orphanaesthesia

Anesthesia recommendations for

Pallister-Hall syndrome

Disease name: Pallister-Hall syndrome

ICD 10: D33.0

OMIM: 146510

Synonyms: Hypothalamic hamartoblastoma syndrome

Disease summary: Pallister-Hall syndrome (PHS) is a rare autosomal dominant congenital disorder that is characterized by polydactyly, hypothalamic hamartoma, hypopituitarism, bifid epiglottis, and imperforate anus [1]. Gelastic seizures are sometimes present.

PHS is caused by mutations of the GLI3 gene (7p13). Typical facial features are normal, but some patients have short nose, cleft palate, gingival cysts, cleft larynx or bifid epiglottis, micrognathia and midface retrusion [2].

Most patients with PHS require surgery due to primarily to polydactyly or syndactyly, but a few may need surgery for imperforate anus, or genitourinary malformations. Patients with hypopituitarism need steroid and other hormonal replacement therapy. Renal or ear anomalies, deafness, epilepsy, and intellectual disability mental retardation are uncommon, but are also associated with PHS [3].

Most cases are sporadic; however, autosomal dominant inheritance is also observed.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Translations may not always reflect the most recent updates of the English version

---

Find more information on the disease, its centers of reference and patient organizations on Orphanet: www.orpha.net

A	**AIRWAY / ANESTHETIC TECHNIQUE**	ENT advice may be useful. General anesthesia with tracheal intubation is preferred due to increased risk of pulmonary aspiration. Neuraxial or intellectual disability.
B	**BLOOD PRODUCTS (COAGULATION)**	Patients with PHS may have dysmorphic facial appearance (hard palate malformation, cleft larynx, gingival cysts, and bifid epiglottis). Tracheal intubation may be difficult, and laryngeal clefts increase the risk of pulmonary aspiration; bleeding during direct laryngoscopy may occur.
C	**CIRCULATION**	Congenital heart disease is frequently associated with PHS. Electrocardiogram and echocardiogram are recommended to detect cardiac malformations.
D	**DRUGS**	Some patients receive steroid and other hormonal replacement therapy because of hypopituitarism. Stress doses of steroids should be administered perioperatively. Treatment for epilepsy is necessary in some cases.
E	**EQUIPMENT**	Not reported.

Typical surgery and procedures

Typical surgeries in the PHS patients include treatment for polydactyly, imperforate anus, and genitourinary anomalies such as hypospadias, vaginal atresia or renal anomalies [3]. Surgery for hypothalamic hamartoma is rarely indicated but may be necessary in atypical patients [4].

Type of anesthesia

General anesthesia with tracheal intubation is preferred due to increased risk of pulmonary aspiration in patients with laryngeal cleft [5,6]. Intubation may be challenging due to pharyngeal anomalies. Flexible fiberoptic bronchoscopic intubation is preferred, as direct laryngoscopy may cause bleeding in patients with a bifid epiglottis. Fiberoptic bronchoscopy may be necessary if it appears the patient may not be easily ventilated by mask. Despite the increased risk of aspiration, a supraglottic airway (preferably a second generation one with a gastric channel) can be used either to maintain a patent airway or as a guide for intubation [5]. Videolaryngoscopy can also be used to facilitate tracheal intubation [5].

Neuraxial or regional anesthesia might be difficult because of intellectual disability, but in selected cases, it may avoid airway manipulation [6].

Necessary additional pre-operative testing (beside standard care)

Bifid epiglottis or laryngeal clefts predisposes the patients to pulmonary aspiration of gastric contents [7]. In patients with laryngeal clefts, chest X-ray and oxygen saturation must be evaluated preoperatively, because the patients may have pre-existing lung damage due to recurrent aspiration pneumonia. Other laryngeal anomalies such as anterior synechia of the vocal cords or cricoid fusion have been observed (6). Obtaining an ENT advice is therefore useful.

Congenital heart disease is frequently associated with PHS [1,2]. Electrocardiogram and echocardiogram are recommended to detect cardiac malformations.

Other reported organ malformations such as hypopituitarism and renal anomalies may require further evaluation to exclude any potential issues arising with requirement of stress doses of steroids, fluid management, or renal clearance. Adrenal insufficiency should be ruled out to prevent an adrenal crisis. Neurological examination should exclude the presence of intracranial hypertension. A renal ultrasound may evaluate the presence of renal abnormalities.

A large number of other anomalies have been described in patients with PHS, but each of them are uncommon. It is important that the patient be evaluated by a clinical geneticist for other anomalies prior to elective surgery so that the anesthetist can properly manage the patient for those anomalies.

A gelastic seizure is a sudden outburst of laughter with no apparent cause. It may sound unpleasant and sardonic rather than joyful. It usually lasts for less than a minute. During or shortly after a seizure, the patient might display some twitching, strange eye movements, lip smacking, fidgeting or mumbling. The child's parents should be asked for the specificities of these crises in their child to inform caregivers in the PACU and the ward.

In case of thoracic surgery necessitating one-lung ventilation, a CT-scan may be necessary as abnormal lung lobulation is observed in PHS.

Particular preparation for airway management

Patients with PHS may have dysmorphic facial appearance (hard palate malformation, cleft larynx, gingival cysts, and bifid epiglottis) [1,2]. Tracheal intubation may be difficult, and laryngeal clefts increase the risk of pulmonary aspiration; bleeding during direct laryngoscopy may occur [7]. Pretreatment with a histamine (H2) antagonist or proton pump inhibitor and a non-particulate antacid is recommended: no evidence for efficacy. Appropriate difficult airway equipment should be prepared in the operating room; a surgical airway may be needed emergently, and appropriate personnel should be immediately available.

Pre-induction gastric ultrasound may be useful to evaluate the amount of residual gastric content and the associated risk of regurgitation/aspiration.

Particular preparation for transfusion or administration of blood products

Not reported. The general rules for perioperative blood management may be applied.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilization

Not reported.

Interactions of chronic disease and anesthesia medications

Some patients receive steroid and other hormonal replacement therapy because of hypopituitarism [1,2]. Stress doses of steroids should be administered perioperatively.

Some patients require anticonvulsant drugs to minimize seizure risk. Long term use of certain anticonvulsant agents may induce rapid metabolism of neuromuscular blockers and opioids by up-regulating hepatic P450 enzymes.

Anesthetic procedure

Special caution should be paid to avoid pulmonary aspiration during the induction of general anesthesia in patients with laryngeal clefts [7].

Muscle relaxants and opiates may be metabolized more rapidly due to use of anticonvulsant drugs.

Particular or additional monitoring

Neuromuscular function monitoring is recommended.

Invasive hemodynamic monitors may be considered in patients with congenital heart disease depending on their severities [7]. Intracranial pressure may be monitored in patients with intracranial hypertension.

Possible complications

Aspiration pneumonia may occur after surgery, especially in patients with laryngeal clefts.

Postoperative seizures may occur. Continuation of anticonvulsant drugs is recommended perioperatively.

Adrenal insufficiency may occur: hypotension, hypoglycemia, hyponatremia with mild hyperkalemia. Secondary adrenal insufficiency should be considered when unexplained perioperative hypotension is present.

Post-operative care

Respiratory monitors (oximetry, capnography) should be used postoperatively, due to risks of respiratory complications.

Blood pressure may be very labile because of adrenal insufficiency and should be monitored closely.

Disease-related acute problems and effect on anesthesia and recovery

Stress doses of corticosteroids should be administered when unexplained perioperative hypotension is seen. Secondary adrenal insufficiency is diagnosed if corticosteroids are effective.

Ambulatory anesthesia

Not reported. Ambulatory anesthesia is not recommended because patients with moderate to severe manifestations of PHS may require extensive postoperative care, as mentioned above.

Patients with mild PHS might be appropriate for ambulatory anesthesia.

Obstetrical anesthesia

Women with a seizure disorder are at greater risk for mortality during pregnancy, and antiepileptic therapy reduces that risk; however, antiepileptics also increase the risk of fetal death or congenital malformations.

References

1. Hall JG, Pallister PD, Clarren SK, Beckwith JB, Wiglesworth FW, Fraser FC, Cho S, Benke PJ, Reed SD. Congenital hypothalamic hamartoblastoma, hypopituitarism, imperforate anus and postaxial polydactyly - a new syndrome? Part I: clinical, causal, and pathogenetic considerations. Am J Med Genet 1980; 7: 47-74.
2. Biesecker LG, Graham JM, Jr. Pallister-Hall syndrome. J Med Genet 1996; 33: 585-9.
3. Al-Qattan MM, Shamseldin HE, Salih MA, Alkuraya FS, GLI3-related polydactyly: a review. Clin Genet. 2017; 92: 457-466.
4. Boudreau EA, Liow K, Frattali CM, Wiggs E, Turner JT, Feuillan P, Sato S, Patsalides A, Patronas N, Biesecker LG, Theodore WH, Hypothalamic hamartomas and seizures: distinct natural history of isolated and Pallister-Hall syndrome cases. Epilepsia. 2005; 46: 42-7.
5. Oe Y, Godai K, Masuda M, Kanmura Y. Difficult airway associated with bifid glottis and coexistent subglottic stenosis in a patient with Pallister-Hall Syndrome: A case report. JA Clin Rep. 2018; 4: 20.
6. Riutort KT, Feinglass NG, Brull SJ. Anesthetic implications of Pallister-Hall Syndrome in patients with a bifid epiglottis. Rom J Anaesth Intensive Care 2009; 16: 71-4.
7. Kraus M, Diu M. Bifid epiglottis in a patient with Pallister-Hall syndrome. Can J Anaesth 2016; 63: 1197-8.

Date last modified: **October 2025**

This recommendation has been prepared by:

Author:
Kohei Godai, Fellow, Department of Anesthesiology & Critical Care Medicine, Graduate School of Medical & Dental Sciences, Kagoshima University, Saguragaoka, Kagoshima, Japan
kxg179@icloud.com

Disclosure: *The author(s) has no financial or other competing interest to disclose. This recommendation was unfunded.*

This recommendation was reviewed by:

Reviewer:
Sorin J Brull, Mayo Clinic, College of Medicine, Jacksonville, FL, USA
sjbrull@me.com

Reviewer:
Leslie G Biesecker, Medical Genomics and Metabolic Genetics Branch, National Human Genome, Research Institute, National Institutes of Health, Bethesda, Maryland, USA
lesb@mail.nih.gov

Disclosure: *The reviewer(s) have no financial or other competing interest to disclose.*

Update and revision (October 2025)

Author:
Kohei Godai, Fellow, Department of Anesthesiology & Critical Care Medicine, Graduate School of Medical & Dental Sciences, Kagoshima University, Saguragaoka, Kagoshima, Japan
kxg179@icloud.com

Disclosure: *The author(s) has no financial or other competing interest to disclose. This recommendation was unfunded.*

Reviewer
Francis Veyckemans, Retired pediatric anaesthesiologist and honorary professor UCLouvain Medical School, Ottignies-Louvain-la-Neuve, Belgium
veyckemansf@gmail.com

Editorial Review
Christine Gaik, Specialist in anaesthesia and intensive care medicine, University Hospital Marburg, Germany
gaikc@med.uni-marburg.de