Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Deafness Corneal and lenticular opacities Vertigo Mucosal lesions	Difficulty hearing Light sensitivity Dizziness Nausea (vertigo)	Impaired pupillary constriction, hearing loss, oropharyngeal mucosal lesions	Audiometry, ophthalmologic exam including slit lamp, visual acuity, and fields
RESP	Obstructive ventilatory defect Exercise intolerance Airway obstruction (bronchospasm)	Dyspnea Cough	Tachypnea Wheezing	CXR Spirometry Oximetry Treadmill exercise testing
CV	LVH, RVH, aortic dilation Diastolic dysfunction LVOT obstruction Mild valvular insufficiency Coronary artery stenosis	Palpitations, angina, dyspnea	Irregular heartbeat, heart murmur	ECG ECHO Stress imaging Holter monitor
GI	Difficulty gaining weight Delayed gastric emptying Achalasia	Postprandial abdominal pain, N/V, early satiety	Smaller height and weight compared with unaffected siblings	Endoscopic or radiographic evaluations
CNS	TIA/stroke Mild dementia (late finding) Autonomic dysfunction Acroparesthesias	Pain in extremities, cold/heat intolerance, joint pain, stroke symptoms	Neurologic exam, pain inventory, hypohydrosis, orthostatic hypotension	Brain CT or MRI with T1, T2, and FLAIR images
HEME	Abnormal vascular reactivity Prothrombotic state	Angina, stroke, DVT	Thrombophlebitis	Proteins C & S, factor V Leiden, prothrombin G20210A, ATIII, lupus anticoagulant, anticardiolipin antibody
RENAL	Renal failure Proteinuria Impaired concentration ability	Fluid retention	Edema	Electrolytes, BUN, creatinine, GFR, 24-h urine for total protein/Cr
MS	Angiokeratomas, osteopenia, osteoporosis	Osteoporotic fractures	Raised skin lesions	Bone mineral density

Key References: Eng CM, Germain DP, Banikazemi M, et al.: Fabry disease: guidelines for the evaluation and management of multi-organ system involvement, *Genet Med* 8(9):539–548, 2006; Woolley J, Pichel AC: Peri-operative considerations for Anderson-Fabry disease, *Anaesthesia* 63(1):101–102, 2008.

Perioperative Implications

Preoperative Preparation

- Cardiac evaluation with ECG and echocardiogram should be obtained. Consider noninvasive cardiac stress imaging in pts older than 30 y and with concerning symptoms.
- Consider sodium citrate for gastric prophylaxis in pts with symptoms of achalasia.
- Consider preop sedation to avoid excessive activation of abnormal autonomic nervous system.
- Obtain baseline visual exam to differentiate from new deficit after surgical positioning or hemodynamic instability.
- Recurrent pain in extremities may be a relative contraindication for regional anesthesia.

Monitoring

- Consider arterial line given potential autonomic instability and cardiac history.
- Consider CVP or PA cath as indicated.
- Temperature monitoring is especially important.

Airway

- Risk for difficult direct laryngoscopy as a result of TMJ stiffness leading to limited mouth opening.
- Inspect airway for oropharyngeal lesions.
- Risk of bronchospasm.

Preinduction/Induction

- Be prepared for BP swings.
- Anticipate need for bronchodilators and avoid drugs that may cause histamine release when possible.

Maintenance

- Monitor ECG vigilantly given risk for arrhythmias and conduction abnormalities.
- Vasoactive medications should be ready to treat both hypotension and Htn.
- Avoid nephrotoxic medications and administer judicious IV fluids accounting for any renal impairment.
- Warming and cooling equipment should be available given autonomic instability.
- If taking carbamazepine for pain control, increased amounts of nondepolarizing neuromuscular blockade may be required.

Extubation

- Pts with achalasia or delayed gastric emptying should be considered at risk for aspiration.
- Ensure neuromuscular blockade not prolonged from renal insufficiency.
- Anticholinergics may exacerbate hypohidrosis.

Postoperative Period

- Analgesia plan critically important for those with chronic pain

Anticipated Problems/Concerns

- Dose medications appropriately in those with renal impairment.
- Amiodarone can exacerbate lysosomal abnormalities and should be avoided.

Factor V Leiden Mutation

S. Nini Malayaman | Henry Liu

Risk

- Most common hereditary thrombophilia
- Autosomal dominant inheritance pattern
- Heterozygous form in 5% of white population in USA (up to 15% in Europe), 2% of Hispanic Americans, 1% in both African and Native Americans
- Homozygosity in white population 1:5000
- May account for 85–95% of pts with APC resistance
- Relative risk of venous thrombosis sevenfold in heterozygous and 80-fold in homozygotes

Perioperative Risks

- VTE: DVT most likely; lower risk of PE
- Risk of arterial thrombosis unknown

Worry About

- Hypercoagulability
- DVT
- Recurrent fetal loss (twofold to fivefold increased relative risk)
- Conflicting data regarding association with placental abruption, severe preeclampsia, IUGR
- Cerebral vein thrombosis
- Renal transplant rejection
- Risk of thrombosis increased by protein S deficiency, prothrombin 20210 gene mutation, hyperhomocysteinemia, OCP use, pregnancy, increasing age, immobilization, and obesity

Overview

- Factor Va is a procoagulant that is inactivated by APC, with protein S as cofactor, causing less thrombin generation during the propagation phase.

- FVL is resistant to inactivation by APC so thrombin generation is allowed to continue and subsequent clot formation.
- FVL paradox describes the higher prevalence of FVL in pts with DVT compared with FVL pts with pulmonary embolism.
- In CPB, FVL pts found to have less blood loss and need less blood transfusion during hospital stay.
- Testing in FVL is the same as other causes of thrombophilia: Venous thrombosis and age <50 y; unusual sites of thrombosis (hepatic, mesenteric, cerebral); recurrent venous thrombosis; venous thrombosis with strong history of thrombotic disease, venous thrombosis in pregnant women taking oral contraceptives, relatives of pts who had venous thrombosis <50 y, MI in female smokers <50 y.
- Screening test: Modified APC resistance functional assay (sensitivity and specificity for FVL close to 100%).
- Confirmation test: DNA test. In liver transplant pts, DNA test positive, plasma FVL negative. In bone marrow transplant pts, DNA test negative, but plasma shows APC resistance.

Etiology

- SNP 1691 G >A on factor V gene that predicts a single amino acid substitution Arg >Gln.
- The mutated factor V protein is resistant to inactivation by APC.

Usual Treatment

- Treat acute thrombosis event according to standard guidelines.
- Long-term anticoagulation not recommended for heterozygotes if no prior thrombosis.
- Prophylactic anticoagulation (heparin, warfarin) considered for high-risk clinical setting.
- Newer oral anticoagulants (dabigatran [Pradaxa], rivaroxaban [Xarelto], apixaban [Eliquis]) may be considered for prophylaxis.
- Consider minimizing other risk factors for VTE: Stopping oral contraceptives (progesterone) in women with VTE, encouraging obese pts to lose weight, and minimize extended travel.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Cerebral vein thrombosis	Headache Abnormal vision Seizures	Stroke signs, weakness	CT/MRI with contrast
RESP	Pulm embolus	Chest pain Shortness of breath	Tachypnea	ABG, CXR, CT scan
HEME	Thrombosis	Pain at site of thrombosis		Prolonged aPTT, PTT
GU	Renal vein thrombosis	Flank or lower back pain	Hematuria, oliguria	Ultrasound, CT scan
MS	DVT most common Upper extremity thrombosis	Calf pain	Calf pain with DVT	Venography, compression ultrasound of legs
OB	Miscarriage Postpartum thrombosis	Bleeding, spotting		Ultrasound, FHR (Doppler)

Key References: Kujovich JL: Factor V Leiden thrombophilia, *Genet Med* 13(1):1–16, 2011; Van Cott EM, Khor B, Zehnder JL: Factor V Leiden, *Am J Hematol* 91(1):46–49, 2016.

Perioperative Implications

Preoperative Preparation

- Preop screening not recommended if asymptomatic.
- Anticoagulation should follow standard guidelines.
- In FVL heterozygotes, risk of bleed from warfarin is greater (1–3%) than risk of thrombosis (<1%).
- Avoid CVC if possible. FVL heterozygotes have twofold to threefold increase in CVC-related thrombosis.
- Sequential compression devices may decrease incidence of DVT.
- Consider consultation with hematology; may require temporary treatment with anticoagulation during periods of high-risk settings: surgery, cast, immobilization, pregnancy, etc.

Monitoring

- If arterial line indicated, use cautiously in homozygous pts.

Airway/Induction/Maintenance/Extubation

- No special precautions

Postoperative Period

- Standard anticoagulation protocols if no prior history of VTE
- Target INR 2.5 effective anticoagulation even in homozygous pts

Anticipated Problems/Concerns

- No need to alter periop management if asymptomatic.
- Confirmation test is a genetic test, so implications for pt and family members should be discussed.
- Aprotinin, an inhibitor of APC, has been used safely in FVL pts undergoing cardiac surgery without increased risk of thrombosis, although caution is often advised.

Familial Dysautonomia (Riley-Day Syndrome)

Thomas J. Ebert | Craig E. Cummings

Risk

- Autosomal recessive transmission
- Complete penetrance, marked variability in expression
- Predominantly affects Ashkenazi Jewish population (incidence 1:10,000–20,000; carrier frequency 1:27-32)

Perioperative Risks

- Intraop: Primarily cardiovascular with hemodynamic variability
- Postop: Primarily cyclic vomiting and pulmonary complications

Worry About

- Paroxysmal dysautonomic crisis triggered by physiologic or psychologic stress characterized by intractable vomiting, Htn, tachycardia, diaphoresis, erythematous macular rash
- Resp status compromised by dysfunctional swallowing, leading to repeated aspiration pneumonias, and restrictive lung disease secondary to scoliosis
- QTc prolongation and dysrhythmias, including bradycardia and asystole
- Insensitivity to hypoxemia and hypercarbia, including apnea to mild hypoxia
- Increased sensitivity to acetylcholine and catecholamines

Overview

- HSAN type III
- Differentiated from other HSAN types by profound autonomic dysfunction, Htn, orthostatic hypotension, and excessive or decreased sweating
- Characterized by recurrent pulmonary infections, esophageal dysmotility, spinal abnormalities, and thermal dysregulation
- High morbidity and mortality, with only 50% of newborns expected to reach age 40 y

Etiology

- Mutations of gene coding IKBKAP on chromosome 9q31
- Incomplete neuronal development and progressive neuronal degeneration in the peripheral and autonomic nervous systems
- Symptoms due to denervation of peripheral blood vessels and dysfunctional parasympathetic nervous system, baroreceptors, and chemoreceptors

Usual Treatment

- Dysautonomic crisis: Benzodiazepines are first-line therapy.
- Hemodynamic instability: Managed with hydration and direct-acting vasoactive therapies.