

A&I

ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

Offizielles Organ: Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e.V. (DGAI)
Berufsverband Deutscher Anästhesisten e.V. (BDA)
Deutsche Akademie für Anästhesiologische Fortbildung e.V. (DAAF)
Organ: Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin e.V. (DIVI)



PURA syndrome

Rubinstein-Taybi syndrome

orphan**a**nesthesia

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

SUPPLEMENT NR. 11 | 2022

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 Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

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 Anästhesisten damit keine Erfahrungen gesammelt haben, so dass 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 ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass 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.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

Find a survey of the recommendations published until now on:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu



Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin

www.dgai.de



ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

www.ai-online.info

Projektleitung

Prof. Dr. Tino Münster, MHBA

Chefarzt
Klinik für Anästhesie und
operative Intensivmedizin
Krankenhaus Barmherzige
Brüder Regensburg
Prüfeninger Straße 86
93049 Regensburg,
Deutschland

Tel.: 0941 369-2350

E-Mail: Tino.Muenster@barmherzige-regensburg.de

orphananesthesia

Anaesthesia recommendations for **PURA syndrome**

Disease name: PURA syndrome

ICD 10: Q93.5

Synonyms: PURA-related neurodevelopmental disorder, 5q31.3 deletion syndrome

Disease summary: Genetic mutations of the gene coding for purine-rich element binding protein A (PURA, 5q31.2) lead to a developmental disorder, named PURA syndrome. PURA is thought to play a role in the control of DNA replication and transcription, neuron proliferation, dendrite maturation, and mRNA transportation to translation sites during neuronal development. The gene is relevant in brain development and may be involved in the automatic regulation of breathing by the brainstem. PURA defects affect the development of neurons and may also affect the formation of maturation of myelination, leading to developmental problems and seizures, although the exact mechanism is unclear. Early signs of this disorder include hypotonia, hypothermia, swallowing disorders, seizures, central and obstructive sleep apnoea. Later manifestations include neurodevelopmental delay, speech delay or absence, delayed and impaired gross motor development, intellectual disability, and seizure disorder. Challenges for an anaesthesiologist are multifold and the proposed approach is deduced from the above-mentioned clinical problems and from the anaesthetic implications of other phenotypically similar neurodevelopmental disorders. Primary anaesthetic concerns focus on the respiratory, cardiovascular, and neurologic functions of the child as these patients could show an increased sensitivity to sedative medications.

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



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

► **Citation:** Rubin K, Sigler E: PURA syndrome. AnästH Intensivmed 2022;63:S257–S262.
DOI: 10.19224/ai2022.S257

Typical surgery

Gastrostomy, orthopaedic surgery, correction of scoliosis, ophthalmologic procedures.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia.

There are no specific concerns of PURA syndrome being associated with malignant hyperthermia, which helps in determining the type of induction agent or maintenance anaesthetic to use.

Necessary additional pre-operative testing (beside standard care)

Thorough assessment of the respiratory, cardiovascular, and neurologic function with the help of the patient's neurologist or paediatrician is necessary for proper peri-operative care. Additional testing should be guided by the results of such assessment. Lung function testing is probably not feasible and will likely not provide any additional predictive value for post-operative respiratory complications. The dosage and possible side effects (haematologic, metabolic) of the patient's antiepileptic drugs should be checked.

Particular preparation for airway management

Similar neurodevelopmental disorders, such as Rett syndrome and Angelman syndrome, have shown a higher propensity for difficult endotracheal intubation than the general population. However, facial dysmorphism studies of small patient samples do not show facial features that would indicate an increased risk for difficult endotracheal intubation or mask ventilation.

Hypotonia of the oropharyngeal muscles may predispose towards swallowing difficulties and possibly increases the risk of aspiration during induction and awakening.

Particular preparation for transfusion or administration of blood products

There is evidence from similar neurodevelopmental disorders that there may be a higher requirement for blood products in highly invasive surgeries (e.g. scoliosis surgery).

Particular preparation for anticoagulation

No evidence supports the need for particular anticoagulation. Postpubertal patients who are not able to move adequately during the post-operative period should be considered for thromboprophylaxis.

Particular precautions for positioning, transportation and mobilisation

With alterations in muscle tone and potential spasticity/contractures that may develop, positioning should emphasise appropriate padding and avoidance of pressure spots.

Interactions of chronic disease and anaesthesia medications

Not reported.

Anaesthetic procedure

In case of elective procedure, even if short fasting times for clear fluids are currently recommended for healthy children, it is probably safer to ensure a longer than usual fasting time in PURA patients because of their risk of aspiration. Regarding the risk of seizures, the usual antiepileptic drugs should be administered on the day of the procedure and high concentrations of sevoflurane and hyperventilation should be avoided.

An increased risk for apnoea, upper airway obstruction and aspiration should be considered during both induction and recovery of anaesthesia.

Because of PURA's association with central and obstructive sleep apnoea, patients are at increased risk of sedation-related respiratory adverse events. It is likely that patients with PURA syndrome will show delayed recovery from respiratory depressants and increased sensitivity to sedative medications. Minimising the dose of medications that decrease respiratory drive, mainly opioids and benzodiazepines, is recommended.

It seems reasonable to apply principles of anaesthetic management used for patients with severe obstructive sleep apnoea, with reduction of doses of opioids (typically 50 % of usual) accompanied by continuous monitoring, including pulse oximetry, and the use of a prophylactic nasopharyngeal airway during the awakening period.

Altered muscle tone, typically presenting with hypotonia and poor tone of pharyngeal muscles, leads to considerations regarding intraoperative use of a neuromuscular blocking agent: If a neuromuscular blocking agent is needed, its dosage should be titrated to effect (taking into account the reduced muscle tone and mass) using neuromuscular monitoring (train-of-four, TOF) to ensure its adequate effect and reversal. It is likely that there will be variability in the presentation of these patients, leading to alterations in drug dosing and metabolism.

Hypothermia should be actively prevented.

Particular or additional monitoring

No monitoring specific to PURA syndrome.

Possible complications

Sedative drugs, including opioids and benzodiazepines, may cause respiratory insufficiency.

Muscle relaxants dosage should be titrated to effect (taking into account the reduced muscle tone and mass) using neuromuscular monitoring to ensure their adequate effect and reversal.

Post-operative care

Post-operative continuous monitoring with pulse oximetry and respiratory rate is recommended, especially if patient history reveals apnoeas after full term birth or after stress. Following general anaesthesia, admission for 24-hour monitoring is advised to survey that there are no recurrent episodes of apnoea, hypopnoea or desaturation, and that aspiration and reactions are as required.

Multimodal analgesia with an emphasis on non-opioid agents is recommended, with reduction of doses of opioids, should additional analgesia be necessary. Pain should be evaluated using a special scoring system for individuals that are unable to communicate their pain (e.g., the adapted Face, Legs, Activity, Cry, Consolability scale or FLACC scale) and with the help of the child's usual carers (parents).

Patients often have epilepsy with intractable seizures. Antiepileptic medications should be continued on schedule throughout the peri-operative time frame, and IV antiepileptic substitution should be foreseen if the patient needs to remain npo in the post-operative period. It is unlikely that general anaesthesia should be a post-operative seizure trigger in this patient population but hypoventilation, pain and stress could result in an increased risk of seizures.

Disease-related acute problems and effect on anaesthesia and recovery

Pituitary dysfunction may exist. Provide steroid substitution in cases of corticotherapy.

Disease triggered emergency situations are focused on status epilepticus.

Ambulatory anaesthesia

Ambulatory anaesthesia (according to common guidelines) is not recommended. Given the association of the syndrome with both central and obstructive sleep apnoea, we recommend this patient population to be admitted to the inpatient unit.

Obstetrical anaesthesia

Not reported.

References

1. Tanaka AJ, Bai R, Cho MT, Anyane-Yeboah K, Ahimaz P, Wilson AL, et al. De novo mutations in PURA are associated with hypotonia and developmental delay. *Cold Spring Harbor Molecular Case Studies* 2015;1:a000356. DOI: 10.1101/mcs.a000356
2. Reijnders MRF, Leventer RJ, Lee BH, Baralle D, Selber P, Paciorkowski AR, et al. PURA-Related Neurodevelopmental Disorders. In: Adam MP, Ardinger HH, Pagon RA, et al. (editors). *GeneReviews®*. Seattle (WA): University of Washington, Seattle 1993–2018. <https://www.ncbi.nlm.nih.gov/books/NBK426063/> (accessed on: 27.04.2017)
3. Lee BH, Reijnders MRF, Abubakare O, Tuttle E, Lape B, Minks KQ, et al. Expanding the neurodevelopmental phenotype of PURA syndrome. *Am J Med Genet* 2018;176A:56–67. DOI: 10.1002/ajmg.a.38521
4. Pura Foundation. <https://www.purasyndrome.org/family> (accessed on: 26.01.2019)
5. US Department of Health and Human Services. Published 25. Apr 2018. <https://ghr.nlm.nih.gov/condition/pura-syndrome#genes> (accessed on: 26.04.2018)
6. Patino M, Sadhasivam S, Mamoud M. Obstructive Sleep Apnoea in children: perioperative considerations. *BJA* 2013;111;S1:i83–i95. DOI: 10.1093/bja/aet371
7. Liu XF, Wang DX, Ma D. Using General Anesthesia plus Muscle Relaxant in a Patient with Spinal Muscular Atrophy Type IV: A Case Report. *Case Rep Anesthesiol* 2011;743587. DOI: 10.1155/2011/743587
8. Kako H, Martin DP, Cartabuke R, Beebe A, Klamar J, Tobias JD. Perioperative management of a patient with Rett syndrome. *Int J Clin Exp Med* 2013;6:393–403
9. Reijnders MRF, Janowski R, Alvi M, et al. PURA syndrome: clinical delineation and genotype-phenotype study in 32 individuals with review of published literature. *J Med Genet* 2018;55:104–113
10. Rezkalla J, Von Wald T, Hansen KA: Premature Thearche and the PURA Syndrome. *Obstet Gynecol* 2017;129:1037–1039.

Date last modified: **October 2019**

This recommendation was prepared by:

Authors

Kasia Rubin, Anaesthesiologist, Rainbow Babies & Children's Hospital, Cleveland, OH, USA
Kasia.rubin@gmail.com

Elizabeth Sigler, Anaesthesiologist, University Hospitals of Cleveland, Cleveland, OH, USA
elizabethmalloy9@gmail.com

Disclosure The authors have no financial or other competing interest to disclose. This recommendation was unfunded.

This recommendation was reviewed by:

Reviewers

Francis Veyckemans, Anaesthesiologist, Department of Paediatric Anaesthesia, Jeanne de Flandre Hospital, University Hospitals of Lille, Lille, France

Richard Leventer, Paediatric neurologist, Children's Neuroscience Centre, Murdoch Childrens Research Institute, University of Melbourne Department of Paediatrics, Australia

Lía Mayorga, Pediatrician, Inborn Errors of Metabolism, Instituto de Histología y Embriología de Mendoza (IHEM), Universidad Nacional de Cuyo, CONICET-UNCuyo, Mendoza, Argentina

Disclosure The reviewers have no financial or other competing interest to disclose.

Herausgeber



DGAI

Deutsche Gesellschaft
für Anästhesiologie und
Intensivmedizin e.V.
Präsident: Prof. Dr.
F. Wappler, Köln



BDA

Berufsverband Deutscher
Anästhesisten e.V.
Präsident: Prof. Dr.
G. Geldner, Ludwigsburg



DAAF

Deutsche Akademie
für Anästhesiologische
Fortbildung e.V.
Präsident: Prof. Dr.
H. Bürkle, Freiburg

Schriftleitung

Präsident/in der Herausgeberverbände
Gesamtschriftleiter/Editor-in-Chief:
Prof. Dr. Dr. Kai Zacharowski, Frankfurt
Stellvertretender Gesamtschriftleiter/
Deputy Editor:
Prof. Dr. T. Volk, Homburg/Saar
CME-Schriftleiter/CME-Editor:
Prof. Dr. W. Zink, Ludwigshafen

Redaktionskomitee/Editorial Board

Prof. Dr. G. Beck, Wiesbaden
Prof. Dr. A. Brinkmann, Heidenheim
Prof. Dr. H. Bürkle, Freiburg
Prof. Dr. B. Ellger, Dortmund
Prof. Dr. K. Engelhard, Mainz
Prof. Dr. M. Fischer, Göppingen
Prof. Dr. U. X. Kaisers, Ulm
Prof. Dr. T. Loop, Freiburg
Prof. Dr. W. Meißner, Jena
Prof. Dr. C. Nau, Lübeck
RAin A. Pfundstein, Nürnberg
Dr. M. Rähmer, Mainz
Prof. Dr. A. Schleppers, Nürnberg
Prof. Dr. M. Thiel, Mannheim
Prof. Dr. F. Wappler, Köln
Prof. Dr. M. Weigand, Heidelberg

Redaktion/Editorial Staff

Carolin Sofia Kopp B.A.
Korrespondenzadresse:
Neuwieder Straße 9 | 90411 Nürnberg |
Deutschland | Tel.: 0911 9337812
E-Mail: anaesth.intensivmed@dgai-ev.de

Verlag & Druckerei

Aktiv Druck & Verlag GmbH

An der Lohwiese 36 |
97500 Ebelsbach | Deutschland
www.aktiv-druck.de



Geschäftsführung

Wolfgang Schröder | Jan Schröder |
Nadja Schwarz
Tel.: 09522 943560 | Fax: 09522 943567
E-Mail: info@aktiv-druck.de

Anzeigen | Vertrieb

Pia Müller | Robert Kux
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: anzeigen@aktiv-druck.de

Verlagsrepräsentanz

Jürgen Distler
Neuwieder Straße 9 | 90411 Nürnberg
Tel.: 0171 9432534
E-Mail: jdistler@bda-ev.de

Herstellung | Gestaltung

Pia Müller | Robert Kux |
Stefanie Triebert
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: ai@aktiv-druck.de

Titelbild

Gestaltung: Klaus Steigner
Paumgartnerstraße 28 | 90429 Nürnberg
E-Mail: mazyblue@klaus-steigner.de
www.klaus-steigner.de

Erscheinungsweise 2022

Der 63. Jahrgang erscheint jeweils zum
Monatsanfang, Heft 7/8 als Doppelausgabe.

Bezugspreise (inkl. Versandkosten):

• Einzelhefte	30,- €
• Jahresabonnement:	
Europa (ohne Schweiz)	258,- €
(inkl. 7 % MwSt.)	
Schweiz	266,- €
Rest der Welt	241,- €

Mitarbeiter aus Pflege, Labor, Studenten und Auszubildende (bei Vorlage eines entsprechenden Nachweises)

Europa (ohne Schweiz)	94,- €
(inkl. 7 % MwSt.)	
Schweiz	90,- €
Rest der Welt	94,- €

**Für Mitglieder der DGAI und/oder
des BDA ist der Bezug der Zeitschrift
im Mitgliedsbeitrag enthalten.**

Allgemeine Geschäfts- und Liefer- bedingungen

Die allgemeinen Geschäfts- und Liefer-
bedingungen entnehmen Sie bitte dem
Impressum auf www.ai-online.info

Indexed in **Current Contents®/Clinical
Medicine, EMBASE/Excerpta Medica;
Medical Documentation Service;
Research Alert; Sci Search; SUBIS
Current Awareness in Biomedicine;
VINITI: Russian Academy of Science.**

Nachdruck | Urheberrecht

Die veröffentlichten Beiträge sind urhe-
berrechtlich geschützt. Jegliche Art von
Vervielfältigungen – sei es auf mechani-
schem, digitalem oder sonst möglichem
Wege – bleibt vorbehalten. Die Aktiv
Druck & Verlags GmbH ist allein auto-
risiert, Rechte zu vergeben und Sonder-
drucke für gewerbliche Zwecke, gleich
in welcher Sprache, herzustellen. An-
fragen hierzu sind nur an den Verlag zu
richten. Jede im Bereich eines gewerbli-
chen Unternehmens zulässig hergestellte
oder benutzte Kopie dient gewerblichen
Zwecken gem. § 54 (2) UrhG. Die Wie-
dergabe von Gebrauchsnamen, Handels-
namen, Warenbezeichnungen usw. in
dieser Zeitschrift berechtigt auch ohne
besondere Kennzeichnung nicht zu der
Annahme, dass solche Namen im Sinne
der Warenzeichen- und Markenschutz-
Gesetzgebung als frei zu betrachten wä-
ren und daher von jedermann benutzt
werden dürften.

Wichtiger Hinweis

Für Angaben über Dosierungsanwei-
sungen und Applikationsformen kann
vom Verlag und den Herausgebern keine
Gewähr übernommen werden. Derartige
Angaben müssen vom jeweiligen An-
wender im Einzelfall anhand anderer
Literaturstellen auf ihre Richtigkeit über-
prüft werden. Gleiches gilt für berufs-
und verbandspolitische Stellungnahmen
und Empfehlungen.

Allein aus Gründen der besseren Les-
barkeit wird auf die gleichzeitige Ver-
wendung männlicher, weiblicher und
weiterer Sprachformen verzichtet. Sämt-
liche Personenbezeichnungen gelten für
alle Geschlechterformen. Dies impliziert
keinesfalls eine Benachteiligung der je-
weils anderen Geschlechter, sondern ist
als geschlechtsneutral zu verstehen.

CONTACT US

Please do not hesitate to contact us. We will be glad to answer and provide further information to you at any time.

.....
Name

.....
First Name

.....
Department / Hospital

.....
Place

.....
Telephone

.....
E-Mail

.....
Date / Signature

Please contact me for further information

I would like to participate in the project

ADDRESS

German Society of Anaesthesiology and
Intensive Care Medicine
Ursula Homberg
Neuwieder Straße 9 | 90411 Nuremberg | Germany
Tel.: +49-911-9337828
Email: uhomberg@orphananesthesia.eu