men) and high fasting transferrin saturations (>50% in women and >60% in men).
- Genetic testing may reveal mutations in the HFE gene on chromosome 6.

Usual Treatment

- Dietary changes to avoid red meat, vitamin C, and alcohol.
- Weekly or biweekly phlebotomy is initiated in symptomatic pts.
- Iron chelation therapy if phlebotomy is not tolerated (i.e., anemic pts).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Hepatic encephalopathy	Confusion, lethargy		MMSE
ENDO	Diabetes mellitus Hypoparathyroidism Impotence/infertility	Hypoglycemia Hypocalcemia Amenorrhea	Foot examination Chvostek and Trousseau signs	Glucose Calcium FSH/ LH, TSH
CV	Cardiomyopathy Arrhythmias Heart failure	Poor functional status (Pre) syncope Orthopnea	Displaced PMI Peripheral edema Elevated JVD	ECG, Holter monitor ECHO, CXR
RESP	Hepatopulmonary syndrome	Dyspnea	Pleural effusions	CXR
GI	Cirrhosis/hepatocellular carcinoma	Malaise Weight loss Indigestion	Hepatomegaly Splenomegaly Spider nevus	Serum ferritin LFTs, INR, CBC, albumin
MS	Arthralgia	Pain with activity	Swollen joints	
DERM	Bronzed pigmentation (late manifestation)		Bronze/gray skin	

Key References: Shander A, Berth U, Betta J, Javidroozi: Iron overload and toxicity: implications for anesthesiologists, *J Clin Anesth* 24(5):419–425, 2012; Ajloka RS, Kushner JP: Clinical consequences of iron overload in hemochromatosis homozygotes, *Blood* 101(9):3351–3354, 2003.

Perioperative Implications

Preoperative Preparation

- Consider risk for potentiation or precipitation of hepatic encephalopathy and plan to mitigate risk through careful selection of drugs, maintaining normal acid-base status, normalizing electrolytes, and avoiding hypoglycemia and hypotension.
- ECG, low threshold, to obtain ECHO.
- Assess bleeding risk by checking INR, PTT, and platelets, especially if considering RA.

Monitoring

- Decision on invasive lines should be based upon degree of cardiac and liver dysfunction as well as surgical risk.
- Avoid instrumentation of the esophagus (TEE, esophageal stethoscope, temperature probe) in advanced liver disease.

Airway

- Pts may require preoxygenation in the sitting position when orthopnea is present.
- Expect poor preoxygenation and quick desaturation with advanced liver or heart disease.
- If there is evidence of coagulopathy, employ gentle airway manipulation.

Preinduction/Induction

- Consider RSI (with H_2 antagonist and cricoid pressure) if evidence of ascites or gastroparesis associated with diabetes mellitus.
- In pts with severe liver disease, sensitivity to induction agents and anxiolytics may be increased and metabolism of succinylcholine may be slowed.
- Pts with a diseased liver may require a larger initial dose of nondepolarizing neuromuscular blocking agent due to altered protein binding and a larger volume of distribution.

Maintenance

- Consider blood-sparing strategies such as acute normovolemic hemodilution or using colloids, as blood transfusions are especially bad in this population.
- Intraop hourly glucose checks; consider background infusion of dextrose containing crystalloid.
- All volatile agents decrease hepatic blood flow and have minimal hepatic metabolism. All are likely safe.
- Consider cisatracurium as it does not rely on hepatic metabolism.
- Consider the potentiation of morphine, meperidine, alfentanil, benzodiazepines, and dexmedetomidine in pts with advanced liver disease.

Extubation

- Gentle oropharyngeal suctioning due to risk of coagulopathy and bleeding.
- Consider taking the pt intubated to the ICU for chelation therapy in pts that receive large volumes of blood.

Postoperative Period

- Careful glycemic management.
- Surgery and/or anesthetic may result in worse liver function. Remain vigilant for postop coagulopathy, renal impairment, or cognitive dysfunction.
- Pts with cardiac disease should have 24-h telemetry.
- Generally avoid NSAIDs and acetaminophen for pain control.

Hemophilia

Vincent S. Cowell

Risk

- Incidence of hemophilia A, factor VIII (FVIII) deficiency is 1:5000 male births; for hemophilia B, factor IX (FIX, Christmas disease) deficiency, it is 1:25,000 male births.
- Number of people affected with hemophilia in USA is estimated at approximately 20,000.
- Von Willebrand disease is the most common hereditary bleeding disorder, with a prevalence of about 1%.
- Hemophilia A, FVIII deficiency, affects 80–85% of hemophiliacs; the remainder has hemophilia B because of factor IX deficiency.
- Hemophilia A and B are X-linked recessive hereditary disorders, which occur in males and are transmitted by females who may be heterozygous for the gene mutation.
- Females may be asymptomatic carriers of the hemophilia gene and may have partial deficiency of FVIII of FIX, resulting in increased bleeding tendency.
- Hemophilia is without ethnic or geographic predilection.

Perioperative Risks

- Prolonged and potentially fatal hemorrhage may occur both during and after surgery.
- Closed-space bleeding can lead to nerve injury and vascular or airway obstruction.
- Surgery should not proceed without adequate supply of coagulation factor replacement to support the procedure and postop course.

Worry About

- Venous access issues may lead to central venous access.
- Spontaneous bleeding and intraop and postop hemorrhage despite optimal replacement therapy of deficient coagulation factor.
- FVIII and FIX inhibitor antibodies (up to 33% for FVIII and 3% for FIX).

Overview

- Hemophiliacs can have severe deficiency (<1% nml levels) approximately 40%, moderate deficiency (1–5% of nml levels) approximately 10%, or mild deficiency (5–40% of nml levels) approximately 50%.
- This congenital disorder is inherited as an X-linked recessive trait, affecting males almost exclusively.
- Acute and chronic complications often are due to recurrent spontaneous bleeding, the hallmark of which is bleeding into the joints (e.g., cycle of joint hemorrhage, inflammation, synovial proliferation, and erosion of cartilage, causing pain and disability).
- Hemophilia pts generally have normal PT, normal bleeding times, and a prolonged aPTT. Specific laboratory factor assays make the distinction, and plasma concentrations of FVIII or FIX determine the severity.
- Early prophylaxis is now the standard of care for pts with severe hemophilia.
- Plasma and recombinant factor products are now considered safe and equally effective.

Etiology

- Hereditary disorder that is X-linked recessive.
- Acquired hemophilia is the development of FVIII inhibitors (autoantibodies) in persons without a Hx of FVIII deficiency.

Usual Treatment

- Desmopressin (DDAVP injection or Stimate nasal spray) whenever possible for mild hemophilia A.
- Treatment includes clotting factor replacement therapy and recombinant FVIII and FIX products; plasma and recombinant factor products are now considered safe and equally effective; and there is no reported seroconversion to HIV, HVB, or HVC.
- Plasma concentrations of deficient factors are maintained at a minimum of 40–70% throughout the periop period; for major procedures, 100% is recommended before surgery and is maintained for 24–48 h.
- Cryoprecipitate is no longer recommended as a treatment alternative.
- Thrombin is produced via alternative pathways; prothrombin complex concentrate and recombinant factor VIIa (NovoSeven) is used in pts with inhibitors to FVIII of FIX.
- Gene insertion therapy shows a promising future.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Pharyngeal bleeding	Often seen in children	Tongue and mouth lacerations	Exam
GI	GI bleeding not common	When it occurs, bleeding can be excessive	Stool exam and endoscopy	Hemoccult, angio
HEME	Anemia, hematoma formation, and bruising	Lethargy, SOB, and skin discoloration	Hematomas	PT/PTT, plt count, bleeding FVIII and FIX assay, gene analysis
GU	Hematuria	Blood in urine		UA, cysto, IVP
CNS	Intracranial hemorrhage	Head trauma, headache, and change in mental status	Any sign or symptom of head injury or trauma	Head CT
MS	Joint hemorrhage Joint deformities Muscle hemorrhage Compartment syndrome Chronic pain	Painful distention of the joint Bruising Restricted movement Narcotic dependence	Hemarthroses Limited ROM Tenderness	Physical exam X-ray

Key References: Franchini M, Mannucci PM: Past, present and future of hemophilia: a narrative review, *Orphanet J Rare Dis* 7:24, 2012; Cabani LM, Ramsey G: Hemostasis and transfusion medicine. In Barash PG, Cullen BF, Stoelting RK, et al, editors: *Clinical anesthesia*, ed 7, Philadelphia, PA, 2013, Lippincott Williams & Wilkins, pp 433–434.

Perioperative Implications

Preoperative Preparation

- Preparation for the care of a pt with hemophilia should include consultation with a hematologist and when available, a hemophilia treatment center.
- Ideally, the anesthesiologist should have experience treating pts with bleeding disorders.
- A comprehensive detailed plan should be in place that outlines the type of hemophilia, factor levels, and dosing strategy for replacement of coagulation factor deficiencies.
- In elective surgery, levels of deficient coagulation factor should be restored to 40–70% of normal before surgery.
- Inhibitor screening and inhibitor assay assessments are essential to preop preparation.
- Adequate quantities of clotting factor concentrates should be available for surgery and the postop course.
- One unit of factor concentrate per kilogram of body weight normally increases the factor concentration by 2%. For factor VIII the half-life is 6 to 10 h, and for factor IX the half-life is 8–16 h, and thus approximately 1.5 U/h per kg of factor VIII or 1.5 U/2 h per kg of factor IX should be given.

Airway

- Care with laryngoscopy to avoid any trauma and thus bleeding to the airway is essential.
- Avoid nasal cannulations (i.e., endotracheal and nasogastric tubes).

Maintenance

- Noninvasive monitoring is optimal; risk/benefit ratio of invasive monitoring vs. site bleeding risk deserves significant consideration.
- Incorporate techniques to minimizing blood loss relative to the procedure.
- Antifibrinolytic drugs such as tranexamic acid are effective as adjunctive treatments for mucosal bleeds and dental extractions.

Adjuvants

- Risk of uncontrolled bleeding detracts from the selection of regional anesthetic technique. However, brachial plexus blocks performed at the axilla without complications have been reported.

Anticipated Problems/Concerns

- Blood bank support for plasma components, if needed, should be included in plans.
- Minimal risk of transmitting hepatitis and AIDS accompanies transfusion of blood components.

Hemosiderosis, Pulmonary

Fredrick Ntumy | Roy G. Soto

Risk

- Classically affects infants and children (80% manifest before 10 y old), but can affect any age group.
- No predilection for males or females.

Worry About

- Restrictive lung disease
- Pulm Htn
- Cor pulmonale
- Alveolar hemorrhage
- Increased need for transfusion secondary to acute and chronic anemia
- Adrenal insufficiency secondary to chronic steroid use

Overview

- Rare disorder of unknown etiology characterized by repeated episodes of intraalveolar hemorrhage and deposition of hemosiderin in alveolar macrophages. The cycle of recurrent hemorrhage frequently leads to the development of pulm fibrosis, pulm Htn, and cor pulmonale. Disease course is variable and can be marked by multiple spontaneous remissions, and the extent of pulm hemorrhage can be massive, leading to early death, or can be clinically insignificant.
- Presents with classically with the triad of hemoptysis, anemia, and pulm infiltrates on CXR.

Etiology

- Unknown; thought to be immune-mediated due to its responsiveness to immunosuppressive therapy
- Associated with immune-mediated disorders such as Goodpasture syndrome, SLE, Heiner syndrome, and Wegener granulomatosis, which can cause diffuse alveolar hemorrhage via immune-mediated mechanisms

Usual Treatment

- Immunosuppression with steroids (IV and PO) and supportive care. Other immunosuppressive agents such as azathioprine, chloroquine, and cyclophosphamide may be tried in steroid-unresponsive pts.