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Wolf-Hirschhorn syndrome

orphan**anesthesia**

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

SUPPLEMENT NR. 15 | 2026

OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

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orphan**a**nesthesia

Anesthesia recommendations for **Wolf-Hirschhorn syndrome**

Disease name: Wolf-Hirschhorn syndrome

ICD 10: Q 93.3

Synonyms: 4p deletion syndrome, 4p-syndrome, del (4p) syndrome, monosomy 4p, partial monosomy 4p, WHS

Disease summary: The disease was first described by Hirschhorn and Cooper in 1961, the second case was published in 1965 by Wolf et al.

Wolf-Hirschhorn syndrome (WHS) is a congenital disorder with specific clinical features mostly caused by de novo microdeletion of the distal short arm of chromosome 4 (del 4p 16.3) among Wolf-Hirschhorn candidate gene (WHSC1 and WHSC2). Only 10 % are caused by translocation [2,3]. The prevalence of the WHS is estimated at 1:50 000 births with a 2:1 female to male ratio. The severity of the phenotypic manifestation of WHS correlates with the amount of chromosomal deletion. The mortality rate is about 30% within the first two years of life mainly due to aspirations leading to pulmonary infections, epileptic seizures or cardiac failure. The seizures are often hard to control, but tend to decline with age.

The typical clinical features can vary [1,12].

More than 75% of patients have typical facial feature of "Greek warrior helmet" appearance (wide bridge of nose, high forehead), microcephaly, low set ears, growth retardation with prenatal onset, muscular hypotonia, failure to thrive, seizures, febrile convulsions, EEG abnormalities, mental disability of variable degree.

50-75% of patients have skeletal abnormalities as scoliosis, congenital hip dislocation or clump feet, craniofacial asymmetry, microstomia, abnormal teeth, IgA or IgG2 deficiency.

25-50% of patients have hearing loss, heart defect (mostly atrial or ventricular septal defect), eye or optic nerve anomalies, cleft lip and cleft palate, genitourinary tract anomalies, structural brain anomalies and stereotypies. Congenital heart defects usually are not complex.

Less than 25% of patients have anomalies concerning liver, gallbladder, gut, diaphragm, esophagus, lung and aorta, malignancies of liver or hematopoietic system.

► **Citation:** Sabbahi A, Kaltofen H: Wolf-Hirschhorn syndrome. Anästh Intensivmed 2026;67:S175–S182.
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Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this guideline Perhaps new knowledge.



Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

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

Emergency information

A	AIRWAY / ANESTHETIC TECHNIQUE	All types of anesthesia are optional. Regional anesthesia could be challenging in case of skeletal deformities. Preparation for difficult airway management because of facial dysmorphism. Susceptibility to respiratory infections. Higher risk of aspiration due to gastroesophageal reflux. Sensitivity to muscle relaxants in case of muscular hypotonia.
B	BLOOD PRODUCTS (COAGULATION)	IgA deficiency might predispose to allergic reactions in case of transfusion of plasma-containing blood products. Potential platelet dysfunction and impaired coagulation factors in case of valproic acid therapy as antiepileptic drug.
C	CIRCULATION	Congenital heart disease is common. Consider ECG and Echocardiography for evaluation. Cardiac arrhythmias and heart failure due to the severity of the underlying cardiac defect can occur.
D	DRUGS	Antiepileptic drugs should be continued. Consider interactions with anesthetics. EEG Monitoring might be useful. Sensitivity to premedication substances. Distinct association between WHS and malignant hyperthermia possible, yet unproven.
E	EQUIPMENT	Careful patient positioning in case of skeletal deformities is advised. Presence of caregivers in PACU / IMC / ICU might be useful in case of mental disability, hearing loss or visual impairment.

Typical surgery and procedures

Gastrostomy tube placement, fundoplication for gastroesophageal reflux disease, repair of cleft palate, dental treatment, ophthalmological procedures, cardiac surgery, tympanoplasty, myringotomy, hypospadias correction, cystoscopy, hip correction.

Type of anesthesia

Successful perioperative management has been reported with both inhalational and intravenous anesthesia in patients with WHS [5,6,10,13,15]. However, two case reports describe a distinct association between WHS and malignant hyperthermia, one of them with delayed onset [4,16]. Children with WHS often present with infections, therefore perioperative hyperthermia could have other etiologies. Association of malignant hyperthermia with WHS is yet unproven and very unlikely, as the generalized hypotonia is not caused by the muscular system [9]. The ryanodine receptor is genetically not involved [12].

Regional anesthesia like thoracic epidural anesthesia for fundoplication is reported [17], but special care should be taken in case of vertebral abnormalities like scoliosis.

Necessary additional preoperative testing (beside standard care)

A thorough history and examination of the patient is important, as many organ systems (see above) can be involved. Careful evaluation of the airway patency and pulmonary function is essential. In case of congenital cardiac disease, ECG and echocardiography help to evaluate the cardiac function. Blood coagulation and thrombocyte function should be checked if the patient receives valproate therapy. Seizures should be well controlled by antiepileptic therapy.

Particular preparation for airway management

Due to craniofacial deformities equipment for difficult airway management must be prepared. The use of a video-assisted intubation technique is recommended. Some reports also mention successful conventional endotracheal intubation without difficulties. A higher risk of aspiration and susceptibility to airway infections should be kept in mind. The size of the endotracheal tube should be chosen smaller than calculated per age due to growth retardation. In case of low risk of aspiration, a laryngeal mask can be used [7,8].

Particular preparation for transfusion or administration of blood products

If the patient has IgA deficiency, then he might be at risk of allergic reactions when receiving a transfusion with a plasma-containing blood product [14].

Particular preparation for anticoagulation

Coagulation disorders can develop in case of therapy with valproic acid. Careful review of coagulation parameters is recommended, as valproic acid influences both thrombocyte function (acquired von Willebrand's disease) and coagulation factors [11]. Therapy according to the laboratory test results is recommended in case of operations with anticipated significant blood loss, if valproic acid cannot be replaced.

Particular precautions for positioning, transportation and mobilization

Careful attention to intraoperative patient positioning is indicated in case of skeletal deformities like kyphosis, scoliosis or hip dysplasia.

Interactions of chronic disease and anesthesia medications

Most patients are under antiepileptic therapy, which should be continued through the perioperative period. The anesthesiologist must keep in mind possible interactions, especially older antiepileptic drugs like carbamazepine, phenobarbital, phenytoin that induce hepatic enzymes leading to decreased plasma concentrations of many medications. Valproate is an inhibitor of microsomal hepatic enzyme systems and decreases the metabolism of medications.

Anesthetic procedure

As WHS patients tend to be less cooperative and hearing loss is common, the anesthesiologist may wish to have a parent/ caregiver attending the induction of anesthesia. If necessary, premedication substances should be given carefully under monitoring of vital signs and medical surveillance as the patients can be very sensitive, and respiratory complications may occur. Successful inhalational inductions are described, but it should be kept in mind that patients with WHS often present with gastroesophageal reflux disease. The plan for management of the potentially difficult airway must be balanced against the increased risk of aspiration in WHS patients.

Recurrent respiratory infections may lead to bronchial irritability especially at anesthesia induction and during the extubation phase. Difficulties of ventilation and increased peak airway pressure may occur. The use of sevoflurane and bronchodilators such as beta-2-agonist aerosols can be helpful.

Smaller doses of neuromuscular blocking agents may be required. They should be titrated carefully when the patient presents with generalized hypotonia. Use of qualitative and quantitative neuromuscular monitoring is recommended as hypotonic WHS patients have increased sensitivity to neuromuscular blocking drugs. Successful application of sugammadex for reversal of non-depolarizing neuromuscular blocking agents, such as rocuronium and vecuronium, is reported [6].

Regional anesthesia may be applied using ultrasound visualization as malformations of the bony system are common, for example kyphoscoliosis, occult spina bifida [12]. The safety margin of local anesthetic dosage could be less due to susceptibility to seizures.

Particular or additional monitoring

According to the severity of cardiac disease, appropriate hemodynamic monitoring should be planned for the surgical procedure.

Temperature monitoring is advisable to detect fever caused by infections or a rare event of malignant hyperthermia.

Possible complications

Respiratory complications as pulmonary infection, aspiration pneumonia, atelectasis are common.

Prolonged duration of neuromuscular block is possible.

Perioperative seizures can occur, if the patient has a history of severe convulsion disorder.

Cardiac arrhythmia and heart failure due to the severity of possibly underlying cardiac defect may occur.

Hyperthermia should be treated promptly to avoid febrile seizures.

Postoperative care

Continuous respiratory monitoring is recommended until the patient is fully awake and stable. Prolonged surveillance is advisable due to possible complications as mentioned above.

Disease-related acute problems and effect on anesthesia and recovery

If intra- or postoperative hyperthermia occurs, there are many differential diagnoses to be considered: infections, malignant hyperthermia, iatrogenic overheating, drug induced fever etc.

Ambulatory anesthesia

Usually, ambulatory anesthesia may not be advisable. In case of mild presentation of the disease and very short procedure, ambulatory anesthesia may be considered on an individual base. If surgery is performed under peripheral regional anesthesia alone, outpatient management can be considered.

Obstetrical anesthesia

No reports found.

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