Toxicity of Chemotherapeutic Agents

Chemotherapy Treatment	Indication	Toxicity
Anthracyclines (e.g., daunorubicin, doxorubicin)	Hodgkin lymphoma	Myocarditis, leukopenia
Alkylating agents (e.g., cyclophosphamide, ifosfamide)	Lymphoma, solid tumors	Hemorrhagic cystitis, left ventricular dysfunction, immunosuppression, hyponatremia
Bleomycin	Hodgkin lymphoma	Pneumonitis, pulmonary fibrosis
Platinum analogues (e.g., carboplatin, cisplatin)	B-lymphoma	Bone marrow suppression, neurotoxicity/ototoxicity/nephrotoxicity
Monoclonal antibodies (rituximab)	B-cell lymphoma	Cytokines release syndrome, anaphylaxis, interstitial fibrosis

Assessment Points

System	Effects	Assessment by Hx	PE	Test
HEENT	Obstruction, mediastinal mass, tracheomalacia	Dysphagia, odynophagia	SVC obstruction signs, neck ROM	CXR, CT thorax indirect laryngoscopy
RESP	Pneumonitis, pulmonary fibrosis	Poor exercise tolerance	Auscultation	PFTs, CXR, ABGs
CV	Myocarditis, left ventricular dysfunction	Exertional dyspnea, PND, orthopnea	Signs of CHF, Pemberton sign	ECG, CXR, ECHO
RENAL	Nephrotoxicity	Orthostatic hypotension, swelling, somnolence	Edema, pallor, ascites	BUN, Cr, lytes
HEME	Anemia, pancytopenia	Tiredness, SOB	Pallor, tachycardia	FBC, bone marrow biopsy
CNS	Leptomeningeal disease	Headache, CN abnormalities	Nerve palsy, weakness	CT, MRI, lumbar puncture
GI	Aspiration	Regurgitation, dyspepsia	Palpable mass	CT, MRI

Key References: Swerdlow SH: *World Health Organization classification of tumours*, ed 4, Geneva, 2008, World Health Organization; Cullen M, Steven N, Billingham L, et al.: Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. *N Engl J Med* 353(10):988–998, 2005.

Perioperative Implications

Preoperative Preparation
- Aspiration prophylaxis; Assess and prepare for airway challenge and cardiopulmonary status.

Monitoring
- Depending upon condition of pt and level of surgery

Airway
- Rule out mediastinal masses; possible difficult intubation.

Induction
- May be hypovolemic with limited cardiopulmonary reserves as per disease severity.
- Consider deep inhalation induction with sevoflurane and O_2 initially to evaluate whether lower airway instruction occurs: if so, wake pt up and reevaluate.

Maintenance
- CV instability and obstructive or restrictive pulmonary disease

Extubation
- Risk of tracheal collapse, airway obstruction, and aspiration

Postoperative Period
- May require HDU/ICU admission.

Anticipated Problems/Concerns
- Airway challenges: Mechanical obstruction (tumor mass effect)
- High risk of thromboembolism, DVT, infection, and bleeding

Lysosomal Storage Disorders

Jacqueline Cade

Risk
- Individually rare, but as a group the incidence is approximately 1:8000.

Perioperative Risks
- Difficult airway management
- Cardiac or respiratory failure
- Hemorrhage

Worry About
- Difficult or failed intubation
- Coexisting cardiac or respiratory disease
- Difficult vascular access
- Neurologic involvement and pt cooperation

Overview
- Lysosomal storage disorders are rare, inherited, metabolic connective tissue disorders (often autosomal recessive) with variable anesthetic risk.
- Caused by a variety of mutations in lysosomal enzymes in macrophages, impairing normal cellular debris scavenging.
- Retained debris thus accumulates in various tissues throughout the body.
- Includes MPS types I to VII and lipid storage disorders (including Tay-Sachs and Gaucher disease).
- Depending on disease type and severity, many die in early childhood; others can expect to survive well into adulthood.
- MPS most feared from anesthetic point of view primarily due to airway issues (thus the primary focus of this chapter is on these conditions).

Usual Treatment
- Many of these conditions have no specific treatment, and therapy is targeted towards improving quality of life.
- Some more recent success with enzyme replacement therapy (depending on specific condition) and stem cell transplant.

Assessment Points

System	Effect	History	PE	Tests
HEENT (most effects in MPS pts, less so in those with lipid storage disorders)	Facial dysmorphism Macroglossia Micrognathia Enlarged supraglottic tissues Narrowed nasopharynx Excessive secretions Short neck Cervical spine stenosis Floppy or malformed tracheal cartilage High, elongated epiglottis	Previous anesthesia records, history of difficult airway (note usually gets worse with age)	Facial features Mallampati score Thyromental distance Neck ROM Anterior anatomical landmarks	Cervical spine imaging (plain films, MRI)
RESP	Sleep apnea Restrictive lung disease Recurrent URTIs	Snoring, apneic episodes Hx of lung disease	Coarse facial features, macroglossia Pectus excavatum	Sleep study LFTs
CV	Valvular insufficiency (especially mitral and aortic) Cardiomyopathy Cor pulmonale (less common)	Exercise tolerance	CV examination	ECG ECHO 6-min walk test
MS	Flexion deformities Myopathy Short stature Overweight	Variable mobility ranging from independent to wheelchair-bound		
CNS	Developmental delay Neurobehavioral problems Cognitive impairment Visual or hearing loss	Variable spectrum according to specific condition. Some are cognitively intact.		
HEME	Hepatosplenomegaly Possible bleeding tendency Lymphadenopathy, pancytopenia (lipid storage disorders)		Abdominal exam	Baseline full blood count and coagulation profile

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; Cade J, Jansen N: Anesthetic challenges in an adult with mucopolysaccharidosis type VI, *A Case Rep* 2(12):152–154, 2014.

Perioperative Implications

Preoperative Preparation

- Tertiary center with ICU facilities ideal.
- Experienced anesthesia team.
- Consult previous anesthesia records.
- Multidisciplinary team approach (pediatrician, geneticist, and orthopedic or neurosurgeon if cervical spine an issue).
- Optimize: No concurrent infection, consider investigations as appropriate (ECG, ECHO, sleep study, lung function tests, cervical spine imaging), continue enzyme replacement therapy if pt already on it.

Lines

- May have claw deformities (implications for radial arterial lines and peripheral IV lines)

Airway

- Pre-med: Avoid sedatives. An antisialagogue, such as glycopyrrolate, is useful.
- Equipment: Difficult airway equipment prepared, including fiberoptic bronchoscope, video laryngoscope, surgical airway equipment, and second anesthetist.
- Bag-mask ventilation: Can be difficult because prone to obstruction; oropharyngeal airway may not help due to elongated epiglottis.
- Laryngoscopy: Cervical stenosis may limit safety of neck manipulation, and direct laryngoscopy may be difficult. Narrow trachea may necessitate smaller tube.
- Nasal intubation: Narrow nasopharynx may make nasal intubation difficult. Some success with nasopharyngeal airways to relieve airway obstruction during induction, but choose smaller size and beware bleeding from prominent nasal turbinates.
- Bronchoscopy: Consider awake fiber optic intubation if feasible and older pt. Variable success with both inhalational induction maintaining spontaneous ventilation and asleep fiber optic techniques in children. Confirming endotracheal placement with bronchoscope can be misleading due to abnormal tracheal anatomy.
- Surgical airway: Short, stiff neck can make identification of anatomical landmarks for surgical airway difficult. ENT surgeon present if high risk.
- LMA may be useful to relieve obstruction or as a conduit for intubation.

Maintenance

- Ventilation management for restrictive lung disease if present (higher RR, low TV).
- Careful pressure care and padding, especially if pt has flexion deformities.
- Maintain normothermia, especially if coexisting myopathy.

Drugs

- Consider routine dexamethasone, particularly in children (thickened glottic tissues more prone to swelling).
- Risk of hyperkalemia with suxamethonium if pt has prolonged immobility or significant myopathy.
- Ensure nondepolarizing relaxants are fully reversed prior to attempted extubation (use nerve stimulator or consider sugammadex if available).
- Care with opioids and other long-acting sedative drugs. Consider regional analgesia and multimodal approach.
- May have increased bleeding tendency; judicious use of anticoagulants.

Extubation

- Extubate fully awake, reversed, and with minimal or no airway swelling; consider leaving exchange wire in older pts if extreme difficulty encountered with intubation.

Postoperative Period

- Consider ICU/HDU.
- Longer monitoring in recovery room for postextubation complications.
- Risk for postop pulm edema.

Malignant Hyperthermia and Other Anesthetic-Induced Myodystrophies

Michael R. King | Ronald S. Litman

Risk

- Incidence of MH impossible to know because of lack of reporting mechanisms; Malignant Hyperthermia Association of the US hears of approximately 1–2 cases per week in North America.
- More common in males (approximately 2:1).
- Family Hx of MH or unexplained death during surgery associated with MH occurrence.

Perioperative Risks

- Mortality with MH unknown. Malignant Hyperthermia Association of the US hears of approximately 1–2 deaths directly related to MH every 1–2 years.
- Occurrence of MH reduced by avoidance of triggering agents in MH susceptible individuals, and use of succinylcholine only when indicated.
- Immediate availability of dantrolene has greatly reduced morbidity and mortality from MH.
- Myopathies associated with MH are those associated with mutations in RYR1; most common is central core disease.
- Some obscure myopathies associated with risk of MH when caused by mutations in RYR1, STAC3, or CACNL1A3 genes. These include