- 5–12% have anomalous origin of LAD from RCA and cross the RVOT inferiorly. Must confirm prior to OR.
- 25% have right aortic arch.
- Severity of symptoms correlates with degree of RVOT obstruction, as this determines the degree of R-to-L shunting.
  - RVOT obstruction has fixed components (degree of infundibular obstruction, size of pulm valve annulus, size of PA) and dynamic components (infundibular muscle bundle spasm, PVR, SVR).
- Fixed factors determine amount of chronic cyanosis.
- Dynamic factors determine tet spells.
- Pink tets have minimal amount of PS.
- Avoid hypoxia, acidosis, high airway pressures, excitement, and agitation.
- Dx by ECHO, cardiac cath, and/or MRI.
- Associated with chromosome 22 deletions and diGeorge syndrome, VACTERL, CHARGE, and velocardiofacial syndrome.

Usual Treatment

- Primary repair: Usually done at 3–12 mo
- If not immediately operable (low birth weight, prematurity, other disease processes), palliative shunts to increase pulm blood flow (Blalock-Taussig shunt, aortopulmonary shunts)
- Beta-blockers to decrease infundibular spasm and spelling
- Treatment for tet spell:
  - 100% O_2 (pulm vasodilator)
  - Sedation (morphine/fentanyl)
  - Increased SVR (squatting, phenylephrine)
  - Propranolol (decreased contractility of infundibulum; decreased RVOTO)
  - Bicarbonate to correct metabolic acidosis

Assessment Points

System	Effect	Assessment by Hx	Test
GENERAL		FTT, clubbing	Growth charts
CHEST	RVH	Signs of right heart failure	CXR with boot-shaped heart
CV	See Overview	Frequency and severity of tet spells	ECHO, cath, MRI ECG-RVH, RA
HEME	Polycythemia from chronic hypoxemia Plt count may be low from polycythemia	Chronic cyanosis	Hct, plt count

Key References: Doyle T, Kavanaugh-McHugh A: Pathophysiology, clinical features, and diagnosis of tetralogy of Fallot. In Connolly HM, Triedman JK, Armsby C, editors, Waltham, MA, *UpToDate*, 2016. www.uptodate.com/contents/pathophysiology-clinical-features-and-diagnosis-of-tetralogy-of-fallot. (Accessed 13.06.16.); Schmitz ML: Anesthesia for right-sided obstructive lesions. Tetralogy of Fallot. In Andropoulos DB, editor: *Anesthesia of congenital heart disease*, ed 2, Hoboken, NJ, 2010, Wiley-Blackwell, pp 427–432.

Perioperative Implications

Preoperative Preparation

- Heavy premedication to avoid agitation, crying

Monitoring

- Standard monitors plus radial arterial line, CVP, and TEE

Airway

- Standard oral or nasal intubation

Preinduction/Induction

- Mask induction with sevoflurane and oxygen. Ketamine (1–2 mg/kg) with fentanyl (10 mcg/kg) and rocuronium (1 mg/kg) if IV present. AVOID decrease in SVR.

Maintenance

- Phenylephrine appropriately drawn up and diluted.
- Avoid increase in PVR and decrease in SVR.

Extubation

- Pts are taken to the ICU monitored and intubated.

Anticipated Problems/Concerns

- Intraop tet spells
- Arrhythmias

Thalassemia

Sohail Bampoe | Michelle R. Cole

Risk

- Over 60,000 children are born annually with severe beta-thalassemia.
- Global regions that are primarily affected include the Mediterranean, North Africa, and Southeast Asia, where alpha thalassemia is more common.
- Beta-trait carrier status has a global prevalence of approximately 1.5%.
- Over 200,000 pts are currently receiving treatment for thalassemias.
- In endemic areas with highest frequency, carrier status is present in as many as 1:7 individuals, and thalassemia major can occur in 1:158 live births.

Perioperative Risks

- Abnormal globin chains result in severe anemia (mild microcytic anemia in those with carrier status).
- CHF is the leading cause of death.
- End-organ effects of hemochromatosis from chronic iron therapy: Cardiomyopathy, cirrhosis, endocrinopathies (e.g., diabetes, hypopituitarism).
- Diabetes mellitus is common.
- Restrictive lung dysfunction and pulm Htn.
- Airway difficulties, including maxillofacial abnormality secondary to bone marrow expansion.
- Hypercoagulopathy in asplenic pts, and coagulopathy in pts with cirrhosis.
- Alloimmunization secondary to multiple blood transfusions. Obtaining appropriately cross-matched blood may require prolonged testing.

Worry About

- Difficult airway secondary to maxillary deformation in up to 19%
- Cardiac arrhythmias or HF
- Hypercoagulability
- Pulm Htn
- Immunocompromisation

Overview

- Thalassemia is a heterogeneous group of inherited microcytic anemias that result from a genetic mutation causing a defect in the synthesis of one or more globin chain subunits of the HbA, which is normally composed of $\alpha 2\beta 2$.
- Thalassemia is classified according to the genotype that correlates with clinical severity.
- Alpha thalassemia: Alpha globin gene deletion leads to a decrease in alpha chain production with a relative overproduction of beta chains. This leads to formation of β4 tetramers, which causes RBCs to be more rapidly removed leading to anemia.
- Alpha thalassemia silent carrier: One gene absent (aa/a-); healthy except occasional mild anemia.
- Alpha thalassemia trait: Two genes absent on the same or different chromosomes (a-/a- or aa/--); mild anemia.
- Alpha thalassemia intermedia (Hb H disease): inactivation of three genes (a-/--) leads to a spectrum for manifestations; mild to moderately severe anemia, splenomegaly, icterus, abnormal RBC indices; recurrent infections. Heinz bodies = beta chain tetramers. Hb H disease results in poor oxygen delivery to the tissues due its high affinity for oxygen.
- Alpha thalassemia major (Hb Barts): Complete deletion of all alpha chain genes resulting in the formation of Hb-Bart's, which has an exceptional affinity for oxygen resulting in extremely limited tissue oxygen delivery. Incompatible with life; hydrops fetalis unless intrauterine blood transfusions.
- Beta thalassemia: Decreased beta chain production relative to the alpha chain production as a result of mutation resulting in either absence (beta o) or decrease (beta+) in the production of beta globin. Alpha chains are in excess and precipitate leading to inadequate erythroid maturation and hemolysis. In most severe forms, this leads to splenomegaly, anemia, massive expansion of medullary and extramedullary erythropoietic tissue leading to skeletal growth, and metabolic abnormalities.
- Beta thalassemia is a silent carrier (beta/beta+); it shows no clinical symptoms except for low RBC counts.
- Beta thalassemia trait (beta/beta+) = beta thalassemia minor: Mild anemia, abn RBC indices, hypochromia, microcytosis.
- Beta thalassemia intermedia (beta/beta o, beta+/beta+, beta+/beta o): A compound heterozygous state; profound anemia, which periodically may require transfusion support and occasionally splenectomy.

- Beta thalassemia major (beta o/beta o) = Cooley's anemia, transfusion-dependent anemia, massive splenomegaly, bone deformities, growth retardation, and abnormal facies. As a result of chronic anemia and ineffective erythropoiesis, bone expansion and extramedullary erythropoiesis may develop in liver and spleen, and marrow space expansion at sites such as the cranium and paravertebral areas can lead to disfiguring bony changes. Deaths are usually secondary to cardiac manifestations, including cardiomyopathies and heart failure. The incidence of pulm Htn and lung fibrosis increase, leading to a restrictive pattern of lung dysfunction.

Etiology

- Genetic mutation associated with ancestry in areas endemic to malaria

Usual Treatment

- Alpha thalassemia carriers (aa/-a) and those with alpha thalassemia trait (a-/a- or --/aa) are usually asymptomatic and require no treatment.
- Alpha thalassemia intermedia (--/-a): folic acid, transfusions, and possible splenectomy for progressive anemia; avoidance of oxidant drugs.
- Beta thalassemia minor (beta/ beta+) usually does not require treatment.
- Beta thalassemia intermedia and major treatment is symptomatic and supportive.
  - Blood transfusion support with leukodepleted blood when Hb <7 g/dL; transfuse up to Hb 11–13 g/dL. Transfusions are usually required several times a week and can result in iron overload.
  - Iron chelation therapy; deferoxamine IV can cause renal toxicity. Deferasirox causes less toxicity.
  - Splenectomy usually needed around age 6–7 y or in adolescence when transfusion treatments required are at 1.5 times normal (e.g., >200 mL/kg/y).
  - Hematopoietic stem cell transplantation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Maxillary hypertrophy Orofacial malformations High arched palate	Prior difficulties with intubation	Airway evaluation	
CV	Cardiomyopathy Arrhythmias Pericarditis Heart failure	Exercise tolerance Palpitations	Dyspnea Dysrhythmias Murmurs	ECG, annual ECHO, CXR Holter
RESP	Restrictive lung disease Pulm Htn Lung fibrosis	Exercise tolerance	Fine inspiratory crackles	PFTs
HEME	Anemia Splenomegaly Alloimmunization	Exercise tolerance H/o splenectomy Blood transfusion reactions	Tachycardia Splenomegaly	CBC Type and screen
	Coagulopathy			Coagulation studies
HEPAT	Cirrhosis		Hepatomegaly	LFTs, coagulation studies, hepatitis serologies
ENDO	Diabetes mellitus	Recurrent infections Poor wound healing		Fasting glucose Glucose tolerance test
	Hypothyroidism	Cold intolerance Lethargy, depression Decreased metabolism		Thyroid function test
	Adrenal insufficiency			Cortisol determination

Key References: Higgs DR, Engel JD, Stamatoyannopoulos G: Thalassaemia. *Lancet* 379(9813):373–383, 2012; Staikou C, Stavroulaki E, Karmaniolou I: A narrative review of peri-operative management of patients with thalassaemia. *Anaesthesia* 69(5):494–510, 2014.

Perioperative Implications

- Thalassemia minor, in general, does not create anesthetic problems. In pts with thalassemia major, consideration has to be given to problems derived from the severity of the anemia itself and the associated cardiorespiratory complications, but also those related to transfusion therapy, and to bony malformations. Pts may present for major surgery, such as splenectomy.

Preinduction

- Detailed airway evaluation and planning.
- Cardiac function evaluation (including echocardiography).
- Pulm function evaluation.
- Hemoglobin level should be determined and preop transfusion considered.
- Cross-matched blood should be available (antibody matched, leukocyte reduced for frequently transfused children); high degree of alloimmunization in this population exists.
- Evaluation for endocrine dysfunction (e.g., DM, hypopituitarism, hypothyroidism) and adequacy of treatment.
- Hepatic function evaluation in light of risk of cirrhosis and iron or viral-induced damage.
- Coagulation studies.
- Presplenectomy antibiotics and immunizations (when appropriate).

Monitoring

- Consider the need for a Swan-Ganz cath and measurements of CI, CO, and mixed-venous oxygenation.
- Consider arterial cath and frequent hemoglobin, lactate, and blood gas analysis.
- Esophageal Doppler or transesophageal ECHO may contribute useful information.

Induction/Maintenance

- Preparation for possible difficult airway.
- Close attention to the positioning in light of demineralization, pathologic fractures, and scoliosis.
- Careful monitoring of CV function, including postsplenectomy Htn.
- Beware of the effects of laparoscopy on circulatory and respiratory function.
- Thromboembolism prophylaxis; SCD and/or pharmacotherapy when applicable.
- Consider cell salvage.
- Prophylactic antibiotics may be indicated.

General Anesthesia

- Facial abnormalities can present a difficult airway.
- Volatile concentrations should be kept low to avoid cardiac depression in those with high cardiac output states.
- Hypoxemia and acidosis will exacerbate pulm Htn.

Regional Anesthesia

- Osteoporosis, osteopenia, and scoliosis are common.
- Vertebral bodies maybe of reduced height as a result of osteoporosis; the segmental portion of conus medullaris may be lower than predicted.
- Extramedullary hematopoiesis is uncommon in the intraspinal location, but if symptoms of spinal compression are suspected, MRI should be performed prior to regional anesthesia.
- Consider epidural versus spinal in pts who need a regional anesthetic but have CV pathology.
- Evaluate closely coagulation studies prior to regional anesthesia.
- Thromboembolism prophylaxis, especially in postsplenectomy pts.
- Spinal and epidural techniques have been performed safely.

Postoperative Period

- Postop monitoring dependent on the preop status.
- Critical care admission may be necessary.
- Prophylaxis for thromboembolism (postsplenectomy pts in particular).

Anticipated Problems/Concerns

- Intubation difficulties
- CV instability secondary to severe chronic anemia, cardiomyopathy, and endocrinopathies
- Pulm insufficiency
- Coagulation abnormalities: Hypercoagulable or hypocoagulable
- Impaired drug metabolism secondary to cirrhosis
- Adrenal insufficiency complications
- Difficulty in obtaining cross-matched blood due to alloimmunization
- Postop infections