- 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

Alan David Kaye | Martin J. Carney | Rachel J. Kaye

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

Overview

- Bipolar disorder made up of four subtypes that differ in the intensity of mania, as well as the presence or absence of depression.
- There can be a reduced need for sleep, racing thoughts, impulsivity, and mood swings.
- Strong link to family history, as well as heightened illicit drug usage and alcohol abuse.
- Treatment often includes a mixture of antipsychotic medication, as well as mood stabilizers (e.g., lithium, anticonvulsants).
- Typical antipsychotics utilize dopamine antagonism and are plagued with EPS (e.g., tardive dyskinesia).
- Atypical antipsychotics utilize serotonin antagonism with less dopamine effect, leading to fewer EPS manifestations.
- EPS can be treated with anticholinergics such as benztropine 2 mg or diphenhydramine 50 to 100 mg.
- Neuroleptic malignant syndrome is a rare but fatal sequelae of large doses of antipsychotics.
- Mood stabilizers such as lithium uniquely cause thirst, polyuria, weight gain, and the gambit of side effects following diabetes insipidus.

Etiology

- Clear genetic association within first-degree family members.
- Environmental factors play into the epigenetic realm of manic breaks in the disease, including stressors, altered sleep cycle, and substance abuse.
- Disruption in neurotransmitters such as serotonin and norepinephrine likely play a role.

Usual Treatment

- Aimed at managing acute manic events, depressive symptoms, and long-term mood stabilization.
- Lithium, the most commonly used mood stabilizer, is dosed at 900 to 1800 mg orally per day, with the second most common being valproate dosed at 1000 to 3000 mg orally per day.
- Additionally, antipsychotic medications added to mood stabilizers for superior effects versus monotherapy alone.
- Most effective drugs for controlling acute manic episodes: Haloperidol (typical), risperidone, olanzapine, and quetiapine (atypical).
- Behavioral and cognitive psychotherapy.
- Electroconvulsive therapy: the treatment of choice for pts with severe mania refractory to pharmacotherapy.
- Indicated when rapid recovery is required.

Assessment Points

System	Effect	Assessment by Hx	PE
CV	QT prolongation Orthostatic hypotension	Dizziness Dizziness	Orthostatic hypotension Postural BP changes
GI	Liver dysfunction	Alcohol and medication use	Bleeding and jaundice
HEME	Agranulocytosis	Frequent infection	Mild fever
ENDO	Diabetes insipidus Hyperlipidemia	Polydipsia, polyuria	Signs of dehydration
NEURO	EPS	Typical antipsychotic usage	Dystonia, bradykinesia,akathisia, tardive dyskinesia
GENERAL	NMS	Medication usage or change	Hyperthermia, rigidity, autonomic instability, cardiac arrhythmia
	Stevens-Johnson syndrome Toxic epidermal necrolysis	Carbamazepine or lamotrigine use	Fever, rash, blisters

Key References: Price AL, Marzani-Nissen GR: Bipolar disorders: a review, *Am Fam Physician* 85(5):483–493, 2012; Geddes JR, Miklowitz DJ: Treatment of bipolar disorder, *Lancet* 381(9878):1672–1682, 2013.

Perioperative Implications

Preoperative Preparation

- Mental status must be assessed in preop planning.
- Mood stabilizers and antipsychotic regimen should remain the same with lithium level; check if concerned.

Monitoring

- Routine

Airway

- Standard protocol

Preinduction/Induction

- Variable outcomes by institution; standard approach needed

Maintenance

- Thermodysregulation risks: monitor temperature and treat symptoms.
- Adequate, but not excessive urine output.
- Hypotension, tachycardia, and arrhythmia.

Extubation

- Standard practice

Anticipated Problems/Concerns

- Polypharmacy is regularly practiced to control bipolar disorder, and these drugs must be carefully titrated and monitored in the preop and postop settings.
- Psychiatric and mental assessment should be regularly performed to monitor compliance and understanding.
- Cardiac arrhythmia, BP instability, and neuropsychiatric symptom exacerbation.
- Hypothyroidism and diabetes insipidus.
- Regional not a good choice with this disorder.
- Postop adherence and medication changes.

Blebs and Bullae

Trent Bryson

Risk

- Prevalence of blebs as high as 6% of young, healthy adults, although spontaneous rupture occurs only in 7.4 to 18 per 100,000.
- Incidence of ruptured bulla is 26 per 100,000.
- Increased incidence of primary disease in young males.
- Increased prevalence with smoking (Hx, including tobacco and illicit substances), COPD, chronic bronchitis, cystic fibrosis, lung cancer, staphylococcal pneumonia, tuberculosis, Marfan syndrome, Ehlers-Danlos syndrome, alpha-1 antitrypsin deficiency, sarcoidosis, fiberglass pneumoconiosis, and BMI <22.

Perioperative Risks

- Pneumothorax
- Bronchopleural fistulae
- Caval compression of nonruptured giant bulla
- Pulm Htn and RV failure
- COPD

Worry About

- CV collapse from tension pneumothorax
- Expanded dead-space ventilation
- Inability to adequately ventilate due to bronchopleural fistula
- Inadequate venous return from caval compression
- Expansion of bulla leading to compressive effects or rupture

Overview

- *Bleb* usually refers to a collection of air caused by ruptured alveoli within the visceral pleura without any other lining that is <1 cm in size.
- Bullae >1 cm in size and arise from various sources, which cause destruction of lung parenchyma.
- Nitrous oxide is contraindicated, and positive pressure ventilation should be avoided if possible.
  - Nitrous oxide 35 times more soluble than nitrogen in blood. Because of this, nitrous oxide readily diffuses into any gas-filled cavity much more rapidly than nitrogen is absorbed, which leads to rapid expansion of pneumothoraces.