RBCs being unable to protect themselves from oxidative stress. This leads to eventual cell death.
- There are over 180 different known mutations to the G6PD gene that lead to deficiency.
- Frequency, risk, and severity of hemolysis varies depending on severity of deficiency.
- Drugs to avoid include sulfonamides, dapsone, methylene blue, nitrofurantoin, phenazopyridine, primaquine, rasburicase, and toluidine blue.

Usual Treatment

- The main treatment for G6PD deficiency is preventative; avoid oxidative stressors.
- If hemolysis were to occur, discontinue the offending agent and maintain urine output with IVF and diuretics.
- Hemodialysis may be indicated in severe acute renal failure.
- PRBC transfusion can be necessary in cases of severe anemia or hemodynamic compromise.
- Folic acid and iron are beneficial.
- Splenectomy and antioxidants are not indicated.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Excess bilirubin buildup		Scleral icterus	
CV	Anemia leading to decreased oxygen delivery, compensatory increased CO, tissue hypoxemia	Substernal pain, fatigue	Tachycardia,Hypotension, flow murmur	ECG, ECHO in severe refractory hypotension
RESP	Hypoxemic hypoxia if severe	Dyspnea	Tachypnea, possibly decreased SpO_2	ABG
GI	Destruction of RBCs in spleen, cholelithiasis	Abdominal pain	Splenomegaly, jaundice, RUQ tenderness	LFTs (increased indirect bilirubin), increased LDH, RUQ ultrasound
RENAL	Excretion of excess hemoglobin leads to nephropathy	Dark brown urine	Hemoglobinuria	BUN/ Cr, UA (+RBC)
HEME	Hemolytic anemia		Pallor	CBC (decreased Hgb/Hct), decreased haptoglobin, peripheral blood smear with Heinz bodies and RBC fragments
CNS	Kernicterus (bilirubin encephalopathy) in neonates with severe disease	Lethargy, eventual mental retardation	Early hypotonia leads to late hypertonia, gaze abnormalities, hearing loss, movement disorders	Brain MRI with high signal in globus pallidus on T-2 weighted images
MS	Increased erythropoietic response of the bone marrow	Lumbar pain		Increased reticulocyte count

Key References: Luzzatto L: Hemolytic anemias and anemia due to acute blood loss. In Kasper D, Fauci AS, Hauser SL, Longo D, Jameson JL, Loscalzo J editors: *Harrison's principles of internal medicine, ed 19,* New York, NY, 2015, McGraw-Hill; Elyassi AR, Rowshan HH: Perioperative management of the glucose-6-phosphate dehydrogenase deficient patient: a review of literature, *Anesth Prog* 56(3):86–91, 2009.

Perioperative Implications

Preoperative Preparation

- Consider anxiolytic premedication.
- Clarify severity of disease if possible. If Hgb/Hct is stable and no other clinical signs of hemolytic anemia are present, no further testing is typically needed.
- Adequately treat any infections prior to surgery.

Monitoring

- Monitor urine output and color.
- Consider A-line for frequent labs.

Induction

- Maintain baseline HR/BP; blunt response to airway manipulation to minimize physiologic stress.

Maintenance

- Reduce surgical stress with adequate anesthesia and analgesia.
- Hypotension, decreased urine output, and tachycardia may be early signs of hemolysis.
- Maintain diligent use of hand hygiene and infection prevention methods.
- Monitor temperature; hypothermia can lead to hemolysis.
- Aggressively treat acidemia and hyperglycemia; both can lead to hemolysis.

Extubation

- Avoid hypercarbia.

Postoperative Period

- Watch for signs/symptoms of hemolytic crises. At minimum, monitor daily CBC.
- Adequate multimodal pain control.

Anticipated Problems/Concerns

- While in vitro studies have shown isoflurane, sevoflurane, diazepam, and midazolam to inhibit G6PD activity, there have been no in vivo cases or studies showing these and other common anesthetic agents causing hemolytic crisis in the G6PD deficient pt.
- Avoid medications that can induce methemoglobinemia, such as benzocaine, nitrates, and metoclopramide. The treatment for methemoglobinemia, methylene blue, is a known oxidative drug that can lead to acute hemolysis.
- If possible, minimize use of cardiopulmonary bypass, a known cause of oxidative stress.

Glycogen Storage Diseases

Jeffrey D. Roizen

Risk

- There are a total of 11 GSDs (0–7, 9, 11, and 12; there is no GSD 8 or 10); the most common are GSD I (Von-Gierke), GSD II (Pompe [3 types]) and GSD III (Cori or Forbe), which may each be as common as 1:50,000 individuals. The least common may occur as rarely as 1:1,000,000 or even less.
- GSDs I and III each account for roughly 25% of GSDs in US.
- All of the described diseases are inherited in an autosomal recessive fashion and molecular diagnosis is available for all aside from GSD 0 (what was once type 8 is now a subtype of type 6 and is x-linked recessive; what was once type 10 is now a subtype of type 6).
- No racial predilection for most types of GSD. Non-Ashkenazi Jews in northern Africa have an increased prevalence of GSD 3 (1:5000), and there may also be an increased incidence of GSD 7.

Perioperative Risks

- These diseases have heterogeneous risks.
  - Several are associated with a risk for hypoglycemia (0, 1, 3, 6), with 1 and 3 requiring careful glucose monitoring.
  - Hepatomegaly and liver failure in 1, 3, and 4.
  - Lactic acidosis in several (most extremely in 1) when too much glucose is given. This is not usually a clinically relevant problem, but when supplementing with glucose-containing fluids, it is ideal to keep glucose above 80 and below 160.
  - Myopathies (and specifically cardiac failure) in several. For cardiac failure, 2, 3, 4, and 7; for 5 (McArdle) tourniqueting can cause muscle damage.
  - The adult form of GSD 2 (Pompe disease) can be associated with sleep apnea later in life (all forms can be associated with limited respiratory reserve. The infantile form has a lethal outcome caused by progressive cardiorespiratory insufficiency, which usually starts by the end of the first year of life. The juvenile form has a slower course with some individuals living into their 20s or 30s).
  - In GSD type 5 and 7, rhabdomyolysis can cause renal failure.
  - In GSD II, macroglossia can be present.

Worry About

- Hypoglycemia in 0, 1, 3, and 6
- Cardiac function in 2, 3, 4, and 7
- Rhabdomyolysis leading to renal failure in 5 and 7
- Coagulopathy and cirrhosis in 4
- Renal function and platelet function in 1

Overview

- Glucose is the primary energy substrate for the majority of the tissues in the body (heart and brain can function well on ketones, but most other organs cannot). When a person is fasting or between meals, serum glucose (and thus intracellular glucose) is maintained primarily by the breakdown of glycogen in the liver.
- The GSDs result from mutations in genes involved in glycogen synthesis and breakdown, leading to the inability to use glycogen (in one way or another—usually tissue-limited).
- Ideally the NPO time should be limited, and for those associated with hypoglycemia, glucose should be monitored and periop glucose-containing fluids administered.
- The consequences of these mutations depend on (1) the tissue where the enzyme is expressed and (2) the effect of the mutation on the pathway. Whether it prevents the synthesis of glycogen, debranching of glycogen, phosphorylation/dephosphorylation of glucose, or other steps in glycogen breakdown.

Etiology

- Caused by homozygous mutations in enzymes involved in the synthesis or breakdown of glycogen.
- Autosomal recessive trait with a few case reports of compound heterozygotes who have mutations in two different enzymes in the pathway.
- Each heterozygous parent has a 50% chance of passing on the gene.
- Long-term prognosis depends on the enzyme affected (type of GSD): 0, Muscle cramping and occasional growth failure; 1, growth failure; 2, infantile—death by 2, juvenile—death by 30, adult—sometimes heart failure or sudden death in adulthood; 3, myopathy; 4, FTT and death by 10; 5, exercise-induced cramps; 6, growth retardation; 7, growth retardation; 9, delayed motor development and growth retardation; 11, pretty normal; 12, exercise intolerance; 13, exercise intolerance and muscle pain with aging.

Usual Treatment

- Several GSDs can be treated with liver transplant with excellent outcomes (1, 3, and 4).
- Several are managed with enteral cornstarch supplementation (1, 3, and 6).
- 2 (Pompe) may be treated with recombinant human α-glucosidase enzyme replacement therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	In 2 (Pompe) macroglossia can occur		Limited ability to visualize glottic opening	
CV	Cardiomyopathy	Determine GSD type		ECG, ECHO
RESP	Decreased resp reserve (in 2)	Sleep apnea	Assess for sleep apnea	Sleep study
GI	Coagulopathy/liver failure in 1		Jaundice and hepatomegaly with a very firm liver raising concern for cirrhosis	LFTs and coagulation studies (PT/PTT/INR)
HEME	Platelet dysfunction (leading to decreased platelets) in 1	Easy bleeding and bruising	Ecchymosis	CBC with plts and plt function tests if possible
RENAL	Renal dysfunction in 1			Comprehensive metabolic panel (CMP) with calculated GFR
MS	Truncal obesity in 1 and 3		BMI	

Key References: Stuart G, Ahmad N: Perioperative care of children with inherited metabolic disorders, *Contin Educ Anaesth Crit Care Pain* 11(2):62–68, 2010; Fleisher L: *Anesthesia and Uncommon Diseases,* ed 5, Philadelphia, PA, 2006, Elsevier, pp 177.

Perioperative Implications

Preoperative Preparation

- Fasting should be minimized to the extent possible.
- Blood glucose should be monitored and periop glucose-containing fluids administered.
- The appropriate tests for GSD type should be performed; where risks are present, they should be managed appropriately (e.g., for decreased platelets or platelet function, the administration of platelets).
- For altered liver function, be aware that some medications may have altered metabolism.
- Conscious sedation is also possible; concern for sleep apnea syndrome.
- Assess individual pt based on systems approach and review relevant studies.
- For pts with decreased cardiac function, avoid myocardial depressants when possible.
- Avoid tourniqueting with type V; some evidence points to an association of MH with type V, so it is recommended to avoid MH-triggering medications (or to do an IVCT test).
- Similarly, there are case reports suggesting avoidance of propofol and sevofluorane in 2.
- There are theoretical preferences for some approaches, but the key factors of a successful outcome are attention to anesthetic technique and close monitoring.

Monitoring

- Standard ASA monitors
- For cases associated with hypoglycemia, glucose monitoring every 30 min (can use CGM)
- For cases associated with rhabdomyolysis leading to renal failure, consider intraop CKs.
- Bispectral index may be misleading in GSD 1.

Airway

- Anticipate difficulty intubating in 2 if macroglossia is present.
- Other diseases with skeletal muscle involvement can predispose pts to upper airway obstruction.

Induction

- As above in preparation

Maintenance

- Careful positioning in types 5 and 7 to avoid rhabdomyolysis

Postoperative Period

- Continuous pulse oximetry due to high incidence of sleep apnea in 2
- Continued glucose-containing fluids and monitoring for 0, 1, 3, 6

Anticipated Problems/Concerns

- Hypoglycemia in 0, 1, 3, and 6
- Cardiac dysfunction in 2, 3, 4, and 7
- Rhabdomyolysis leading to renal failure in 5 and 7
- Coagulopathy and cirrhosis in 4
- Renal function and platelet function in 1

Goldenhar Syndrome

Zulfiqar Ahmed

Risk

- Incidence: 1:5500 live births.
- Second most common facial birth defect after cleft lip and palate.
- Extracraniofacial anomalies can range from one anomaly (13%) to multiple affected organ systems (42%). No gender or side predominance was detected. Central nervous system, cardiac, and skeletal anomalies each occurred in more than 10% of cases. Surgical correction usually takes place in severe cases.
- Cleft palate occurs in 25% of pts

Perioperative Risks

- Difficulties with airway management
- Possible need for tracheostomy
- High risk of anesthesia overdose in premature and low-weight pts

Worry About

- Stabilizing the heart rate.
- Difficulty with airway management.
- Ensuring good mask fit. There are many sizes to choose from, and the mask must fit prior to induction. Mask may have to be changed after induction for better fit. The degree of inflation of the facemask cuff may be adjusted in order to ensure an appropriate seal.
- IV access.
- Associated anomalies, such as cardiac and or cervical spine malformation that may influence decisions.
- Cancelation of procedure owing to inability to intubate.
- Increased severity of microsomia. Pruzansky classification type III is associated with increased intubation difficulties.