- Typically high-dose steroids (1 mg/kg per d prednisone for 2–4 wk) until hearing improves, and then taper over 3–6 mo
- MTX, cyclophosphamide, azathioprine, leflunomide, tacrolimus, and rituximab all with case reports of effectiveness, usually reserved for severe organ or life-threatening presentations
- Surgical repair or bypass of diseased segments: favorable only when activity of the disease is under control with medical treatment
- Cochlear implant use: Very successful

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Inner ear dysfunction Interstitial keratitis	Dizziness, tinnitus Photophobia, redness, tearing, blurry vision, and oscillopsia	Slit lamp exam	Calorics and audiogram with sensorineural hearing loss
RESP	Pulmonary embolism Pneumonia (due to immunosuppression)	Dyspnea Cough	Tachypnea Lung field consolidation Wheezing	CXR, V/Q scan, CT scan Bronchoscopy BAL ABG
CV	Aortitis Coronary arteritis Limb ischemia AI, MR	Chest/back/abdominal pain Dyspnea Orthopnea	Tachycardia Hypotension Disparate limb BP Heart murmur	ECG, TTE CT scan Limb duplex scan Angiography
GI	Mesenteric ischemia	Post prandial abdominal pain N/V	Abdominal tenderness Splenomegaly	CT scan Angiography Abdominal US
CNS	Intracranial manifestations of vasculitis	Weakness Numbness Falling Incoordination Difficulty speaking	Gait instability Dysmetria Functional neurologic deficits	Head CT and MRI to R/O tumor/stroke Carotid duplex US
HEME	Pancytopenia	Easy bleeding and bruising Fatigue Fever	Petechiae Rash Pallor Lymphadenopathy	CBC and differential Reticulocyte count Peripheral smear
METAB/ ENDO	Iatrogenic Cushing syndrome	Poor wound healing Skin changes Body habits changes Emotional/psychiatric changes	Striae Buffalo hump Skin wounds Moon facies Htn Hirsutism	Electrolytes $HgbA_1C$
RENAL	Glomerulonephritis	Hematuria Oliguria Headache Edema	Htn Peripheral edema	BMP, albumin, UA

Key References: Singer O: Cogan and Behçet syndromes, *Rheum Dis Clin North Am* 41(1):75–91, 2015; Gluth M, Baratz K, Matteson E, Driscoll CL: Cogan syndrome: a retrospective review of 60 patients throughout a half century, *Mayo Clin Proc* 81(4):483–488, 2006.

Perioperative Implications

Preoperative Preparation

- Assess disease activity state and screen for concomitant vasculitic processes.
- Ensure adequacy of blood products and IV access.
- Severe neutropenia may warrant prophylactic antimicrobial therapy and reassessment of timing risk/benefit.
- Concomitant steroid therapy and necessity of stress doses should be considered.

Monitoring

- Consider awake arterial line in appropriate limb as indicated.
- Consider CVP, TEE, or PA cath as indicated for disease burden and procedure.
- Consider BIS if cerebral circulation is affected.

Airway

- Use caution with edematous airway mucosa.

Preinduction/Induction

- Tailor afterload and preload management to cardiac function and concomitantly affected organs including cerebral, renal, and mesenteric beds.
- Avoid hypotension in concomitantly affected organs.

Maintenance

- Judicious blood pressure management to preserve diseased organ bed perfusion

Extubation

- Avoid Htn with vascular repairs and aneurysmal burden.

Postoperative Period

- Continue monitoring of hemodynamics.
- Maintain vigilance for hemorrhage.
- Immunosuppressed patients have an increased susceptibility to infection.
- Watch for signs of adrenal insufficiency.

Anticipated Problems/Concerns

- Maintain a low threshold to evaluate the occult disease burden of other organ systems not identified preop.

Complement Deficiency

David Y. Kim | Marshall K. Lee

Risk

- C1 esterase inhibitor–deficiency incidence: 1:50,000-150,000 of the general population.
- Symptoms onset and diagnosis occur approximately at 20 y, and by 30 y approximately 98% of pts have symptoms.
- C2 deficiency incidence: <0.1% of the general
- Male versus female ratio: 1:6.
- Higher incidence (6%) in pts with autoimmune disease (see Immune Suppression).
- Incidence in pts with Hx of *Neisseria* meningitis: 15%.
- C3 and C5–C8 deficiencies have increased risk for infections.

Perioperative Risks

- Possible life-threatening airway compromise
- Increased risk of postop infection, particularly if the deficiency affects the early complement components
- Risk for inflammatory complications (e.g., glomerulonephritis, vasculitis)

Worry About

- Acute airway edema resulting from laryngeal or mucous membrane swelling, which can result in definitive airway obstruction; abdominal pain from intestinal edema, which may be an associated finding on exam
- Increased infectious risk

Overview

- Hereditary angioneurotic edema is associated with a complement deficiency of the enzyme C1 esterase inhibitor. It is a rare genetic deficiency that may lead to uncontrolled production of C2, C3, and C5 complement, resulting in acute noninflammatory, painless, nonpruritc, nonpitting edema. Initial inciting events are often the result of trauma, but may even be attributed to emotional stress.
- Any component of the classical pathway, alternate pathway, or terminal common pathway may be affected.
- Virtually all deficiencies show some ↑ risk of infection and/or autoimmune disease.
- Deficiencies in other complement components, C2 and C3, have also been associated with immunocompromised pts, resulting in recurrent life-threatening infections associated with a variety of organisms.
- Increased risk of autoimmune diseases.
- Deficiency in any of the terminal components C5–C8 show selective risk of recurrent neisserial infections, which usually are not life threatening.

Etiology

- C1 complement results from a heterozygous deficiency of C1 esterase inhibitor. The mediators of the angioedema response result from coagulation, complement, and the kinin pathway. C1 esterase inhibitor is a key regulator for Hageman factor, coagulation, plasmin, and plasma kallikrein. There have been more than 100 mutations on the C1 esterase gene in pts without hereditary angioedema, and 20% of those have been new mutations with no prior history.
- All complement proteins are inherited in an autosomal fashion, with the possible exception of properdin, which appears to be X-linked.

Usual Treatment

- Treatment modalities have included stanozolol, danazol, methyltestosterone, oxymetholone, aminocaproic acid, tranexamic acid, and cinnarizine. Mechanism of action for therapeutics is increased synthesis of C1 esterase inhibitor (for the steroids) and inhibition of plasmin activation (for the antifibrinolytics).
- Acute preop prophylaxis has consisted of fresh frozen plasma and epinephrine. However, caution must be taken because plasma provides substrates that may aggravate the scenario and worsen the edema. Purified concentrates of C1 esterase inhibitor given IV have also been used outside USA.
- Antibiotic treatment dictated by specific infection.

Assessment Points

System	Effect	Test
IMMUNO	Infectious risk for all systems	CH50 screening test for complement-mediated lysis of sheep erythrocytes; tests for specific complement components available at reference labs Assess other specific organs as indicated by autoimmune disease (e.g., renal for SLE)

Key References: O'Neil KM: Complement deficiency, *Clin Rev Allergy Immunol* 19(2):83–108, 2000; Wen L, Atkinson JP, Giclas PC: Clinical and laboratory evaluation of complement deficiency, *J Allergy Clin Immunol* 113(4):585–593, 2004.

Perioperative Implications

Preoperative Preparation

- In pts with C1 deficiency, consider preop administration of 2 units of FFP or C1 concentrate with appropriate consideration to risks and benefits of therapy.
- Sterile technique strictly observed.

Monitoring

- Routine.
- Coagulation profile.
- Minimize invasive lines.

Airway

- Airway management should minimize trauma. Tracheal intubation is acceptable, but preparation for an emergency tracheostomy should be made. Laryngeal mask airway use should be tempered by the concerns for upper-airway edema and resulting ineffective ventilation. Regional anesthesia is an acceptable alternative to prevent airway manipulation.

Induction

- Routine

Maintenance

- Routine

Extubation

- Extubate and remove all lines at earliest opportunity.

Postoperative Period

- Maintain sterile techniques.

Anticipated Problems/Concerns

- If emergency intubation is required, it is recommended that an otolaryngologist or surgical personnel be present for a possible tracheostomy or cricothyroidotomy.
- Ensure meticulous sterile technique to minimize risk of infection.

Congenital Methemoglobinemia

Bronwyn R. Rae

Risk

- Navajo Indians, Alaskan Indians, and people of Puerto Rican and Cuban ancestry
- Normal life span (except for RCM type II)

Perioperative Risks

- Oxidizing agents may increase MetHb to dangerous levels.
- Mild respiratory/cardiac depression may adversely affect pts with already limited reserve.
- Pregnancies not compromised.

Worry About

- Measurement of SpO_2
- Oxidant drugs (e.g., prilocaine, benzocaine, nitroglycerin, sulfonamides, phenacetin, and nitric oxide), which are contraindicated
- Myocardial ischemia due to decreased O_2 delivery
- Blood loss/anemia due to O_2-carrying capacity already reduced

Overview

- Enzyme deficiency: Shift of O_2 dissociation curve to the left leads to mild erythrocytosis (normal RBC life span).
- RCM type I defect restricted to red cell soluble cytochrome b5 reductase only. Cyanosis is sole clinical symptom. Homozygotes have compensatory increase in RBC mass. Heterozygotes may develop acute symptomatic methemoglobinemia after exposure to exogenous MetHb-inducing agents. Defect may be the cause of unexplained periop cyanosis.
- RCM type II: Defect occurs in all cells and involves both soluble and microsomal forms of cytochrome b5 reductase. Results include mental retardation, spasticity, opisthotonos, microcephaly, growth retardation, and death by 2–3 y of age.
- RCM type III: Nonerythroid enzyme deficiency, but CNS spared.
- HbM variations: Alpha chain variants affected from birth, and beta chain variants by 3–6 mo of age. Patients develop mild hemolytic anemia.

Etiology

- RCM types I, II, and III: Occur by autosomal recessive inheritance because of deficient reducing capacity of oxidized heme caused by NADH cytochrome b5 reductase (diaphorase) deficiency.
- HbM variants: Occur by autosomal dominant inheritance due to structural abnormality in globin moiety; amino acid substitutions create abnormal environment for heme residues, displacing the equilibrium toward the ferric state.

Usual Treatment

- RCM types I, II and III: Reducing agents (e.g., riboflavin 20–60 mg orally, methylene blue 1–2 mg/kg IV; the effect lasting 10–14 d) and ascorbic acid used for chronic management
- HbM variants: No available treatment. (In an emergency, hyperbaric O_2 therapy and exchange transfusion may be used.)