- Mineralocorticoid administration as needed; many glucocorticoids have significant mineralocorticoid action (hydrocortisone, prednisone, prednisolone). Methylprednisolone and dexamethasone have no mineralocorticoid activity.

Anticipated Problems/Concerns

- Severe resistant hypotension, hyperthermia, and CNS abnormalities, such as confusion, coma, lethargy, may occur intraop or postop and may be unpredictable.
- Syndrome may occur in severely traumatized pts without history of steroid use, with clinical picture of sepsis and associated abnormalities in adrenal function; Rx is life saving.

Alagille Syndrome

Christopher J. Cullom | Alan David Kaye | Amit Prabhakar

Risk

- Also known as syndromic bile duct paucity
- Affects cardiac, musculoskeletal, ocular, facial, and neurodevelopmental systems
- Most common inherited disorder that causes chronic liver disease in children
- 1:100,000 births with equal gender incidence

Perioperative Risks

- Cardiac congenital anomaly and hemodynamic instability
- Coagulopathy
- Liver dysfunction
- Musculoskeletal injury from positioning

Worry About

- Vertebral abnormalities
- Facial anomalies
- Ocular abnormalities
- Vitamin deficiencies: A, D, E, K
- Neurologic deficits (neuropathy, mental retardation, cerebellar defect)

Overview

- In addition to liver involvement, includes congenital cardiac disease (97%), dysmorphic face (96%), ocular abnormalities (78%), vertebral anomalies (51%), and kidney malformation (40%).
- Disease ranges from mild cholestasis to progressive liver failure.
- Liver involvement results in the loss of intralobar ducts over months to years.
- Elevated serum bile acids, conjugated bilirubin, alkaline phosphatase, and GGT typically seen.
- Malnutrition and growth failure is common, leading to delayed pubertal development.
- Malnutrition may lead to protuberant abdomen, making pts more prone to regurgitation.
- Ineffective absorption of dietary lipids, essential fatty acids, fat-soluble vitamins.
- Vitamin deficiencies: vitamin K (coagulopathy), vitamin D (rickets), vitamin E/A (retinopathy and neuropathy).
- Vitamin K deficiency and liver dysfunction lead to prolonged PT and PTT as well as thrombocytopenia.
- Cardiac abnormalities: Pulm vascular stenosis (most common with up 90% pts), tetralogy of Fallot, truncus arteriosus, patent ductus arteriosus, VSDs.
- Facial characteristics: Prominent forehead, hypertelorism, saddle or straight nose.
- Vertebral anomalies: Butterfly vertebrae (splitting of the bodies sagittally), spina bifida, fusion of adjacent vertebrae.
- Ocular abnormalities: Posterior embryotoxon, microcornea, macular dystrophy.
- Posterior embryotoxon progresses to glaucoma in 50% of pts.
- Neurologic effects: Cerebellar ataxia and peripheral neuropathy usually due to vitamin E and A deficiency. Mental retardation is also associated with the syndrome.
- There is a 12–14% risk of spontaneous intracranial bleed.
- Renal dysplasia found in 40% of pts.
- Halothane should be avoided as it has a myocardial depressant effect, lowering hepatic blood flow.
- Perfusion pressure to liver and kidney should be maintained with periop hydration and blood pressure control.

Etiology

- Characterized by chronic cholestasis, decreased number of interlobar bile ducts, and variety of congenital malformations
- Autosomal dominant mode of transmission involving mutation in *JAG1* gene

Usual Treatment

- Pts typically require procedures to correct various congenital abnormalities, biliary diversion, and ileal exclusion; may also require biopsy or liver transplantation.
- Symptomatic relief of pruritus can be provided with rifampicin or ursodeoxycholic acid.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Pulm arterial stenosis, tetralogy of Fallot, truncus arteriosus, patent ductus arteriosus	Dizziness Palpitations	Murmur	ECG, ECHO
RENAL	Renal dysplasia			Cr, GFR, UA
GI	Cholestasis, liver failure/cirrhosis	Pruritus	Hepatomegaly, splenomegaly	LFTs, abdominal CT
HEME	Coagulopathy			CBC, PT, PTT, INR
MS	Osteodystrophy		X-ray of extremities/DXA	
NEURO	Intracranial hemorrhage, vertebral anomalies		Cervical spine evaluation	X-ray of vertebrae
HEENT	Xerophthalmia, posterior embryotoxon		Ophthalmoscopic exam	
GENERAL	Facial abnormalities		Prominent forehead, hypertelorism	

Key References: Choudhry D, Rehman M, Schwartz R, et al.: The Alagille's syndrome and its anaesthetic considerations, *Paediatr Anaesth* 8(1):7–82, 1998; Subramaniam K, Myers L: Combined general and epidural anesthesia for a child with Alagille syndrome: a case report, *Paediatr Anaesth* 14(9):787–797, 2004.

Perioperative Implications

Preoperative Preparation

- Assessment of airway and neck mobility.
- Standardized bleeding history as well as clotting profile.
- ECHO and ECG to prepare for cardiovascular abnormalities.
- Evaluate neurologic status.
- Avoid succinylcholine if peripheral neuropathy is present.

Monitoring

- Avoid invasive monitoring whenever possible due to bleeding risk.

Airway

- Neck mobility may create difficulties.

Preinduction/Induction

- Potential usage of rapid sequence induction as pts are prone to regurgitation.
- Careful positioning due to osteodystrophy.
- Eye care paramount due to vitamin A deficiency and dry eyes.

Maintenance

- Use of sevoflurane or isoflurane as they have less myocardial depressant effects and preserve hepatic blood flow.
- Blood pressure control and adequate hydration to maintain liver perfusion.
- Use of cisatracurium for muscle relaxation as metabolism is independent of liver and renal function.

Extubation

- Usual criteria

Postoperative Period

- Careful positioning in PACU

Regional Anesthesia

- Used cautiously due to potential risk of bleeding and vertebral anomalies, but not contraindicated

Anticipated Problems/Concerns

- Cardiac pathology/anomalies
- Hemodynamic instability and hypotension
- Airway difficulty due to vertebral anomalies
- Coagulopathy
- Nerve and soft tissue injury due to positioning
- Liver and renal dysfunction
- Ocular abnormalities requiring extra eye protection
- Various neurologic abnormalities to be aware of before anesthesia