orphanaesthesia

# Anaesthesia recommendations for

# Angelman syndrome

**Disease name:** Angelmann syndrome

**ICD 10:** Q93.5

**Synonyms:** (Happy) puppet syndrome

**Disease summary:** Angelman syndrome (AS) is a neuro-genetic disorder consisting of severe developmental delay, movement or balance dysfunction, a “happy demeanor” behavioral phenotype (frequent laughter/smiling, hand-flapping, etc.) and minimal or absent speech (with receptive and non-verbal communication skills more pronounced than verbal ones). Frequently (more than 80% of the time), AS is associated with microcephaly, seizures and an abnormal electroencephalogram (large amplitudes, slow spike waves, triphasic waves). Twenty to 80% of AS patients demonstrate clinical features such as tongue thrusting, prognathia, wide-spaced teeth, strabismus, scoliosis and fascination with water.

Clinically, AS in girls during early childhood can mimic the features of the Rett syndrome and in girls with one of these syndromes it may be difficult to differentiate one from another by clinical exam.

Genetically, AS is related to Prader-Willi syndrome as the two syndromes map to the same 15q11.2-13 chromosome region and both conditions are imprinted. However, the conditions are distinct genetically since AS is due to maternal disruption of the maternally-derived UBE3A gene while Prader-Willi syndrome is caused by disruption of multiple genomic elements on the paternally-derived chromosome. So the PWS gene is "switched off" on the maternally inherited chromosome 15. On the other hand, if the deleted area is maternal in origin, the paternal gene is switched off and the patient will have Angelman syndrome (AS).

Each syndrome, when caused by a chromosome deletion of 15q11.2-13 can also result in concomitant deletion of GABRA5, GABRB3 and GABRG3. Thus, production of the GABA receptor may be abnormal. These abnormal GABA receptors have been implicated in AS patient’s unpredictable responses to GABA agonists.

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Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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

## Typical surgery

Oral surgery; orthopaedic surgery (scoliosis); ophthalmology (strabismus) and otolaryngeal surgery.

## Type of anaesthesia

Abnormal GABA receptor dosage, and hypothetically also dysregulation of NMDA or AMPA receptors (related to disruption of UBE3A) may imply problems with the administration of some anaesthetic agents, but there is no conclusive evidence that any drug or hypnotic might be more appropriate than others. Thus, balanced anaesthesia and total intravenous anaesthesia have been utilized without untoward effects, although the duration of drug effects should be taken into account. The use of dexmedetomidine as a hypnotic substance in total intravenous anesthesia with intraoperative neurophysiological monitoring proved useful in one case report.

In principle, there is no contraindication to regional anaesthesia. However, because of these patients' developmental delays and often agitated behaviour, placement as well as assessment of success or failure of spinal or epidural anaesthesia is difficult. Also, scoliosis could make placement of an epidural catheter difficult.

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

If there is a history of bradycardia, cardiac function should be tested. In cases of severe or frequent epileptic seizures, a paediatric neurologist should be consulted. Coexisting diseases that might lead to perioperative complications have to be evaluated.

Communication with the patient's parents should be integrated right from the start, because verbal communication skills of the patients themselves are poor or nonexistent.

## Particular preparation for airway management

Anatomical facial and oropharyngeal abnormalities such as protruding tongue, overbite and prognathism occur in cases of AS and tend to increase with age. Their evaluation by the anaesthesiologist should be obligatory, but there is no proof that problems with intubation are to be expected.

## Particular preparation for transfusion or administration of blood products

Not reported.

## Particular preparation for anticoagulation

Not reported.

## Particular precautions for positioning, transportation and mobilisation

Not reported.

## Interactions of chronic disease and anaesthesia medications

Not reported.

## Anaesthetic procedure

There is no conclusive evidence that any drug or anaesthetic may be inappropriate.

When muscle relaxants are used, antagonization with anticholinesterase agents should be avoided because of the possibility of bradycardia. In case anticholinesterase agents have to be administered they always have to be accompanied with anticholinergic agents. Bradycardia has been described as potentially life-threatening. The use of sugammadex could cause bradycardia but seems feasible in principle.

## Particular or additional monitoring

Postoperative weakness should be prevented. Monitoring of neuromuscular blockade is recommended to ensure that antagonization with anticholinesterase agents is not necessary.

## Possible complications

Children with AS can experience syncope secondary to vagal hypertonia during laughing spells.

There are also 2 case reports describing AS patients experiencing severe bradycardia during surgery performed under general anaesthesia. Pretreatment with atropine or glycopyrrolate to prevent bradycardia during a procedure performed under general anaesthesia has been advocated by some authors; also bradycardia is not always sufficiently susceptible to atropine. To avoid elevation of the vagal tone, the indications for laparoscopy have to be evaluated carefully.

## Post-operative care

Intensive care is not mandatory. PACU length of stay of AS patients does not differ compared to other postprocedure patients. Degree of postoperative supervision depends on procedure and preoperative condition of the patient.

Because of the lack of verbal communication skills, the degree of postoperative pain has to be evaluated very carefully. The “happy” phenotype is potentially misleading for interpretation. Help of parents to decode pain, especially by recognizing the differential in agitation, is recommended.

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

Although seizures are frequently associated with AS, there is no evidence of problems with epilepsy caused by anaesthesia administered to AS patients.

The most significant life-threatening complication of an anaesthetized AS patient has been bradycardia due to vagal hypertonia which led to asystole with delayed response to atropine. But in both recent studies that were not single case reports (Berlin/Germany; Nashville, TN, USA), no case of bradycardia came about (total of 13 patients, 31 cases of anaesthesia).

Postoperative respiratory function can be depleted due to typical circumstances such as OSAS.

## Ambulatory anaesthesia

Ambulatory anaesthesia is possible according to common guidelines if the procedure itself does not afford a longer phase of supervision. This applies especially for oral surgery.

## Obstetrical anaesthesia

Not reported.

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