Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Distortion of airway structures due to self-mutilation		Examine airway	
CV	Htn, CAD Adrenergic pressor response to stress is absent	Angina, angina-equivalent symptoms, PND	Displaced PMI S_3	ECG Pharmacologic stress testing Coronary angiography and ECHO
RESP	Aspiration pneumonia	SOB following vomiting episode	Rales Wheezing	CXR
GI	Vomiting Athetoid dysphagia	Dysphagia		
RENAL	Decreased renal function due to obstructive uropathy			BUN Cr IVP
CNS	Mental retardation Seizure disorders Decreased MAO activity		Mental status questioning	EEG Mental function tests
MS	Spasticity, contractures		ROM	

Key References: Williams KS, Hankerson JG, Ernst M, et al.: Use of propofol anesthesia during outpatient radiographic imaging studies in patients with Lesch-Nyhan syndrome, *J Clin Anesth* 9(1):61–65, 1997; Salhotra R, Sharma C, Tyagi A, et al.: An unanticipated difficult airway in Lesch-Nyhan syndrome, *J Anaesthesiol Clin Pharmacol* 28(2):239–241, 2012.

Perioperative Implications

Preoperative Preparation
- Antacids.
- H_2 blockers.
- Metoclopramide.
- IV access may be difficult.

Monitoring
- Routine
- ST-segment analysis if CAD present

Airway
- Rapid-sequence induction.
- Avoid succinylcholine.
- Awake fiberoptic intubation.

Preinduction/Induction
- Premedication where appropriate to help with behavioral issues.
- Avoid agents with renal metabolism (adjust dosing).

Maintenance
- Avoid agents with renal toxicity.
- No one agent or technique shown superior.
- Administer exogenous catecholamines with caution (due to associated Htn).

Extubation
- Awake to avoid aspiration

Adjuvants/Postoperative Period
- Make some space accessible to avoid injury to child.
- Benzodiazepines for spasticity.

Anticipated Problems/Concerns
- Hx unavailable or inaccurate because of retardation

Leukemia

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Risk
- Estimated 318,389 individuals living with leukemia or in remission in USA
- Estimated 54,270 new cases and 24,450 deaths of leukemia in 2015
- Males >females
- ALL greater in children (median age of diagnosis 14 y)
- CML, CLL, and AML common in adults and diagnosed in sixth and seventh decades

Perioperative Risks
- Immunocompromised pt, tumor lysis syndrome (metabolic derangement), tumor compression of organs (anterior mediastinal mass), neutropenia (anemia, coagulopathy), hyperviscosity, oral mucositis, sequelae of cytotoxic agents (immunocompromised state, respiratory failure, cardiovascular failure), opportunistic infection, and sepsis
- Hematoma and/or bleeding, thromboembolism, diffuse alveolar hemorrhage from thrombocytopenia and splenic sequestration of platelets

Worry About
- Myelosuppression: Thrombocytopenia, anemia, and neutropenia
- Bone marrow suppression with NO; rare potential for malignant hyperthermia in ALL
- Upper airway edema, anterior mediastinal mass (paralysis, supine position)
- Pleural effusion, pneumonitis, and pulm fibrosis
- Tumor lysis syndrome (especially with dexamethasone), hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia, and renal failure
- Remote anesthesia location, airway difficulty, equipment, and monitoring

Overview
- Four main types of leukemia: ALL, AML, CLL, and CML. No staging system for leukemia.
- From 2004 to 2010, the 5-year relative survival rates overall: CML—59.9%, CLL—83.5%, AML—25.4%, ALL—70%, ALL—93% for children <5 y.
- Usually outpatient treatment, but may require GA or MAC for bone marrow biopsy, bone marrow harvest, central venous access/port placement, lumbar puncture (diagnostic and intrathecal chemotherapy), HSCT, bronchoscopy, pericardiocentesis, and radiation therapy.
- Mortality remains high post HSCT secondary to sepsis, pulmonary complications, and GVHD.

Etiology
- Largely unknown. Greaves hypothesis (in utero mutation and secondary delayed viral exposure).
- Strong suspicion that leukemia and lymphoma are virus-induced (e.g., EBV). Associated with genetic disorders (e.g., Down syndrome).
- Chronic exposure to benzene (primarily from tobacco smoke), extraordinary doses of radiation, and secondary malignancy from certain cancer therapies can be causes of the leukemia.
- Breastfeeding for 6 mo or more could lower childhood leukemia risk.

Usual Treatment
- Treatment varies with type of leukemia, age, and phase (beyond the scope of this chapter)
- Supportive treatment: Antimicrobial, blood transfusion, nutrition, and pain control
- Newer approaches: Monoclonal antibody, experimental cancer vaccines, donor lymphocyte infusion, gene therapy, autologous and allogeneic transplantation, and stem cell transplantation
- AML:
  - Ara-C
  - Anthracyclines: Daunorubicin, idarubicin + cytarabine
  - Gemtuzumab ozogamicin: ATRA
  - Arsenic trioxide: Vinca alkaloids: vincristine/vinblastine
  - Bone marrow transplant
- CML:
  - HSCT
  - Tyrosine kinase inhibitors: Imatinib mesylate (initial treatment of choice)
- Nilotinib
  - Dasatinib
  - Busulfan
  - Hydroxyurea
  - Interferon alfa, allopurinol
  - Splenectomy, radiation, bone marrow transplant
- CLL:
  - Cyclophosphamide
  - Corticosteroid
  - Fludarabine
  - Cytarabine
  - Bendamustine, rituximab
  - Alemtuzumab
  - Radiotherapy
- ALL:
  - Imatinib, clofarabine, L-asparaginase, daunorubicin, vincristine, dexamethasone, doxorubicin, cytarabine (ara-C)
  - Radiation therapy, intrathecal chemotherapy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Ulceration, oral lesions	Dysphagia, pain	Airway assessment	
CV	Rare: Pericardial effusion, conduction defects, murmurs, CHF Mediastinal mass	Dyspnea, fatigue	Narrow pulse pressure, pericardial friction rub, cardiomegaly	CXR, CT scan, ECG, ECHO
GI	Hepatosplenomegaly hypoalbuminemia	Loss of appetite Weight loss	Hepatosplenomegaly	Albumin
HEME	Anemia Leukostasis Thrombocytopenia	Weakness, easy fatigue,	Pallor Ecchymoses Petechiae, easy bruising, nose-bleeds	CBC Bone marrow aspirate results
RENAL	Renal failure from tumor lysis syndrome (acute loss of tumor)	Decreased UO	Decreased UO	BUN/Cr, hyperkalemia ↑ phosphate, ↑ or ↓ Ca^{2+}
CNS	Cranial nerve infiltration (very rare), meningeal leukemia (less common in adults), vincristine neuropathy	Cranial nerve palsies, clouding of mental status, peripheral neuropathy	Weakness	EMG
MS	Infiltration of bony cortex and periosteum, synovial membranes	Bone pain	Bone swelling	X-ray CT scan

Key References: Bryan JC, Jabbour EJ: Management of relapsed/refractory acute myeloid leukemia in the elderly: current strategies and developments, *Drugs Aging* 32(8):623–637, 2015; Latham GJ: Anesthetic considerations for the pediatric oncology patient—part 2: systems-based approach to anesthesia, *Paediatr Anaesth* 20(5):396–420, 2010.

Perioperative Implications

Preoperative Preparation

- Assess volume status, CBC, electrolytes, renal function, N/V, diarrhea, and oral mucositis.
- Review sign and symptoms and imaging reports of mediastinal mass for compromised airway.
- Airway assessment: Oral mucosal ulceration, edema, fibrosis, and neck mobility.
- Neutropenia precaution: Periop isolation, aseptic technique for safe port access, avoidance of per rectum medication and probe.

Monitoring

- Routine

Airway

- Signs of dysphagia, ulcerations, and airway bleeding from chemotherapy and candidiasis.
- Oral leukemia lesions can occur prior to or during therapy.
- Anterior mediastinal mass: Risk of difficult intubation, ventilation, and compromise hemodynamic. Fiber optic intubation, inhalation induction, and rigid bronchoscopy may be required; lateral or prone position may help with ventilation. Avoid muscle relaxants.
- Chronic radiation: Potential for difficult airway; high-dose or chronic radiation to oral cavity, head, and neck cause fibrosis and stiffness of soft tissue resulting in limited mouth opening and neck extension.
- Post radiation changes: Affecting airway mucosal fibrosis, subglottic edema, and supraglottic and subglottic narrowing or stenosis may complicate the airway management.
- Leukemic infiltration of tonsils and adenoids, retropharyngeal lymph nodes, and cervical lymphadenopathy may cause airway obstruction and difficulty in intubation and ventilation.

Induction

- Brief heparinization and thrombocytopenia may influence choice of local, spinal, or epidural
- MAC or deep sedation with propofol and remifentanil infusion preferred over propofol alone
- GA may require in younger pediatric age with special equipment and monitoring in various remote anesthesia locations, such as radiation therapy suite

Maintenance/Extubation

- Routine inhalation technique or TIVA
- Low FIO_2 for during and after bleomycin therapy
- Prophylaxis for N/V
- Multimodal pain management

Anticipated Problems/Concerns

- Risk of infection; aseptic technique with placement of all lines.
- Dexamethasone may precipitate tumor lysis syndrome; anesthesia provider should communicate with oncology team before using dexamethasone for N/V prophylaxis in high-risk pts.
- Caution required for subclinical cardiomyopathy, pericardial effusion, airway management, and pulmonary dysfunction after chemotherapy and radiation therapy.
- Use of epidural blood patch for treatment of PDPH is controversial; may increase risk for infectious complication and CNS leukemia spread.
- Blood products: CMV depleted, irradiated blood, platelets; careful with doses and GVHD.
- ICU admission: Cardiorespiratory failure, pleural effusion, pneumonia, sepsis, compromised airway, GVHD following HSCT, pulmonary complications, and multiple organ failure.

Liddle Syndrome

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Risk

- Extremely rare but described in a variety of populations
- True incidence and prevalence unknown

Perioperative Risks

- Chronically untreated Htn

Worry About

- Undiagnosed cerebrovascular, CV, and/or renal disease secondary to chronic Htn
- Worsening of hypokalemia with hyperventilation and nasogastric suctioning
- Hypokalemia-induced dysrhythmias and potentiation of NMB

Overview

- Monogenic AD gain-of-function mutation in the ENaC resulting in early onset Htn, hypokalemia, and metabolic alkalosis with suppressed plasma renin activity; resembles primary aldosteronism but aldosterone excretion is markedly suppressed (also known as "pseudoaldosteronism").
- Htn results from volume expansion due to increased Na^+ reabsorption via the constitutively active ENaC; urinary secretion of K^+ and H^+ occurs to balance out movement of electrical charges, resulting in a hypokalemic metabolic alkalosis.
- Presentation is variable.
  - Htn may not be early in onset or severe.
  - Hypokalemia may be absent.
  - Family history is not reliable, as spontaneous mutations have been reported.

Etiology

- ENaC is a membrane-bound ion channel located on the apical membrane of the principal cell in the distal tubule, which is selectively permeable to sodium ions; their activity is normally regulated by aldosterone.
- ENaC is composed of three subunits: α, β, and γ.
- NEDD4, a ubiquitin ligase enzyme, negatively modulates ENaC via ubiquitination.
- Gene mutations resulting in deletions or alterations of the carboxy-terminus of the β or γ subunits (located on chromosome 16p) make NEDD4 binding impossible; this prevents channel degradation and removal, resulting in the constitutive activity of ENaC.

Usual Treatment

- Amiloride or triamterene therapy (direct ENaC inhibitors) with a low-sodium diet.
- Kidney transplantation is curative.
- Htn and hypokalemia are not responsive to mineralocorticoid antagonists (e.g., spironolactone) because the increased activity of ENaC is not mediated by aldosterone.