Anemia, Hemolytic

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Risk

- Autoimmune disorders (SLE, RA, scleroderma, cold agglutinin disease).
- Lymphoproliferative disorders (CLL, NHL).
- Prosthetic heart valves (ball-and-cage, and bileaflet valves). Usually subclinical, but can be severe in up to 15% of pts.
- Family history of hemoglobinopathies or RBC membrane defects (thalassemia, sickle cell disease, G6PD deficiency, spherocytosis).
- Exposure to drugs (cephalosporins, penicillins, NSAIDs) or other chemicals (naphthalene, fava beans).
- Infection (*Clostridium perfringens*, *Haemophilus influenza* type B, malaria, HIV).
- Wilson disease (due to toxic effect of copper ions in circulation).

Perioperative Risks

- Anemia, hypoxia.
- Underlying CV compromise.
- Splenomegaly in pts with extravascular hemolysis (within the reticuloendothelial system). Splenectomy is a common surgical procedure in pts with sickle cell disease due to hemolysis and sickling.
- Renal failure due to massive hemolysis (e.g., cold agglutinin hemolysis, sickling, drug reaction)
- Varying levels of liver disease depending on type of hemolytic anemia. Synthetic function of liver is usually normal, but in severe cases can be compromised.

Worry About

- Uncompensated anemia in pts with subacute hemolysis
- Periop hemolysis and/or hypoxia
- Need for transfusion and/or fluids

Overview

- Pts with hemolytic anemia may present with any of the following: fatigue, angina, SOB, tachypnea, tachycardia, or jaundice. The hemolysis can lead to changes in blood viscosity, gallstone production, splenomegaly, and renal failure in severe cases. Many pts will be both iron and folate deficient.
- Epidemiology varies by pt population. For example, G6PD is an X-linked condition and its prevalence is near 50% in Kurdish Jews, but around 1:1000 in North American and European populations.
- Other things to consider incl monitoring periodic Hct levels, and administering prophylactic antibiotics/vaccinations to pts who have had a splenectomy.

Etiology

- Multiple causes; see Risk section (e.g., RBC structural abnormalities, autoimmune reaction, enzyme deficiency, hemoglobinopathies, mechanical heart valves, drugs, infection).

Usual Treatment

- Treatment depends on etiology:
  - Autoimmune: Corticosteroids, plasmapheresis, packed RBC transfusion for symptomatic pts, supportive care;
  - Drug induced: Discontinuation of offending medication, corticosteroids, supportive care;
  - Prosthetic valve: Cardiology consult and transfusion if symptoms rapidly worsen;
  - RBC membrane defect: Splenectomy and supportive care;
  - Enzyme deficiency: Avoidance of triggers, splenectomy, supportive care;
  - Infection: Treatment of underlying infection and supportive care;
  - Wilson disease: Rapid removal of copper, early consideration for liver transplant.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dehydration	Fatigue, dizziness	Hypotension, weak pulses, increased capillary refill	CBC, BNP
HEME	Anemia	Fatigue, SOB, dizziness	Jaundice, pallor, splenomegaly	Hgb, Hct, reticulocyte count, indirect bilirubin, LDH
RENAL	Hemoglobinuria, acute renal failure	Dark urine (episodic)	Possible Htn, resp rate changes	Urine analysis, BUN, Cr
GI	Liver disease		Hepatosplenomegaly	Liver function tests (LFTs)

Key Reference: Eckman JR: Disorders of red cells. In Lubin MF, Dodson TF, Winawer NH, editors: *Medical management of the surgical patient: a textbook of perioperative medicine,* ed 5, Cambridge, 2013, Cambridge University Press, p 215.

Perioperative Implications

Preinduction/Induction/Maintenance

- Preop management and treatment of underlying cause of hemolytic anemia.
- The test obtained periop depends on the etiology, severity, and chronicity of the hemolytic anemia.
- Avoidance of hypoxia, hypercarbia, acidosis, low-flow conditions, and hypothermia (particularly in cold agglutinin disease).
- Optimize CV status with adequate hydration; consider IV fluid treatment the day before surgery if hypovolemic.
- RBC transfusion may be considered to improve O_2 carrying capacity depending on etiology (must be warmed for pts with cold agglutinin disease).
- Normothermia should be strictly maintained in any pt requiring transfusion(s).
- Possible plasmapheresis for acute removal of IgM antibodies in pts with uncontrolled cold agglutinin disease.

Monitoring

- Standard monitors and urine output, CV status, O_2 saturation (pulse oximetry), and temp regulation (avoiding hypothermia)

General Anesthesia

- Choice of anesthetic technique can vary, but all approaches should have the goal of avoiding hypoxia, hypercarbia, acidosis, stasis, low-flow conditions, and hypothermia.
- Avoidance of hypoventilation.

Regional Anesthesia

- Goals for regional anesthesia are the same as for general anesthesia. No specific contraindications.

Postoperative Period

- Supplemental O_2 therapy
- Adequate hydration
- Early ambulation
- Continued temperature regulation
- Active pulm toilet
- Aggressive evaluation and treatment of fever or infection

Anticipated Problems/Concerns

- Acute periop hemolysis; may warrant transfusion.
- Periop sickling event due to hypoxia, acidosis, hypothermia, or low flow. Sickling can be decreased by increasing arterial oxygen tension.
- Hypothermia-induced cold agglutinin hemolysis; decreased by maintaining normothermia.
- Hypoxia and end-organ damage.
- Venous thrombosis, pulm embolism.

Anemia, Megaloblastic

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Risk

- Prevalence: Estimates ranging from 1.7-3.6%.
- Most common cause is vitamin deficiency: 65% vitamin B12; 12% combined folate/vitamin B12; 6% folate.
- Pernicious anemia is less common: 1 in 7500 people in USA develops pernicious anemia each year.
- Prevalence increases with advanced age and in countries with higher rates of malnutrition.

Perioperative Risks

- Risk of severe anemia and coagulopathy.
- Risk of coronary, cerebral ischemia secondary to severe anemia.
- Increased plasma volume as compensatory mechanism can predispose pts to CHF.

Worry About

- Exaggerated effect of myocardial depression from anesthesia.
- Preoperative treatment should include supplementation of B12 and folate or transfusion in setting of severe anemia and emergent surgery.
- Decreased platelet count and coagulopathy.
- Anemia causing MI, stroke, or resp failure.

Overview

- An anemia caused by a failure of DNA synthesis which results in large, structurally abnormal and immature red blood cells called megaloblasts (MCV >100 fL/cell).
- Often WBC and platelet counts are also decreased.

- Anemia develops insidiously and due to physiologic compensatory mechanisms it may not cause symptoms until it is severe.
- Symptoms: Fatigue, pallor, dyspnea on exertion, headache, dizziness, tachycardia, nausea, diarrhea, glossitis, and jaundice.
- Vitamin B12 deficiency can interfere with myelination and produce peripheral neuropathy which varies from subtle loss of vibratory sensation and proprioception to frank dementia.

Treatment

- The treatment of megaloblastic anemia depends upon the underlying cause of the disorder.
- Diagnose with complete blood counts, red cell indices, and assays of the vitamin B12 and folate.
- Dietary insufficiency of cobalamin and folate can be treated with appropriate changes to the diet and the administration of supplements.
- Vitamin B12 1000-2000 µg orally can be given once per d but if pts have neurologic signs, vitamin B12 1 mg IM is usually given 1 to 4 times/wk for several wk.
- Folate 400-1000 µg orally once per d.
- Vitamin B12 deficiency must be ruled out before treating with folate alone as this would treat anemia but not the neurologic manifestations.

Etiology

- Most common cause is vitamin B12 and/or folate deficiency due to:
  - Decreased absorption due to gastric or intestinal disease (pernicious anemia, Crohn disease);
  - Decreased intake seen in strict vegan diet, elderly, or alcoholics;
  - Increased requirements seen in pregnancy, patients on hemodialysis, and hemolytic anemia.
- Some drugs and toxins impair vitamin absorption, including methotrexate, chemotherapeutic agents, phenytoin, antacids, and nitrous oxide.
- Much rarer causes include enzyme deficiencies, myelodysplastic syndromes, and acute myeloid leukemia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Headaches and dizziness or vertigo, sore tongue	Yellow eyes, large beefy red tongue	
CV	Increased cardiac output Increased plasma volume	Angina, chest pain, palpitations, tachycardia	Hypotension and tachycardia	Decreased Hgb and Hct, red cell count MCV >100 May have decreased WBC and platelet count
RESP/HEME		Poor exercise tolerance Resp distress	Pallor, DOE, SOB	Large oval cells with hypersegmented neutrophils and large platelets in bone marrow diagnostic feature; Howell-Jolly bodies, nuclear fragment, may be seen in RBCs; low reticulocyte count
GI	Splenomegaly	Symptoms of liver disease, nausea, vomiting, diarrhea	Splenomegaly, jaundice	Liver enzymes, increased LDH
ENDO	Low erythropoietin levels			Bone marrow—macrocytosis, low folate, and B12 stores
CNS		Headaches, fatigue, dizziness, confusion	Dementia, neuropsychiatric disease	Low B12
PNS	Peripheral neuropathy		Loss of vibratory and proprioception especially in LE	Low B12
MS		Fatigue	Easy bleeding, bruising	

Key References: Khanduri U, Sharma A: Megaloblastic anaemia: prevalence and causative factors, *Natl Med J India* 20(4):172–175, 2007; Aslinia F, Mazza J, Yale S: Megaloblastic anemia and other causes of macrocytosis, *Clin Med Res* 4(3):236–241, 2006.

Perioperative Implications

Preoperative Preparation

- Preop workup of cause of megaloblastic anemia; treat cause and any vitamin deficiencies.
- Schilling test was used to identify origin of vitamin B12 deficiency but is no longer available in most hospitals and has been replaced with antiparietal cell and anti-intrinsic factor antibody assays.
- Treatment with folate alone with correct hematologic but not neurologic manifestations.
- May benefit from periop hematology/oncology consult.
- Bone marrow megaloblastic changes are reversed within 12 h after treatment with folate and vitamin B12, and bone marrow morphology appears to be normal within 2 to 3 d.
- Watch for hypokalemia and hypophosphatemia after treatment.

Monitoring

- ST segment changes for myocardial ischemia.
- Large-bore access to facilitate transfusion.

Induction/Maintenance

- Both regional and general anesthesia are options.
- Caution with neuraxial anesthetics or regional anesthetics in case of bleeding diathesis or preexisting neuropathy.
- Avoid nitrous oxide as it inactivates vitamin B12, even with short exposure.

Intraoperative Management

- Intraoperative transfusion as clinically indicated.
- Some pts at risk for increased bleeding and transfusion.

Postoperative Period

- Increased risk for anemia and bleeding diathesis.
- If transfusion given, worry about volume overload due to compensatory increased plasma volume.

Anticipated Problems and Concerns

- Vigilance for prevention, diagnosis, and treatment of ischemic events.
- Be prepared to treat bleeding diathesis.
- Treat symptoms (e.g., resp distress, fatigue, angina, heart failure, tachycardia).

Angina, Chronic Stable

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Risk

- Incidence in USA: 3 million.
- Annual rates per 1000 new episodes of angina for non-African American men are 28.3 for ages 65–74, 36.3 for ages 75–84, and 33.0 for age 85 and older. For non-African American women in the same age groups, the rates are 14.1, 20.0, and 22.9, respectively. For African American men, the rates are 22.4, 33.8, and 39.5, and for African American women, the rates are 15.3, 23.6, and 35.9, respectively.
- African Americans have highest death rates, although overall death rates are decreasing over time.

Perioperative Risks

- Increased risk of periop MI and death varies, depending on study (3–12%).
- Risk of LV dysfunction, myocardial ischemia, hypotension, and MI.

Worry About

- Increasing frequency of symptoms (i.e., unstable angina)
- Signs of LV dysfunction with ischemia
- Silent myocardial ischemia

Overview

- Chronic stable angina identifies pts at risk for developing myocardial ischemia and MI.
- Angina is present in <25% of episodes of myocardial ischemia.
- Symptoms should be stable for previous 60 d for "stable" diagnosis.
- Can result from
  - Inadequacy of myocardial O_2 supply in pts with critical coronary artery stenosis.