Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	UAO secondary to septal deviation, choanal stenosis, and nasopharyngeal narrowing Ocular hypertelorism and proptosis Cleft lip or palate rarely	Sleep apnea snoring, daytime somnolence	Hypoplastic maxilla, relative mandibular prognathism Mallampati scoring difficult in toddlers Exposure keratopathy of cornea	3D cranial CT planning Polysomnography (sleep studies) or overnight oximetry
CV	FGFs involved in cardiac cushion proliferation and valvulogenesis	Exercise tolerance or arrhythmias	PDA or ASD murmurs	ECHO
RESP	Choanal atresia	OSA snoring		Nasoendoscopy
HEME	No known bleeding diatheses			
RENAL	Nil reported			
ORTHO	Cervical fusion (18%), usually C2-C3, occasionally C3-C4, C5-C6 Scoliosis Subluxation of the radial heads Ankylosis of the elbows.		Reduced range of movement of cervical spine	Cervical spine lateral x-ray or craniocervical CT
CNS	Chiari malformation Cerebellar tonsil herniation (73%) Progressive hydrocephalus (47%). Intracranial hypertension	Headaches Seizures	Gait disturbance Paresthesia	Craniocervical CT and MRI
PNS	Mild to moderate mental retardation	Developmental delay		
MS	Usually normal		Metacarpophalangeal shortening	Hand x-ray

Key References: Stricker PA, Shaw TL, Desouza DG, et al.: Blood loss, replacement and associated morbidity in infants and children undergoing craniofacial surgery, *Paed Anesth* 20(2):150–159, 2010; Hughes C, Thomas K, Johnson D, et al.: Anesthesia for surgery related to craniosynostosis: a review. Part 2, *Paediatr Anaesth* 23(1):22–27, 2013.

Perioperative Implications

Preoperative Preparation
- Caution with sedative premedication in presence of OSA or intracranial hypertension
- Cooperation limited in younger age groups

Monitoring
- Invasive pressure monitoring warranted for major craniofacial surgery

Airway
- Difficult BMV and intubation
- Mandibular hypoplasia more prominent postmaxillary advancement and may worsen glottic view

Induction
- Upper airway obstruction common on gas induction may require NPA

Maintenance
- Protection of orbits and corneas
- Reliable venous access mandatory
- Risk of excessive bleeding, dural tears, and gas embolism during vault surgery

Adjuvants
- Antifibrinolytics, surgical hemostasis with topical agents, and cell salvage have been described to reduce transfusion requirements

Extubation
- RED frame impedes access to upper airway. Wire cutters and spanner required to be with pt at all times.

Postoperative Period
- Increased risk of upper airway obstruction on emergence and in PACU
- Difficult BMV with RED frame in situ

Anticipated Problems/Concerns
- Multiple surgeries in first year of life to reduce risk of hydrocephalus or intellectual impairment
- Upper airway obstruction with postop facial edema; may require ICU/PACU care overnight

Cryptococcus Infection

Pierre Moine

Risk
- In general population: 0.4–1.3 cases per 100,000; AIDS pts: 2–7 cases per 1000.
- Impact of cryptococcosis: Approximately 625,000 deaths each year worldwide.
- Underlying immunocompromised conditions and risk factors: AIDS, systemic lupus erythematous, prolonged treatment with corticosteroids, organ transplantation, advanced malignancy, hematologic malignancy, diabetes, sarcoidosis, cirrhosis, idiopathic CD4 lymphocytopenia, or use of immune-modifying monoclonal antibodies (alemtuzumab, infliximab, etanercept, or adalimumab).
- More and more pts with cryptococcosis are described as immunocompetent.

Perioperative Risks
- Respiratory insufficiency, severe ARDS
- Elevated ICP

Worry About
- Underlying immunocompromised, genetic, or other conditions

Overview
- Systemic mycosis and third most prevalent disease in HIV-positive individuals
- *Cryptococcus neoformans*/*C. gattii* typically infect immunocompromised persons, essentially HIV and transplant-recipient pts, but also pts who do not have underlying HIV infection or are not transplant recipients. These pts tend to have a delayed diagnosis compared with the HIV and transplant groups and are remarkably currently the highest risk group for mortality in resource-available countries
- Wide range of clinical presentations from asymptomatic respiratory colonization to dissemination of infection into any organ. In severely immunosuppressed pts, involvement of multiple body sites. Common sites for infection are the lungs and CNS
- Pulmonary cryptococcosis/cryptococcal pneumonia: Mainly underestimated, not often recognized, multiple clinical presentations—asymptomatic solitary or multiple nodules, lobar infiltrates, interstitial infiltrates, cavities, endobronchial colonization or masses, mediastinal adenopathy, hilar adenopathy, miliary pattern, cavitary lesions, or pleural effusions/empyema, pneumothorax, and life-threatening pneumonia with ARDS
- Cryptococcal meningitis/meningoencephalitis: Primary life-threatening infection, most frequent and most severe form. Mortality rate approximately 12%. Other CNS clinical manifestations: Cryptococcomas (abscesses) of brain, spinal cord granuloma, chronic dementia (from hydrocephalus)
- Laryngeal cryptococcosis: hoarseness, cough, or acute airway obstruction

Etiology
- Seven species are described in the *C. neoformans* species complex: *C. neoformans*, *C. deneoformans*, *C. gattii*, *C. bacillisporus*, *C. deuterogattii*, *C. tetragattii*, and *C. decagattii*. *C. neoformans* and *C. gattii* are the agents highlighted in cryptococcal meningitis fungal infection. Other species, *C. laurentii* and *C. albidus*, are reported.
- Cryptococcus species are encapsulated heterobasidiomycetous fungi. The presence of a polysaccharide capsule is considered one of the reasons for the virulence of the yeast, increasing its invasiveness, pathogenicity, and conferring resistance to the host.
- Cryptococcus infection occurs by the inhalation of infectious cells and is considered a primary pulmonary infection, which may lead to a disseminated infection, with a special predilection for invading the CNS causing meningitis, encephalitis, or meningoencephalitis.
- Skin/subcutaneous, ophthalmic, bone, and prostatic disease also occur. Any pt with a diagnosis of cryptococcosis should be investigated for disseminated disease.

- No human-to-human transmission, except in cases of contaminated transplant tissue
- The most accurate diagnosis method is a LFA, which relies on antibody detection of the fungal glucuronoxylomannan in the capsule.

Usual Treatment

- An essential step in the treatment of cryptococcosis is first being able to make an accurate diagnosis and to so as quickly as possible.
- It has been shown that 89% of the pts with a relapse of cryptococcosis are reinfected by the original strain for a second time, raising concerns for gains in drug resistance (temporarily through heteroresistance or permanently through genetic mutations) or inefficiency of current drug regimens to clear fungus.
- Multiple challenges to effective antifungal treatment may include diagnosis, timing of treatment, cost of treatment, efficacy of the drugs, and availability of drugs.
- Cryptococcal meningitis/meningoencephalitis or CNS infection: The gold standard antifungal regimen is the combination of IV amphotericin B deoxycholate (polyene antifungal agent AMB) 0.7–1 mg/kg/day (or its liposomal derivatives, such as liposomal amphotericin B [AmBisome] 3–6 mg/kg/day with less nephrotoxicity) with 5-fluorocytosine (pyrimidine analogs 5-FC) 100 mg/kg/day for 2–4 wk. Adding flucytosine to amphotericin B reduces the rates of failure and relapse compared with amphotericin B monotherapy. Then fluconazole 400–800 mg/day for at least 8–10 wk. In HIV pts, maintenance fluconazole 200–400 mg/day PO therapy lifelong. Currently the issue of using azoles is developing resistance. Itraconazole is the second drug chosen for a maintenance dose. New-generation azoles (voriconazole, posaconazole) have demonstrated potent activity against *Cryptococcus* species.
- Despite the effectiveness of AMB, it has a high toxicity causing nephrotoxicity, hepatotoxicity, and myelotoxicity. In addition, 5-FC has hematologic toxicities.
- In resource-limited regions, fluconazole is the commonly used alternative therapy to AMB. However, fluconazole is fungistatic and not fungicidal and has been shown less effective than AMB-based therapy.
- Corticosteroids not recommended for the treatment of cryptococcal meningitis.
- Raised ICP is an extremely common complication of cryptococcal meningitis. Control of increased ICP (external drainage or CSF shunt, or surgical drainage of abscesses) to avert irreversible morbidity.
- Antiretroviral therapy in HIV pts or augmentation and restoration of host immunity through reversal of immunosuppression in other immunocompromised hosts.
- Pulmonary disease: fluconazole 400–800 mg/day for 6–12 mo.
- For more severe disease and immunocompromised hosts, treat like CNS disease.
- Echinocandins have no clinically useful activity against *Cryptococcus*.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
ENT	Laryngeal infection	Hoarseness, cough, or acute airway obstruction	Laryngeal edema and erythema, exophytic lesions	Laryngoscopy, stains, biopsy, cultures, serum cryptococcal antigen
RESP	Pneumonia	Fever, chest pain, cough, weight loss, dyspnea, sputum production	Signs of infection	ABGs, CXR, sputum culture, bronchoscopy, lung biopsy, serum cryptococcal antigen, LFA
CV	Endocarditis, myocarditis	Rare vascular instability		ECG, ECHO
HEME/IIMMUNO	Cryptococcemia		Signs of infection	Blood cultures, serum cryptococcal antigen, LFA
GU	Prostatitis, renal cortical abscess		Signs of infection	UA, urine cultures
CNS	Meningitis, abscesses, dementia	Headache, fever, nausea vomiting, cranial nerve palsies, lethargy, coma, seizures, or memory loss	Mental status, focal signs	CSF India ink stain, CSF cultures and cryptococcal antigen, LFA,CT, MRI

Key References: Perfect JR: Cryptococcosis (*Cryptococcus neoformans* and *Cryptococcus gattii*). In Bennett JE, Dolin R, Blaser MJ, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*, ed 8, Philadelphia, PA, 2015, Elsevier, pp 2934–2948; Idnurm A, Lin X: Rising to the challenge of multiple *Cryptococcus* species and the diseases they cause. *Fungal Genet Biol* 78:1–6, 2015.

Perioperative Implications

Preoperative Preparation

- Disposable anesthetic delivery circuits with bacterial filters.
- Protect and maintain airways for altered mental status, seizures, focal neurologic signs, and cranial nerve palsies.
- Organ system effects of HIV infection or underlying immunocompromised conditions.

Monitoring

- ARDS network low tidal volume protocol in severe ARDS patients.
- Consider monitoring increased ICP.

Airway

- None

Induction/Maintenance

- Anesthetic drugs associated with lower ICP and having neuroprotective qualities
- Possible interaction of antiretroviral drugs with the anesthetics and/or toxicity

Extubation

- Consider if can adequately protect airway.

Adjuvants

- None

Postoperative Period

- Careful observation for respiratory and neurologic compromise

Cushing Syndrome

Kathleen A. Smith | Justin L. Rountree

Risk

- Onset generally occurs in third and fourth decades.
- Approximately 3–5 times more common in women than men.
- 5-y mortality rate from adrenal carcinomas has been estimated to be >70%.

Perioperative Risks

- Lyte abnormalities
- Consequences of untreated Htn
- Hyperglycemia
- Cardiovascular disease more common

Worry About

- Challenges related to obesity, including airway management and IV access.
- Significant osteopenia secondary to impaired calcium absorption, making positioning difficult.
- Htn due to fluid retention.
- Increased risk of infection as a result of corticosteroids' immunosuppressive qualities.
- Hypokalemic alkalosis, commonly seen in ectopic ACTH production.
- Cushing syndrome may also occur with other disease states, including pheochromocytoma, sarcoidosis, pancreatic carcinoma, sarcoidosis, carcinoid lung tumors, and other neuroendocrine carcinomas.

Overview

- Most common cause of Cushing syndrome is iatrogenic administration of exogenous glucocorticoids.
- Spontaneous Cushing syndrome can result from adrenal gland hyperplasia secondary to increased ACTH production from a pituitary tumor or an ectopic nonendocrine ACTH tumor. Pituitary tumors may present with visual disturbances and have symptoms of increased ICP.
- Other causes include primary gland disorders, such as adrenal adenoma or carcinoma.
- Symptoms including Htn, hyperglycemia, increased intravascular volume, hypokalemia, abdominal striae, truncal obesity, telangiectasias, muscle weakness and/or wasting leading to thin extremities, osteoporosis due to impaired calcium absorption, depression, and insomnia.
- Severe metabolic alkalosis is often the first clinical manifestation of ectopic ACTH-secreting tumors and may result in significant hypoventilation, myocardial depression, arrhythmias, decreased cerebral blood flow, and neuromuscular excitability.