HELLP Syndrome

David J. Birnbach

Risk

- Occurs in 0.1–0.9% of all pregnancies.
- Previous history of preeclampsia or HELLP syndrome is a risk factor for HELLP.
- Occurs in 10–20% of women suffering from preeclampsia with severe features.
- May be a form of preeclampsia. Preeclampsia occurs in 2–10% of pregnancies; it is more prevalent in women with diabetes, women who are obese, and older women.

Perioperative Risks

- High maternal and fetal morbidity and mortality
- Increased cesarean delivery rate, increased intraop hemorrhage

Worry About

- Can be confused with hepatitis, thrombotic thrombocytopenic purpura, gallbladder disease, viral illnesses, antiphospholipid syndrome, and acute fatty liver of pregnancy.
- Thrombocytopenia and coagulopathy increase risk of hematoma associated with neuraxial anesthetic.
- High risk of hemorrhagic complications; associated with placental abruption.
- Upper airway and laryngeal edema can lead to airway obstruction and difficult or failed intubation. Fluid management can be difficult; pulm edema may ensue.

Overview

- HELLP is an acronym for the findings that suggest hepatic involvement in preeclamptic pts: **H**emolysis, **E**levated **L**iver enzymes, **L**ow **P**latelets. It typically presents between 28–36 wk gestation but has been reported to occur postpartum.
- Diagnostic criteria include hemolysis, defined by abnormal peripheral smear/microangiopathic hemolytic anemia and increased bilirubin levels; elevated liver enzymes; and thrombocytopenia.
- Failure to treat may lead to eclampsia or death due to hepatic hematoma or rupture.
- Up to 20% of pts with HELLP syndrome do not have antecedent Htn.

Etiology

- Poorly understood; may be severe form of preeclampsia resulting from abnormal prostaglandin control, intravascular platelet activation, and microvascular endothelial damage

Usual Treatment

- Definitive treatment is delivery as quickly as possible.
- After delivery, many experience full recovery and plt counts returning to normal within 1 wk.
- Recent evidence challenges the role of glucocorticoid therapy.
- Platelets, FFP, and cryoprecipitate administered as needed.
- Magnesium sulfate for CNS irritability and antihypertensives for Htn.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Upper airway edema	Dyspnea, voice change	Poor visualization on airway exam	Mallampati assessment
CV	LV failure	Dyspnea, desaturation	Adventitious sounds, desat	CVP and/or LVEDP
RESP	Resp depression	Magnesium administration	Decreased reflexes	$MgSO_4$ level
GI	Liver swelling Subcapsular hematoma	Epigastric pain N/V		Elevated AST, ALT, LDH >600 IU/L
HEME	Thrombocytopenia Hemolytic anemia	Bruising Pallor, jaundice	Bleeding (IV site oozing)	Platelet count <100,000 Bilirubin >1.2 mg/dL Peripheral smear
RENAL	Acute renal failure	Oliguria		Elevated uric acid, BUN, serum Cr
CNS	Eclampsia, cerebral edema	Seizures		

Key References: American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy: Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy, *Obstet Gynecol* 122(5):1122–1131, 2013; Fitzpatrick KE, Hinshaw K, Kurinczuk JJ, Knight M: Risk factors, management, and outcomes of hemolysis, elevated liver enzymes, and low platelets syndrome and elevated liver enzymes, low platelets syndrome, *Obstet Gynecol* 123(3):618–627, 2014.

Perioperative Implications

Preoperative Preparation

- Obtain CBC, PT, PTT, fibrinogen, ALT, AST, LDH, BUN, and Cr.

Monitoring

- Consider arterial line and baseline ABG.
- Consider CVP if oliguria persists despite fluid administration or CHF.

Airway

- Assess airway early and repeat airway exam periodically.
- Laryngeal edema may preclude normal tracheal intubation in the event of emergency C-section. Videolaryngoscopy should be considered for intubation.
- Difficult intubation equipment should be immediately available.
- Consider preemptive epidural or continuous spinal cath before platelet count drops.

Induction

- Control neuraxial anesthesia with incremental dosing of catheter, if not contraindicated. Spinal techniques can be safely used in severe preeclampsia without coagulopathy.
- If GA is required, the hypertensive surge associated with ET intubation can be reduced by pretreatment with magnesium, antihypertensives, and/or opioids.

Adjuvants

- If significant Htn, antihypertensive therapy prior to laryngeal intubation.
- If receiving magnesium sulfate and needs GA, small doses of neuromuscular blocking agents with close neuromuscular blockade monitoring.

Hemochromatosis

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Risk

- Incidence of primary (hereditary) hemochromatosis: In some Caucasian populations, 10% are heterozygous carriers and 0.25–1% homozygous.
- Age: Clinical manifestations typically occur after age 40 in men and later in women due to the protective effect of menses.

Perioperative Risks

- Infection due to accumulation of iron in immune cells
- Glycemic disturbances
- Bleeding risk from low levels of clotting factors or platelet dysfunction
- Decompensated heart failure and/or arrhythmias

Worry About

- Iron deposition in the liver, heart, and endocrine glands leading to dysfunction

Overview

- Primary (hereditary) hemochromatosis is transmitted by genes, and secondary hemochromatosis is acquired.
- HH is an autosomal recessive disorder (HFE gene) that results in excess iron absorption.
- Once excess iron is absorbed, humans have no way to increase excretion. Iron accumulates in organs and results in cell damage. Because 90% of excess iron is deposited in the liver, it is often most affected.
- HCC is one of the most serious complications from untreated HH, responsible for 45% of deaths in pts with HH. Presence of cirrhosis is the greatest prognostic indicator for increased mortality.

Diagnosis

- Diagnosis is made by looking for elevated serum ferritin (>200 ng/mL in women and >300 ng/mL in

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.