Bernard-Soulier Syndrome

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Risk

- Estimated to be <1 in 1 million persons, but may be higher due to misdiagnosis and underreporting
- Rare: Approximately 100 cases reported in literature

Perioperative Risks

- Severe hemorrhage out of proportion to plt count
- Transfusion reactions

Worry About

- Severe periop hemorrhage
- Limited availability of blood products
- Concurrent medical conditions (e.g., uremia, liver disease) or medications (NSAIDs, heparin, and antiplatelet agents) contributing to bleeding

Overview

- Coagulopathy characterized by defects in plt number and function due to an absence or abnormality in plt membrane glycoprotein receptor complex GPIb-IX-V, a four-protein complex responsible for initiating plt adhesion at sites of vascular injury and binding Von Willebrand factor
- Defect in primary hemostasis; mucocutaneous bleeding; often, the bleeding is more severe than expected for the pt's particular plt count
- Clinical phenotype severity varies; manifestations range from easy bruising, purpura, epistaxis, gingival bleeding, and menorrhagia to hematuria, GI bleeding, and fatal hemorrhage
- Severe bleeding associated with menses, trauma, and certain surgical procedures (e.g., tonsillectomy, appendectomy, splenectomy, dental extraction)
- Diagnosed by prolonged bleeding time, presence of a small number of very large plt on blood smears (macrothrombocytopenia), reduced plt counts (20,000–100,000), and absence of RIPA

Etiology

- Autosomal recessive inheritance pattern; a wide spectrum of clinical manifestation based on the degree of glycoprotein complex dysfunction.
- Individual genes have been identified for each of the proteins in the complex and may be the target for future therapy: 17p12 (GPIba), 22q11.2 (GPIbb), 3q29 (GPV), and 3q21 (GPIX).

Usual Treatment

- Bleeding prophylaxis including lifestyle modifications (e.g., personal safety, avoidance of trauma, avoidance of antiplatelet medications [aspirin], adequate dental hygiene, use of contraceptives in females at puberty)
- Bleeding treatment: Plts, PRBCs, and EACA
- Refractory bleeding: DDAVP, gamma globulin, corticosteroids, and recombinant factor VIIa

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oral/mucosal friability	Epistaxis and gingival and cutaneous bleeding	Sores, stomatitis, erythema	See HEME
CV	Vascular access: potential hemorrhage			
GI	GI bleeding	Melena, hematochezia		Stool guaiac, endoscopy
HEME	Coagulopathy: Primary hemostasis, mucocutaneous bleeding Severe hemorrhage Antibodies to blood products	Bleeding gums, bruising easily, menorrhagia, epistaxis Hx of transfusion family Hx of periop bleeding	Petechiae, bruises, gingival hyperemia	PT/ INR, PTT, plt count, blood smear, plt function assay, ristocetin cofactor activity Type and screen, crossmatch, and antibody analysis

Key References: Kostopanagiotou G, Siafaka I, Sikiotis C, et al: Anesthetic and perioperative management of a patient with Bernard-Soulier syndrome, *J Clin Anesth* 16(6):458-460, 2004; Lanza F: Bernard-Soulier syndrome (hemorrhagiparous thrombocytic dystrophy), *Orphanet J Rare Dis* 1:46, 2006.

Perioperative Implications

Preoperative Preparation

- Collaboration with hematology and blood bank.
- Ensure availability and adequacy of blood products.
- Assess and optimize coagulation (coagulation factor analysis, dialysis if uremic, and FFP/vitamin K if increased INR).

Monitoring

- Standard monitors.
- Risk-benefit assessment to evaluate more access or invasive monitoring (A-line or CVP) versus unnecessary or failed attempts leading to sources of potential bleeding.
- Urine output for new-onset hemoglobinuria as first sign of transfusion reaction.
- Avoid undue tension on soft tissues and provide adequate padding of pressure points and mucosal surfaces.
- Consider intraop thromboelastogram.

Airway

- Avoid nasal manipulation.
- Use extreme caution with friable oral and pharyngeal mucosal surfaces.
- Consider video laryngoscopy to ensure first-attempt success.

Induction

- No specific recommendations

Maintenance

- Avoid hemodilution.
- Meticulous surgical hemostasis.
- Normothermia promotes coagulation.
- Analyze clot formation via thromboelastography and transfusion as needed.
- Controlled hypotension may reduce potential blood loss; however, avoid in anemic pts.

Extubation

- Care of mucosal membranes, gentle orotracheal suction under direct visual guidance, and avoid coughing

Adjuvants

- Neuraxial anesthesia is relatively contraindicated in these pts. Individual risk-benefit assessment based on severity of disease and plt function (e.g., thromboelastography).

Postoperative Period

- Continue monitoring coagulation status.

Anticipated Problems/Concerns

- Severe intraop and postop hemorrhage
- Transfusion-related reaction and increased likelihood of infectious bloodborne diseases

Bilirubinemia of the Newborn

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Risk

- A common problem in neonates.
- Some types pathologic and some physiologic.
- Bilirubin may be unconjugated or conjugated; differentiating important for diagnosis.
- If pathologic, varying effect on management (e.g., sepsis, Rh incompatibility, GI obstruction, Gilbert, AVM, sickle cell, biliary atresia).
- Clinical, epidemiologic, and genetic risk factors associated with significant hyperbilirubinemia include preterm gestational age, exclusive breastfeeding, glucose-6-phosphate dehydrogenase deficiency, Rh/ABO incompatibility, East Asian or Native American ethnicity, any jaundice observed in the first 24 h of life (hemolysis until proven otherwise), cephalohematoma or significant bruising after delivery, and Hx of a previous sibling treated with phototherapy.

Perioperative Risks

- Risks specific to a primary pathologic cause of bilirubinemia
- Acute bilirubin encephalopathy (unconjugated bilirubin may penetrate brain cells and cause dysfunction in either pathologic or physiologic states)
- Kernicterus (chronic and permanent sequelae of bilirubin neurotoxicity)

Worry About

- Factors that increase blood-brain barrier permeability to unconjugated bilirubin (hypoxia, hypercarbia, acidosis, hyperosmolality, hypertension, seizure activity, and sepsis)
- Drugs (e.g., sulfonamides, ceftriaxone, ampicillin, salicylates, furosemide, contrast dye) that displace bilirubin from albumin, which can increase free fraction of unconjugated bilirubin in the blood

- Conversely, binding of some drugs to albumin may be altered in the presence of hyperbilirubinemia in the neonatal period
- Physiologic states (dehydration, hypercarbia, and acidosis) may displace bilirubin
- Surgery may increase load of heme to be degraded (e.g., hematoma absorption)
- Primary pathology

Overview

- Bilirubin is derived from the catabolism of proteins that contain heme, usually, from the breakdown of hemoglobin from RBCs.
- Heme is oxidized to biliverdin and then reduced to bilirubin, which is unconjugated, nonpolar, and lipid soluble.
- Unconjugated bilirubin circulates bound to albumin in equilibrium with its unbound fraction that readily crosses the blood-brain barrier and can cause neurotoxicity.
- Bilirubin is conjugated in the liver cell microsomes by the enzyme (UDP)-glucuronyl transferase, to form the polar, water-soluble glucuronide of bilirubin.
- Most of the conjugated bilirubin is excreted as bile, which is metabolized by intestinal flora and excreted in the feces.
- The danger of unconjugated hyperbilirubinemia is bilirubin-induced neurologic dysfunction.
- Bilirubinemia peaks in term infants between 3–5 d; preterm infants 5–6 d
- Clinical features of bilirubin encephalopathy are lethargy, anorexia, nausea, vomiting, and opisthotonic posturing.
- The ability of anesthetic agents to displace bilirubin from albumin has not been well studied.

Etiology

- Nonpathologic, physiologic jaundice due to immature hepatic glucuronyl transferase
- Pathologic hyperbilirubinemia due to many causes (isoimmunization, erythrocyte biochemical defects, erythrocyte structural defects, infection)
- Excess bilirubin production from RBC breakdown (intravascular hemolysis or polycythemia, extravascular bruising or cephalohematoma)
- Decreased removal of bilirubin through gut (decreased meconium evacuation and increased enterohepatic recirculation; decreased bile flow due to liver disease or cholestasis)
- Breastfeeding jaundice (occurs in first wk after birth and implies inadequate hydration or caloric intake)
- Breast-milk jaundice (unidentified factors in normal mature human milk that cause increased reabsorption of UB from gut) can last for 3–4 wk up to 3 mo

Usual Treatment

- Goal of therapy is to prevent indirect-reacting bilirubin–related neurotoxicity.
- Phototherapy and exchange transfusion (for severe cases) remain the primary treatment modalities used to keep the maximal total serum bilirubin below the dangerous levels.
- Phototherapy bypasses the hepatic system and produces photoisomers of bilirubin that are more water-soluble and can be cleared directly in bile or urine without conjugation in the liver.
- Exchange transfusion removes infants' sensitized and destroyed RBCs and circulating antibodies; double-volume exchange replaces 85% of circulating RBC volume, decreases bilirubin level by 50%, and corrects anemia.
- AAP guidelines for healthy term infant: Phototherapy when serum bilirubin >12–15 mg/dL; exchange transfusion >20–25; premature or ill term-infants have lower threshold for starting therapy.
- Several factors are important when determining the bilirubin level above which kernicterus is possible (gestational age, degree of illness, evidence of hemolysis, rate of rise, albumin level, and physiologic stress).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Jaundice resulting from accumulation of unconjugated, nonpolar, lipid-soluble bilirubin pigment in the skin		Jaundice progresses in cephalocaudal direction (face, approximately 5 mg/dL; abdomen, approximately 15 mg/dL)	
RESP	Pleural effusion, pulm edema	Maternal prenatal history	Resp distress	CXR
HEME	Hemolysis	Rh/ABO maternal-fetal incompatibility	Anemia, bruising, cephalohematomas hepatosplenomegaly, jaundice	Maternal ABO and Rh typing Cord blood type, Rh and direct Coomb CBC, diff, retic, and blood smear Fractionated bilirubin, LFTs, ammonia, PT/PTT, blood and urine cultures
CNS	Bilirubin toxic to CNS cells	High levels of bilirubin	Abnormal posture, tonicity, reflexes	

Key References: Kaplan H, Wong RJ, Sibley E, et al: Neonatal jaundice and liver diseases. In Martin RJ, Fanaroff AA, Walsh MC, editors: *Fanaroff and Martin's neonatal-perinatal medicine,* ed 10, Philadelphia, 2015, Elsevier, pp 1618–1673; Bhutani VK, Wong RJ, Stevenson DK: Hyperbilirubinemia in preterm neonates, *Clin Perinatol* 43(2):215–232, 2016.

Perioperative Implications

Preoperative Preparation

- Determine reason for hyperbilirubinemia.
- Weigh risks and benefits of surgery if bilirubin levels are high.
- Ensure adequate intravascular volume.
- Active efforts to lower bilirubin levels.
- Address coexisting disease states.

Monitoring

- Blood sampling may be indicated.

Airway

- Neonatal airway concerns

Induction

- Maintain normal hemodynamics.

Maintenance

- No one agent or technique preferred.
- Few data reflecting effects of anesthetic agents on bilirubin levels.
- Avoid hypoxia, hypothermia, and acidosis.

Extubation

- Standard criteria

Postoperative Period

- Apnea/bradycardia risks.
- Monitor bilirubin levels.

Anticipated Problems/Concerns

- Ultimate goal of therapy and management is to prevent bilirubin encephalopathy and kernicterus.

Bipolar Disorder

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Risk

- Lifetime prevalence within USA 4%
- Vast majority of pts younger than 25 y
- Suicide rates are 20 times higher than that of general population

Perioperative Risks

- Risk of disregard for self care within manic phases, especially in the setting of enhanced stress
- Exacerbation of the disease if certain medications
- Anesthetic considerations focused on drug-drug interactions and altered dosing (e.g., lithium decreases MAC requirements)

Worry About

- Depressed, irrational, irritable pt behavior
- Increased morbidity and mortality due to overlapping medical conditions (e.g., diabetes mellitus, cardiovascular disease, obesity)
- Drug interactions and side effects
  - Extrapyramidal side effects (EPS) (e.g., akathisia, tardive dyskinesia, muscle rigidity)
  - Cardiac effects such as QT prolongation and orthostatic hypotension
  - Rash including Stevens-Johnson syndrome and toxic epidermal necrolysis
  - Lithium risk during pregnancy, thyroid, parathyroid, and diabetes insipidus