and other B-complex vitamins, protein).

FOOD AND NUTRITION

- Provide a normal diet unless renal or hepatic function is altered. Do not consume foods or take supplements high in vitamin C. Read cereal labels and avoid those with 100% or more of the daily allowance for iron and vitamin C. A low-iron diet is not recommended.
- Ensure adequate protein and sufficient energy intake to meet estimated needs and activity levels.
- Avoid alcohol because of potential damage to a vulnerable liver.

Common Drugs Used and Potential Side Effects

- Avoid use of multivitamin supplements that contain iron and vitamin C because these can increase iron absorption.
- An iron chelator may be needed, such as deferoxamine (DFO). This is given intravenously 8–12 hours for up to five times in a week. It can be neurotoxic.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- All blood relatives of the patient must be evaluated and monitored yearly for iron overloading.
- Genetic testing of other family members is also recommended for those with inherited type.
- Discuss avoidance of alcohol and raw seafood. *Vibrio vulnificus* in some raw seafood kills people every year; many are those with undetected iron overload.
- Discuss nutrient sources as appropriate for the individual.

Patient Education—Food Safety

- If tube feeding or CPN is needed, careful handwashing procedures should be followed.
- Avoid eating raw seafood.

For More Information

- Iron Disorders Institute
  http://www.irondisorders.org
- Iron Facts
  http://ods.od.nih.gov/factsheets/iron.asp
- Iron Overload Diseases Association, Inc.
  http://www.ironoverload.org/
- Iron Tests
  http://www.irondisorders.org/Forms/irontests.pdf

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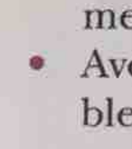
Dever JB, et al. Phenotypic characteristics and diagnoses of patients referred to an iron overload clinic. *Dig Dis Sci.* 2009 Dec 24. [Epub ahead of print]

MedlinePlus. Porphyrias. Web site accessed December 28,2009, at http://www.nlm.nih.gov/medlineplus/ency/article/001208.htm.

POLYCYTHEMIA VERA

NUTRITIONAL ACUITY RANKING: LEVEL 1



DEFINITIONS AND BACKGROUND

Polycythemia vera (PV) is a chronic, progressive disease in which increased blood volume and increased erythrocyte production occur. Other names include erythremia, Osler–Vasquez disease, and polycythemia rubra vera. Hematological disorders like PV can result in elevated levels of cobalamin, which is released during hepatic cytolysis.

The cause of PV is unknown, and the disease is considered a hematological malignancy. The disease develops

slowly and may progress to acute myelogenous leukemia. The average age at diagnosis is 50–60 years. Incidence is highest among those of Jewish ancestry, occurring in 2 of 100,000 of the population. Increased viscosity of the blood and number of platelets result in a high risk for clot formation and stroke, hemorrhage, or myocardial infarction.

Patients with PV frequently develop hyperhomocysteinemia due to discrete depletion of cobalamin or folate; vitamin therapy should be considered. With treatment, individuals with this condition may live for 15–20 years. Phlebotomy or medications may be used.

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: The somatic V617 F mutation in the Janus kinase (JAK) 2 gene, which causes a valine to phenylalanine substitution at position 617, has recently been found in the majority of patients with PV (Meyer, 2009).

Clinical/History

Height
Weight
BMI
Diet history
I & O
BP (hypertension?)
Belching, fullness
Flatulence
Peptic ulcer?
Constipation
Headache
Vertigo
Lassitude
Tinnitus
Pruritus after bathing
Transient blurred vision, diplopia
Dyspnea
Chest pain
Dusky reddish skin on face and hands
Hemorrhagic tendency
Seizures, confusion
Splenomegaly
Tinnitus
Paresthesias
Gout

Lab Work

Hgb (>18 g/dL)
Hct (>52% for men; >47% for women)
Platelets (elevated)
Leukocytes (elevated)
Serum B_{12} (elevated)
Erythropoietin (low)
TIBC
Erythrocyte sedimentation rate (ESR)
Leukocyte Alk phos
Serum ferritin
Gluc
RBC (7–12 million)
Oxygen saturation >92%
CRP
Alb, transthyretin
CRP
Chol, Trig
BUN, Creat
Uric acid (elevated)
Bone marrow biopsy

INTERVENTION

OBJECTIVES

- Prepare patient for phlebotomy by ensuring adequate nutrient stores.
- Prepare, as needed, for chemotherapy or radiation therapy, which may be provided.

SAMPLE NUTRITION CARE PROCESS STEPS

Abnormal GI Function

Assessment Data: BMI 20. Constipation, flatulence, history of gastric bleeding, and ulceration.

Nutrition Diagnoses (PES): Abnormal GI function related to discomfort and pain as evidenced by constipation, flatulence, GI ulceration, and bleeding.

Interventions: Food–nutrient delivery—use comfort foods and adequate CHO, fiber, and fluid intake; reduce acidic foods and items not well tolerated. Educate about good nutrition and inclusion of B-complex vitamins. Counsel about individualizing tolerance for medications with appropriate food, fluid, and snacks.

Monitoring and Evaluation: Daily use of prescribed medications. Improvement in GI function; resolution of constipation and flatulence. No additional GI bleeding.

- Correct or control condition.
- Manage any side effects such as heart failure, peptic ulcer disease, gastric bleeding, gout, leukemia, and seizures.

FOOD AND NUTRITION

- A high CHO diet with preferred foods and balanced meals should be offered. Monitor for the need for vitamin or mineral supplementation. Include foods rich in beta carotene.
- Extra fluids will be helpful (35–40 mL/kg, unless contraindicated, as with heart failure).
- Changes in dietary texture or content may be needed if radiation or chemotherapy alters nutrient or dietary needs.

Common Drugs Used and Potential Side Effects

- Myelosuppressive agents may be prescribed. Anagrelide hydrochloride (Agrylin) is an oral imidazoquinazoline agent that has been shown to reduce elevated platelet counts and the risk of thrombosis. Interferon alpha may be used in younger patients; pegylated interferon alpha-2a (PEG-IFN-alpha-2a) is beneficial (Quintas-Cardama et al, 2009).
- The antimetabolite hydroxyurea may be used. Side effects include anemia and skin ulcers.
- Chemotherapeutic agents (busulfan, chlorambucil, and cyclophosphamide) may cause nausea and vomiting or weight loss.
- Low-dose aspirin is sometimes used in patients with thrombotic or ischemic conditions. It can relieve some of the burning sensations in the feet and hands. Antihistamines can help reduce itching sensation.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Discuss need to maintain a healthy lifestyle and to eat adequate protein and calories because of the frequent phlebotomies, where completed.
- Discuss ways to make meals that are nutritious yet simple to prepare.
- Tepid oatmeal baths may help reduce pruritus.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- Mayo Clinic – PV
  http://www.mayoclinic.com/health/polycythemia-vera/DS00919
- Merck Manual–Blood Disorders
  http://www.merck.com/mmhe/sec14/ch178/ch178b.huml
- Myeloproliferative Disorders
  http://www.acor.org/diseases/hematology/MPD/

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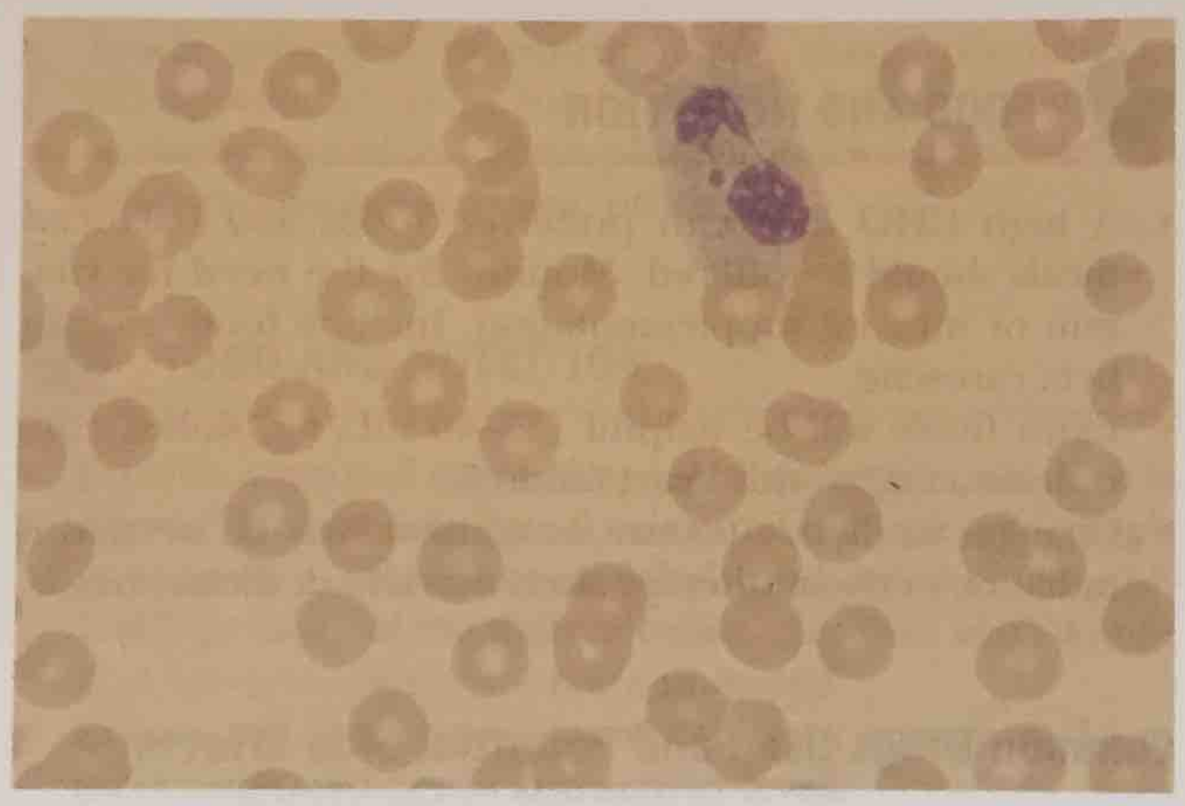
Quintas-Cardama A, et al. Pegylated interferon alfa-2 a yields high rates of hematologic and molecular response in patients with advanced essential thrombocythemia and polycythemia vera. *J Clin Oncol.* 27:5418, 2009.

THROMBOCYTOPENIA

NUTRITIONAL ACUITY RANKING: LEVEL 1



Adapted from: *Anderson's Atlas of Hematology;* Anderson, Shauna C., PhD. Copyright 2003, Wolters Kluwer Health/Lippincott Williams & Wilkins.

DEFINITIONS AND BACKGROUND

Thrombocytopenia purpura, a myeloproliferative disorder, is a blood disease affecting the clotting factor (platelets) of the blood, with an abnormally low platelet count and shorter than normal (10 days) platelet survival time. Thrombocytopenia is the most common cause of bleeding, usually from small capillaries. Women are more affected than men.

There are many reasons for the development of decreased marrow production or platelet destruction that causes thrombocytopenia, including some hereditary causes. These can sometimes be determined by examination of bone marrow. Idiopathic thrombocytopenic purpura (ITP) is caused by platelet destruction by antibodies. Thrombotic thrombocytopenic purpura (TTP) is manifested by vascular lesions.

Plasma exchange (plasmapheresis) is used to remove the abnormal antibody from the blood and replace the missing enzyme. Mortality of TTP has decreased from 90% to 10% (George, 2009); survival improved dramatically with plasma exchange treatments after the 1980s (Kremer-Hovinga et al, 2009). Unfortunately, adults with TTP of any etiology have a high risk for persistent minor cognitive abnormalities (George, 2009).

ASSESSMENT, MONITORING, AND EVALUATION

CLINICAL INDICATORS

Genetic Markers: Mutations in the ADAMTS13 gene cause the familial form of TPP. Alterations in the ADAMTS13 gene reduces instructions for the normal process of blood clotting.

Clinical/History

- Height
- Weight
- BMI
- Diet history
- I & O
- BP
- Nosebleeds
- Bleeding from other sites
- Bruising
- Pinpoint red spots on skin
- Headache
- Slurred speech
- Numbness and weakness of extremities
- Fever?
- Pallor
- Jaundice
- Shortness of breath

Lab Work

- CBC (low platelets)
- H & H (decreased)
- Alb, transthyretin
- N balance
- PT and PTT (normal)
- Casts in urine
- Proteinuria
- CRP
- Ca^{++}
- Na^{+}, K^{+}

SAMPLE NUTRITION CARE PROCESS STEPS

Self-Feeding Difficulty

Assessment Data: BMI at lower end of normal, but some weight loss noted. Dx of TPP with numbness and weakness in hands and feet. Inability to feed self and remain independent; depression and easy frustration noted at mealtimes.

Nutrition Diagnoses (PES): Self-feeding difficulty related to numbness in hands as evidenced by inability to hold traditional utensils.

Interventions: Food–nutrient delivery—alter food choices to simplify options and offer more finger foods. Educate about use of adaptive feeding equipment that can be used for more independence. Counseling with tips on meal simplification.

Monitoring and Evaluation: Improved ability to feed self independently. No further weight loss. Less depression and frustration at mealtimes.

INTERVENTION

OBJECTIVES

- Avoid infections, especially upper respiratory infections and flu to prevent coughing, which increases intracranial pressure.
- Reduce bleeding tendency and complications, such as intracranial hemorrhage or GI bleeding (Goldman, 2007).
- Rest frequently.
- Prepare patient for splenectomy, if indicated. Ensure adequate nutrient stores.

FOOD AND NUTRITION

- Maintain diet of preference. Use small, frequent feedings if patient has nausea or vomiting.
- Adequate folic acid will be needed.
- Increase fluids (e.g., 3 L/d) unless contraindicated.
- After splenectomy, patient will need adequate protein, energy, zinc, and vitamins A and C for wound healing. Vitamin K from the diet and supplements may need to be monitored.

Common Drugs Used and Potential Side Effects

- Most drugs are stopped because nearly any drug may aggravate the condition.
- Corticosteroids such as prednisone may be used to control bleeding. Side effects are numerous and may affect nutritional status (e.g., decreased serum calcium, potassium, and nitrogen; increased serum sodium; and glucose intolerance may occur).
- Myelosuppressive agents are often prescribed. Anagrelide hydrochloride (Agrylin) is an oral imidazoquinazoline agent that has been shown to reduce elevated platelet counts and the risk of thrombosis. Interferon alpha may be used.
- Rituximab seems to be a promising drug in the treatment of refractory autoimmune thrombocytopenia.

Herbs, Botanicals, and Supplements

- Herbs and botanical supplements should not be used without discussing with the physician.

NUTRITION EDUCATION, COUNSELING, CARE MANAGEMENT

- Discuss altering nutrients as needed, depending on medications ordered and their use over time; surgery, if required; and ability to eat adequately.

Patient Education—Food Safety

If tube feeding or CPN is needed, careful handwashing procedures should be followed.

For More Information

- The ITP Society of the Children's Blood Foundation
  http://www.childrensbloodfoundation.org/
- Platelet Disorder Support Foundation
  http://www.pdsa.org/

THROMBOCYTOPENIA—CITED REFERENCES

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