**Anemia**

* Reduction in [Hb] more than 2 standard deviations below the mean, adjusted for sex and age
* Men <135g/L, Women <120g/L
* Normals may differ for certain populations
	+ High altitude, smokers, exposure to carbon monoxide, African Americans
* Associated with increased risk of hospitalization, death in older adults living in the community

**Signs and symptoms of Anemia**

**Underlying Causes**

1. Hemorrhage
2. Hemolysis
3. Defects in haemoglobin, RBC membrane
4. Suppression of bone marrow
5. Alcohol use
6. Dietary deficiencies
7. Chronic kidney disease
8. Hypothyroid, hypogonadism
9. Leukemia
10. Myelodysplastic syndrome
11. Infiltrative diseases (cancer, sarcoidosis)

**History and Physical**

* Bleeding
* FHx of anemia
* Medication use
* Alcohol intake
* Comorbid conditions
* GI symptoms
* Menorrhagia
* Glossitis, angular cheilitis, koilonychias, paresthesias

**Algorithms for Microcytic, Normocytic, and Macrocytic Anemias**

**Treatment of Common Anemias**

**Iron Deficiency Anemia**

* Assess underlying cause of anemia
* Rule out occult GI bleeding
* Menorrhagia must be convincing before being accepted as sole cause of iron deficiency
* If not obvious GI blood loss, consider screening for celiac disease
* If Hb fails to respond as anticipated, consider ongoing blood loss, medications that impair iron absorption, different / concurrent cause of anemia, impaired erythropoietic response
* To increase adherence to oral supplements: slowly increase dose, start with a tablet after meals, then change timing to before meals
* Avoid enteric-coated products -> poor absorption
* Treat until iron stores replenished

|  |  |
| --- | --- |
| Nonpharmacologic | Pharmacologic |
| * Diet: foods rich in heme iron (liver, lean red meats, seafood: oysters, clams, tuna, salmon, sardines, shrimp)
* Takes longer to replete iron stores than supplements
* Ascorbic acid (vitamin C) enhances absorption of non-heme iron
* Polyphenols and phytates (found in tea / coffee) can inhibit non-heme iron absorption
 | * Oral iron salts: variety of forms with varying concentration of elemental iron
	+ Absorption enhanced when given on empty stomach, but side effects (nausea, epigastric pain) more common this way
	+ Target dose = 105-200 mg/d of elemental iron, in divided doses
* Parenteral iron: for patients with malabsorption or true intolerance to oral iron, or if ongoing losses exceed capacity of GI tract to absorb oral iron
	+ Low risk of anaphylaxis
* Reticulocyte response should be evident w/in 1 week, Hb expected to increase by 10g/L every 7-10d
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**Megaloblastic Anemia**

* Due to impaired DNA synthesis caused by deficiencies of vitamin B12 or folate, or due to impaired DNA / RNA metabolism (drugs, myelodysplasia)
* Characterized by hypersegmented neutrophils on blood film
* Reticulocyte response evident in 3-4d, Hb improves by day 10, full resolution in 2 months
* Neurologic deficits may take 6 months or more to resolve, some may persist
* Risk of hypokalemia in older patients on diuretics for heart failure (obtain baseline potassium, monitor, and supplement as needed)
* Vitamin B12 deficiency: can present with anemia, macrocytosis, pancytopenia, neurologic complications e.g. dementia, weakness, sensory neuropathy, paresthesias
	+ Low-normal or normal serum vitamin B12 may be seen when deficient and responds to supplements
	+ Need high index of suspicion, especially in older adults
	+ Meat and dairy are the only diet sources
	+ Strict vegans at risk
	+ Vegetarians may be at risk during high demand (e.g. pregnancy)
	+ Most common cause of deficiency is malabsorption due to pernicious anemia, gastrectomy, gastritis, ileal resecrtion, Crohn’s, pancreatic insufficiency, certain drugs (e.g. metformin, PPIs)
* Folate deficiency
	+ Most commonly caused by dietary deficiency and alcoholism
	+ Increased requirements in pregnancy, haemolytic anemia, and with use of certain medications (e.g. methotrexate, phenytoin, trimethoprim)
* Nonpharmacologic Choices: normal dietary intake of vitamin B12 and folate
	+ In case of neurologic deficits due to B12 deficiency -> need pharmacologic treatment
	+ Abstinence from alcohol may be necessary

Pharmacologic Choices

|  |  |
| --- | --- |
| Vitamin B12 | Folic Acid |
| * Treat with either cyanocobalamin or hydroxocobalamin
* Daily requirement: 6-9 mcg
* Doses > 100 mcg/d not absorbed but not tocity
* Tend to give more than less, especially if neurological deficits
* High dose oral vitamin B12 effective, but limited by compliance and need for monitoring
* Approach: parenteral vitamin B12 until neurologic and hematologic findings resolve, maintenance route based on patient’s circumstances
 | * Replacement doses: 1-5 mg/d
* Give only for confirmed folate deficiency or in situations of increased demand
* Ensure patients do not have concomitant vitamin B12 deficiency
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**Anemias Responsive to Erythropoiesis Stimulation**

* Chronic renal failure, HIV patients on ARVs, chronic Hep C patients on ribavirin, chemotherapy patients (for non-hematologic cancers), surgery patients, low-risk myelodysplasia
* Select patients to treat based on endogenous EPO levels
* Ensure adequate iron supply along with EPO use
* Choices: Epoetin (Eprex) given 3x/wk, Darbepoetin (Aranesp) given once per 1-4 weeks
* Significant potential for toxicity
* Rapid/excessive correction of anemia can lead to HTN, seizures (monitor HTN 3x/wk initially, then after each dose)
* Erythrocytosis can predispose to thrombosis
* Risk of pure red cell aplasia -> profound anemia

**CCFP Objectives**

1. Assess the risk of decompensation of anemic patients (e.g., volume status, the presence of congestive heart failure [CHF], angina, or other disease states) to decide if prompt transfusion or volume replacement is necessary.
2. In a patient with anemia, classify the anemia as microcytic, normocytic, or macrocytic by using the MCV (mean corpuscular value) or smear test result, to direct further assessment and treatment.
3. In all patients with anemia, determine the iron status before initiating treatment.
4. In a patient with iron deficiency, investigate further to find the cause.
5. Consider and look for anemia in appropriate patients (e.g., those at risk for blood loss [those receiving anticoagulation, elderly patients taking a nonsteroidal anti-inflammatory drug]) or in patients with hemolysis (mechanical valves), whether they are symptomatic or not, and in those with new or worsening symptoms of angina or CHF.
6. In patients with macrocytic anemia:
	1. Consider the possibility of vitamin B12 deficiency.
	2. Look for other manifestations of the deficiency (e.g., neurologic symptoms) in order to make the diagnosis of pernicious anemia when it is present.
7. As part of well-baby care, consider anemia in high-risk populations (e.g., those living in poverty) or in high-risk patients (e.g., those who are pale or have a low-iron diet or poor weight gain).
8. When a patient is discovered to have a slightly low hemoglobin level, look carefully for a cause (e.g., hemoglobinopathies, menorrhagia, occult bleeding, previously undiagnosed chronic disease), as one cannot assume that this is normal for them.
9. In anemic patients with menorrhagia, determine the need to look for other causes of the anemia.

**Resources**

BC Guidelines. Iron Deficiency - Investigation and Management.

Therapeutic Choices. Sixth Edition. Common Anemias.

Mayo Clin Proc 2005;80(7):923-36. How to interpret and pursue an abnormal complete blood cell count in adults.