Aktiv Druck & Verlag GmbH | ISSN 0170 - 5334 | 02330

www.ai-online.info

63. Jahrgang | Juli / August 2022

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)

Pallister-Hall syndrome

Paroxysmal nocturnal haemoglobinuria

orphan anesthesia

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

SUPPLEMENT NR. 10 | 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.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

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

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 recommenations 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.

Find a survey of the recommendations published until now on:

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

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

DGAI
Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin
www.dgai.de

A&I
ANÄSTHESIOLOGIE & INTENSIVMEDIZIN
www.ai-online.info

orphananesthesia
a project of the German Society of Anaesthesiology and Intensive Care Medicine
www.orphananesthesia.eu

orphananesthesia

Anaesthesia recommendations for

Paroxysmal nocturnal haemoglobinuria

Disease name: Paroxysmal nocturnal haemoglobinuria (PNH)

ICD 10: D59.6

Synonyms: Marchiafava-Micheli disease

Disease summary: Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired clonal haematopoietic stem cell disease caused by somatic mutations in the PIGA gene (Xp22.1), encoding a protein involved in the biosynthesis of the glycosylphosphatidylinositol (GPI) anchor. The mutation occurs in one or several haematopoietic cells and leads to a lack (total or partial) of all GPI-anchored cell membrane proteins (the most important being CD55 and CD59). PNH had a prevalence of up to 1.6/100,000, a 5-years mortality about 35 % and a median survival of 10–5 years. After bone marrow transplant, the majority of deaths occur within the first years of transplantations while the probability to survive at 2 years is 56 %. Symptoms and complications of PNH are caused by the deficiency of CD55 and CD59, proteins regulating and stabilising the complements cascade, on PNH erythrocytes. The lack of CD55 and CD59 is responsible for a complement mediated intravascular haemolysis mainly associated to haemoglobinuria, thrombosis and bone marrow failure. Furthermore, cell-free plasma haemoglobin in PNH leads to depletion of nitric oxide causing smooth muscle dystonia and altering the vascular tone. For these reasons, in a clinical context, haemolysis of PNH is associated with anaemia, weakness, dyspnoea, fatigue, renal impairment, need for transfusions, pulmonary hypertension, abdominal pain and thromboembolic complications.

The main anaesthetic concerns in PNH consist in preventing the activation of complement cascade during the peri-operative period. Any stressful situations may activate or exacerbate the complement cascade.

An optimal peri-operative management of patients with PNH includes the use of eculizumab, a novel antibody blocking the terminal complement cascade, blood cells transfusion and antibiotic prophylaxis, the avoidance of hypoxaemia, acidosis, dehydration and drugs known to activate complement cascade.

▶ **Citation:** Vargas M, Servillo G: Paroxysmal nocturnal haemoglobinuria. Anästh Intensivmed 2022;63:S248–S256. DOI: 10.19224/ai2022.S248

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

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

Typical surgery

Literature review is limited to case reports of PNH patients presenting cholecystectomy, Caesarean section, coronary artery bypass, cardiac valve repair and peripheral vascular surgery.

PNH patients have an increased risk of venous and arterial thromboembolic complications or haemorrhages in different organs and systems of the body, so surgical and/or invasive procedure may take place in these situations.

Type of anaesthesia

Literature reported case reports about the use of general anaesthesia for different surgical procedure in PNH patients. General anaesthesia in PNH patients must eliminate the stress response to surgical stimuli, achieving a deep anaesthetic and analgesic level.

General anaesthesia in PNH patients should avoid or minimise:

1) complement activation
2) hypoxaemia
3) acidosis
4) dehydration.

Regional anaesthesia may be difficult to apply in PNH patients depending on their degree of thrombocytopenia and their need of immediate anticoagulation in case of acute exacerbation of this disease or thromboembolic complications.

Necessary additional pre-operative testing (beside standard care)

PNH is associated to aplastic and/or iron-deficiency anaemia, haemolysis and thrombosis. Patients should have full blood count, coagulation screening including d-dimers, blood chemistry test including LDH, electrolytes, kidney and liver function. LDH is a very good parameter to estimate the ongoing haemolytic activity. A urine test is helpful to assess the presence of an active haemoglobinuria. An analysis of complement components, as C3 and C4, might be useful to evaluate the basal complement activity before the surgical procedure.

PNH is associated with cerebral, abdominal, pulmonary and liver complications due to its pathogenesis. As a result, further investigations will be needed in case of previous complications or focused symptoms. For example, in case of recurrent abdominal pain or thrombosis of abdominal vessels, a (duplex) ultrasound evaluation of the site should be done. In case of suspected or confirmed pulmonary hypertension, more specific tests to assess functional or haemodynamic impairment is required (BNP, echocardiograph).

Particular preparation for airway management

Difficult swallowing and breathing may appear during haemolytic crisis in PNH patients.

Literature has not reported cases of difficult airway management in PNH.

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

The main concern about the airway management in PNH patients is to apply a good analgesia to prevent the stress response to endotracheal intubations.

However, if a difficult airway is suspected, a protocol according to national and international guidelines should be applied.

Particular preparation for transfusion or administration of blood products

PNH patients required blood transfusions due their state of anaemia. After transfusions haemolysis may occur in PNH patients when using ABO incompatible plasma or prolonged storage of blood cells, although with lower incidence.

Washing blood transfusions could be avoided by using group-specific fresh blood and blood products. However, if patients need a large volume of blood within a short period of time, e.g. in case of acute bleeding or emergency situations, the role of washed red cells needs to be reconsidered.

Particular preparation for anticoagulation

Prophylaxis with heparin or LMWH should be used during the peri-operative period. Aggressive anticoagulation with heparin or LMWH in combination with eculizumab should be used in an acute thrombotic episode. However, when the platelet count is less $10x10^9$/L, anticoagulation is contraindicated while it should be used with a platelet count greater than $50x10^9$/L. In patients with platelet counts between 30 and $50x10^9$/L, a reduced dose of LMWH is probably appropriate.

Particular precautions for positioning, transportation and mobilisation

Not reported.

Interactions of chronic disease and anaesthesia medications

Eculizumab, a human monoclonal antibody approved by the US Food and Drug Administration and EMA, which binds C5 preventing its activation to C5b and thereby inhibiting MAC formation, is used as a standard treatment of symptomatic PNH.

For PNH patients chronically treated with eculizumab, surgery should be planned right after the last infusion of eculizumab (e.g. next day). Eculizumab administration during the peri-operative period may give a better control of complement activity. This monoclonal antibody may elicit synergistic effects on complement regulation, however, it has no direct effect on the pharmacokinetics and pharmacodynamics of anaesthetic drugs. It is suggested that the reduction of complement levels in the peri-operative period may be due to a synergistic effect of anaesthetic management and monoclonal antibody therapy. Extra dosing of eculizumab should be considered for PNH patients with breakthrough haemolysis/uncontrolled haemolysis.

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

Anaesthetic procedure

Antibiotic prophylaxis could be administered before starting surgery. For general anaesthesia, propofol in lipid emulsion is suitable for induction because it is not associated with complement activation. Since haemoglobinuria is frequently associated to dark colour urine, long-time infusion of propofol causing urine discoloration should be discouraged in PNH patients. Sevoflurane should be suitable for anaesthesia maintenance because it showed that this volatile anaesthetic significantly reduces complement activation and the levels of complement fragment. N_2O should be avoided because of its myelosuppressive effects. Analgesia during surgery may be obtained with remifentanil TCI or intermittent fentanyl with the aim to firmly reduce the stress response to surgical stimuli. Neuromuscular blockade should be considered using drugs with a lower rate of cross-reactivity and anaphylaxis. Accurate fluid management should be obtained with crystalloids, avoiding colloids because of their effects on complement activation.

Particular or additional monitoring

Bispectral index or other non-invasive cerebral monitoring may be useful to assess the level of anaesthesia.

Neuromuscular relaxation monitoring using patterns of electrical nerve stimulation such as train-of-four, tetanic or post-tetanic count, double burst stimulation, are controversial in PNH because their continuous or alternate stimulation may trigger complement activation. Furthermore, it is better to evaluate neuromuscular relaxation by means of a clinical or capnographic curve.

When needed according to the level of surgical risks, it is better to use noninvasive monitoring instead of invasive monitoring to avoid further complication from complement and coagulation activation.

The analysis of haemolytic parameters, especially LDH levels and haemoglobin, is useful to evaluate the haemolytic and complement activity during surgery.

Possible complications

Haemolytic crisis and -aemia, haemoglobinuria, infection, thromboembolic complication, acute bleeding may complicate the post-operative period.

Post-operative care

Post-operative analgesia is needed to avoid post-operative pain. Pain may be treated with NSAIDs and opioids according to pain levels and patient characteristics.

A urine test after surgery is needed to assess possible haemoglobinuria.

Analysis of LDH levels is useful to evaluate the level of haemolysis and complement activity after the surgical procedure.

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

Full blood count and coagulation screening including d-dimers are useful to check for any possible exacerbation of anaemia, infection and thrombosis.

Disease-related acute problems and effect on anaesthesia and recovery

Fulminant haemolysis, thrombosis of abdominal vessels, deep vein thrombosis, pulmonary embolism, sinus-vein thrombosis, meningococcal infection during eculizumab treatment.

Ambulatory anaesthesia

Ambulatory anaesthesia should be done in non-symptomatic and well-controlled PNH patients in low-risk surgery, in spite of which the patients should be protected against all causes of complement activation such as pain, anxiety, infection, radiocontrast agents, etc.

Obstetrical anaesthesia

Pregnancy is possible for women with PNH, but it is potentially hazardous for mother and infant. Pregnancy in PNH patients is risky and leads to complications such as cytopenia, transfusion dependency, thrombosis, need of anticoagulation, eculizumab treatment and immunosuppression (for cytopenia due to bone marrow failure).

Literature reported cases of Caesarean section in PNH patients treated with general or regional anaesthesia. The choice of the type of anaesthesia must take into account the risk of acute bleeding, coagulation disorders and the need of a high dose of anticoagulation in PNH thrombocytopenic patients.

Vaginal delivery is still possible in PNH patients, but the analgesic administration by epidural catheter must consider the risk of anticoagulation dosage and coagulation disorders. Literature reported a case of vaginal delivery in which a regimen of regular pethidine injections was used to minimize labour stress.

Blood transfusion, anticoagulation and eculizumab may reduce the risk and complications of fulminant haemolysis and thrombosis.

A close control of blood counts, coagulation screening including d-dimers and a clinical evaluation should be performed after delivery to prevent and reduce further complications. Need for anticoagulation is recommended during pregnancy and at least 6 weeks postpartum.

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

References

1. Pu JJ, Brodsky RA. Paroxysmal nocturnal hemoglobinuria from bench to bedside. Clin Transl Sci 2011;4:219–224
2. Vargas M. Lallo C. Marra A. Servillo G. Anaesthesia and orphan disease: Laparoscopic cholecystectomy with paroxysmal nocturnal hemoglobinuria and human mAb therapy. Eur J Anaesthesiol 2013;30:770–772
3. Lee JW, Jang JH, Lee JH, et al. Clinical symptoms of haemolyses are predictive of disease burden and mortality in Asian patients with paroxysmal nocturnal hemoglobinuria. Haematologica 2010;95:506
4. Hillmen P, Modupe E, Kelly R, et al. Long-term effect of the complement inhibitor eculizumab on kidney function in patients with paroxysmal nocturnal hemoglobinuria. Am J Hematol 2010;85:553–559
5. Smith LJ. Paroxysmal nocturnal hemoglobinuria. Clin Lab Sci 2004;3:172–177
6. Lindorfer MA, Pawluckowycz AW, Peek EM, et al. A novel approach to preventing the hemolysis of paroxysmal nocturnal hemoglobinuria: Both complement-mediated cytolysis and C3 deposition are blocked by a monoclonal antibody specific for the alternative pathway of complement. Blood 2010;115:2283–2293
7. Parker C. Eculizumab for paroxysmal nocturnal haemoglobinuria. Lancet 2009;373:759–767
8. Ogin GA. Cholecystectomy in a patient with paroxysmal nocturnal hemoglobinuria: Anaesthetic implications and management in the perioperative period. Anesthesiology 1990;4:761–764
9. Brustolin S, Giugliani R, Felix M. Genetics of homocysteine metabolism and associated disorders. Braz J Med Biol Res 2010;43:1–7
10. Den Heijer M, Lewington S, Clarke R. Homocysteine, MTHFR and risk of venous thrombosis: A meta-analysis of published epidemiological studies. J Thromb Haemost 2005;3:292–299
11. Shay H, Frumento RJ, Bastein A. General anesthesia and methylenetetrahydrofolate reductase deficiency. J Anesth 2007;21:493–496
12. Doenicke A, Lorenz W, Stanworth D, et al. Effect of propofol on histamine release, immunoglobulin levels and activation of complement in healthy volunteers. Postgrad Med J 1985;61:15–20
13. Allen TK, George RB, Olufolabi AJ, et al. The management of caesarean delivery in a parturient with paroxysmal nocturnal hemoglobinuria complicated by severe eclampsia. Can J Anesth 2007;54:646–651
14. Winterhalter M, Brandl K, Rabe-Meyer N, et al. Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanil infusion to intermittent fentanyl. Eur J Anesth 2008;25:326–335
15. Warltier DC, Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy. Anesthesiology 2006;104:835–846
16. Pu JJ, Brodsky RA. Paroxysmal nocturnal hemoglobinuria from bench to bedside. Clin Transl Sci 2011;4:219–224
17. Rosse WF, Nishimura J. Clinical manifestations of paroxysmal nocturnal hemoglobinuria: Present state and future problems. Int J Hematol 2003;77:113–120
18. Bjorge L, Ernst P, Haram OK. Paroxysmal nocturnal hemoglobinuria in pregnancy. Acta Obstet Gynecol Scand 2003;82:1067–1071
19. Roeth A, Duehrsen U, Schrezenmeier H, Schubert J. Paroxysmale nächtliche Haemoglobinurie (PNH) – Pathogenese, Diagnostik und Therapie. Dtsch Med Wochenschr 2009;134:404–409

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

20. Roeth A, Duehrsen U: Treatment of paroxysmal nocturnal hemoglobinuria in the era of eculizumab. Eur J Haematol 2011;87:473–479

21. http://www.dgho-onkopedia.de/de/onkopedia/leitlinien/paroxysmale-naechtliche-haemoglobinurie-pnh

22. Hill A, Kelly RJ, Hillmen P. Thrombosis in paroxysmal nocturnal hemoglobinuria. Blood 2013;121:4985–4996

23. Kelly R, Arnold L, Richards S, Hill A, Bomken C, Hanley J, et al. The management of pregnancy in paroxysmal nocturnal haemoglobinuria on long-term eculizumab. Br J Haematol 2010;149:446–450

24. Hillmen P, Muus P, Dührsen U, Risitano AM, Schubert J, Luzzatto L, et al. Effect of the complement inhibitor eculizumab on thromboembolism in patients with paroxysmal nocturnal hemoglobinuria. Blood 2007;110:4123–4128

25. Carrier M, Lazo-Lagner A, Shivakumar S, Tagalakis V, Gross PL, Blais N, et al. Clinical challenges in patients with cancer-associated thrombosis: Canadian expert consensus recommendations. Curr Oncol 2015;1:49–59.

Date last modified: **September 2015**

This recommendation was prepared by:

Authors

Maria Vargas, Department of Anaesthesia and Intensive Care Medicine, University of Naples Federico II, Naples, Italy
Vargas.maria82@gmail.com

Giuseppe Servillo, Department of Neuroscience and Reproductive and Odontostomatological Sciences, University of Naples Federico II, Naples, Italy

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

This recommendation was reviewed by:

Reviewers

Alexander Roeth, Department of Haematology, University Hospital Essen, Germany
Alexander.Roeth@uk-essen.de

Lazo Lagner, Department of Medicine, University of Western Ontario, Ontario, Canada
alejandro.lazolangner@lhsc.on.ca

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

Please note that this recommendation has not been reviewed by an anaesthesiologist and a diseases expert but by two disease experts instead.

© Anästh Intensivmed 2022;63:S248–S256 Aktiv Druck & Verlag GmbH

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

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) (inkl. 7 % MwSt.) 258,- €
  Schweiz 266,- €
  Rest der Welt 241,- €

  Mitarbeiter aus Pflege, Labor, Studenten und Auszubildende (bei Vorlage eines entsprechenden Nachweises)
  Europa (ohne Schweiz) (inkl. 7 % MwSt.) 94,- €
  Schweiz 90,- €
  Rest der Welt 94,- €

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

Die Beiträge aus der A&I finden Sie online unter: **www.ai-online.info**

Allgemeine Geschäfts- und Lieferbedingungen
Die allgemeinen Geschäfts- und Lieferbedingungen 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.**

Wichtiger Hinweis
Für Angaben über Dosierungsanweisungen und Applikationsformen kann vom Verlag und den Herausgebern keine Gewähr übernommen werden. Derartige Angaben müssen vom jeweiligen Anwender im Einzelfall anhand anderer Literaturstellen auf ihre Richtigkeit überprüft werden. Gleiches gilt für berufs- und verbandspolitische Stellungnahmen und Empfehlungen.

Allein aus Gründen der besseren Lesbarkeit wird auf die gleichzeitige Verwendung männlicher, weiblicher und weiterer Sprachformen verzichtet. Sämtliche Personenbezeichnungen gelten für alle Geschlechterformen. Dies impliziert keinesfalls eine Benachteiligung der jeweils 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
Roritzerstrasse 27 I 90419 Nuremberg I Germany
Tel.: +49-911-9337828
Email: uhomberg@orphananesthesia.eu