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# A&I

# ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

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## Anti-NMDA-receptor encephalitis

## Birt-Hogg-Dubé syndrome

orphanaesthesia

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

## SUPPLEMENT NR. 14 | 2023

## 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.

**Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:**

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## 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.

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orphananesthesia

# Anaesthesia recommendations for

# Anti-NMDA-receptor encephalitis

**Disease name:** Anti-NMDA-receptor encephalitis

**ICD 10:** G04.81 (Other encephalitis, myelitis and encephalomyelitis)

**Synonyms:** Anti-N-methyl-D-aspartate-receptor encephalitis, Anti-NMDAR encephalitis

**Disease summary:** Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is an autoimmune, neuroinflammatory process that is caused by antibodies against the NMDA-receptor 2A subunit in the central nervous system (CNS). While this is an aquired disease (either post-infectious or paraneoplastic), there may be a component of genetic vulnerability. Since the first paediatric case report in 2009, it has become the second most common cause of autoimmune encephalitis in children. Patients present with psychosis, neurologic deficits and seizures. There can be a progressive decline to decreased responsiveness, catatonia and paroxysmal sympathetic hyperactivity (PSH). Autonomic instability is a hallmark of the disease. Most children recover completely, but a small percentage are left disabled or die from cardiac arrhythmia. These patients almost always require anaesthesia during diagnostic workup and occasionally for therapeutic measures, such as excision of teratoma. The NMDA-receptor is also a common target for anaesthetic agents.

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**

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## Typical surgery

Imaging (MRI or CT), diagnostic lumbar puncture, placement of plasmapheresis catheter and excision of teratoma (if tumour is found) comprise the most common indications for anaesthesia.

The adult literature describes this disease as a paraneoplastic process in young women that is typically related to an underlying teratoma (mostly ovarian). The two largest paediatric studies reported that none of the paediatric patients had an associated tumour. This suggests that the pathogenesis of anti-NMDA receptor encephalitis may be different in children and adults. This may have implications for the indications of anaesthesia.

In older patients with high suspicion of an underlying tumour, anaesthesia may be indicated for long MRIs or tumour resection. In younger patients with low suspicion of a tumour, imaging modalities such as CT or ultrasound (US) can be utilised. Anaesthesia exposure time can be minimised or avoided with modalities such as CT or US and should be considered when choosing appropriate imaging.

## Type of anaesthesia

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

Regional or local anaesthesia can be provided. There are case reports of neuraxial anaesthesia and transverse abdominis plane blocks being performed without complication. Local anaesthetics inhibit nerve transmission by binding to voltage-gated sodium channels; they are devoid of NMDA-receptor activity.

There are multiple case reports of anti-NMDA-receptor encephalitis patients who underwent general anaesthesia with various agents. While there is insufficient evidence in the literature to recommend one anaesthetic technique over the other, there is consensus to avoid direct NMDA-receptor antagonists such as ketamine, nitrous oxide, methadone and tramadol. There do not appear to be published reports that describe the effects of direct NMDA-receptor antagonists in this population.

Volatile anaesthetics and propofol have indirect action on the NMDA-receptor. Propofol and inhalational agents (except nitrous oxide) have been used successfully in case reports and case series. Opioids, muscle relaxants, benzodiazepines, dexmedetomidine and local anaesthetics comprise the agents that are considered free of NMDA-receptor activity.

A case series on paediatric patients with this disease, who underwent general anaesthesia showed, that the majority of patients did not appear to have clinically relevant haemodynamic lability during the peri-operative period. There were no additional interventions necessary in paediatric patients, other than standard titration of anaesthetics.

## Necessary additional pre-operative testing (beside standard care)

Autonomic instability is a hallmark of anti-NMDA-receptor encephalitis. The small percent of patients who do not recover from this disease can suffer fatal arrhythmia. It is important to note pre-operative vital signs for paroxysmal sympathetic hyperactivity (tachycardia, hypertension, fever) and to assess disease severity. Pre-operative electrocardiogram might be indicated.



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## Particular preparation for airway management

The patients' age and symptoms, such as psychosis, may inhibit the patients' ability to cooperate. Patients with severe or late-stage anti-NMDA-receptor encephalitis can experience altered upper airway control and altered central control of breathing. There is no evidence that this disease is associated with increased difficulty masking or intubating. Patients with severe disease may have difficulty clearing secretions.

Face mask, nasal canula, LMA or endotracheal tube can be used for imaging or minor diagnostic procedures such as lumbar puncture. Airway choice depends on the respiratory condition, procedure and aspiration risk of the patient. The preoperative consciousness level should also be considered. For major procedures such as laparotomy, laparoscopy or central line placement, endotracheal intubation may be necessary.

## Particular preparation for transfusion or administration of blood products

There do not appear to be special considerations for transfusion or administration of blood products beyond standard care.

## Particular preparation for anticoagulation

There is no evidence to support the need for particular preparation for anticoagulation beyond standard care.

## Particular precautions for positioning, transportation and mobilisation

Not indicated or reported. Patients with neuropsychiatric symptoms may be combative or unable to cooperate with positioning and mobilisation.

## Interactions of chronic disease and anaesthesia medications

With the interplay of disease and anaesthesia on the NMDA-receptor, potential exists for the exacerbation of neurologic symptoms or paroxysmal sympathetic hyperactivity (PSH).

There seems to be a general consensus to avoid direct NMDA-receptor antagonists (ketamine, nitrous oxide, methadone, tramadol). Agents with indirect NMDA-receptor activity have been used successfully in this population (propofol, sevoflurane, desflurane, isoflurane). Opioids, muscle relaxants, benzodiazepines, dexmedetomidine and local anaesthetics are devoid of NMDA activity.

The effects of direct NMDA-receptor antagonists have not been studied.



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## Anaesthetic procedure

Anaesthesiologists should be prepared to manage paroxysmal sympathetic hyperactivity (PSH) that can be seen with this disorder. It would be prudent to have vasopressors, beta-blockers, antihypertensives and anticholinergics readily available to treat autonomic instability in a timely fashion. Neuraxial anaesthesia may avoid further NMDAR antagonism. While there is concern for neuraxial anesthesia in any patient with active encephalitis, there are case reports of its successful use.

## Particular or additional monitoring

These patients are at risk for arrhythmias, hypertension, hyperthermia and altered central ventilation. The standard ASA monitors are essential. Arterial line monitoring may be indicated for patients who are experiencing severe symptoms, PSH or who are undergoing major surgery. BIS monitoring could potentially be helpful in the titration of anaesthesia. However, some anti-NMDAR encephalitis patients have abnormal EEGs and the value of BIS monitoring in these patients is controversial. Cerebral oximetry has not been studied in this population, but its use can provide a target for the support of oxygen delivery to the brain.

## Possible complications

In a paediatric case series, there was one death within twenty-four hours of anaesthesia. That patient was experiencing fever, tachycardia and severe neuropsychiatric symptoms pre-operatively. Post-operatively, the patient experienced ventricular tachycardia followed by pulseless electrical activity.

There are a few case reports of adult patients who experienced severe bradycardia and required cardiac pacemaker placement over the course of their disease. The bradycardias were not related to anaesthetic exposure.

## Postoperative care

The presence of severe pre-operative symptoms may be a risk factor for perioperative complications due to the dysautonomia that can be seen in anti-NMDA-receptor encephalitis. Hypertension, tachycardia and dysthermia could be indications for postoperative admission and monitoring. Neurologic symptoms can also include decreased consciousness and central hypoventilation.

## Disease-related acute problems and effect on anaesthesia and recovery

As mentioned above.

According to a multi-institutional observational study on patients of all ages, 80–88 % of patients had good outcomes after 24 months. The long-term effect of anaesthesia on the disease process is unknown.



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## Ambulatory anaesthesia

Ambulatory anaesthesia should only be considered in patients with mild disease and no signs of paroxysmal sympathetic hyperactivity.

## Obstetrical anaesthesia

There are case reports of neuraxial anaesthesia being successfully performed for delivery and caesarean section.



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