

## Anaesthesia recommendations for **Phelan-McDermid syndrome**

**Disease name:** Phelan-McDermid syndrome

**ICD 10:** Q93.5

**Synonyms:** 22q13.3 deletion syndrome, Chromosome 22q13.3 deletion syndrome, Deletion 22q13 syndrome. Monosomy 22q13.3.

**Disease summary:** Phelan-McDermid syndrome, 22q13 deletion syndrome, is a genetic condition caused by the deletion of the terminal end of chromosome 22 or mutation of the SHANK3 gene. The genetic changes that cause PMS vary from person to person and can occur from a de novo mutation or be inherited (autosomal dominant). Global developmental delay, intellectual disability of varying degrees, autism or autistic-like behavior, hypotonia, epilepsy, absent or severely delayed speech, gastroesophageal reflux, syndactyly, genitourinary abnormalities, brain structural abnormalities such as microcephaly, and distinctive facial features with possible tracheal stenosis may occur. Chromosomal microarray is the most common method for diagnosing Phelan-McDermid syndrome. Fluorescence in situ hybridisation (FISH) may detect larger deletions. If a diagnosis of Phelan-McDermid syndrome is suspected, but no deletion of 22q13 is detected through microarray, targeted DNA sequencing may detect mutations of the SHANK3 gene.

Mitochondrial abnormalities, specifically abnormalities in complex I and IV activity, may explain some phenotypic variation in PMS individuals.

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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](http://www.orpha.net)

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## Typical surgery

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Patients may present at different ages, for different types of surgeries/procedures and exams: such as magnetic resonance imaging, CT scans, otorhinolaryngology or plastic surgery, brainstem auditory evoked response (BAER) study, urology and dental surgery among many others.

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## Type of anaesthesia

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Each patient should be evaluated on an individual basis. The anaesthetic management of patients with Phelan-McDermid syndrome may be complicated by airway problems such as difficult laryngoscopy secondary to dysmorphic features (microcephaly, synophrys, midface hypoplasia, hypertelorism) and a possible high arched palate. Tracheal stenosis has been described. Gastroesophageal reflux and swallowing problems may be present. A careful evaluation and management of possible difficult airway should be planned. In the presence of a difficult airway, induction of anaesthesia with maintenance of spontaneous ventilation and tracheal intubation under safe conditions is highly recommended.

Patients with Phelan-McDermid syndrome usually present with global developmental delay, hypotonia and possible seizures. They commonly have an autistic-like behaviour (Mouthing/chewing and teeth grinding are common) with absent or severely delayed speech.

A decreased sensitivity to pain has been described in patients with Phelan-McDermid syndrome. Increased sensitivity to anaesthetics has been documented in animal studies of Phelan-McDermid syndrome genetic model. The choice and dosages of anaesthesia medications should be adjusted accordingly.

Patients with Phelan-McDermid syndrome may be predisposed to increased body temperature secondary to decreased perspiration. Special caution should be exerted in maintaining adequate hydration and normothermia. Careful positioning secondary to seizure risk should be applied.

A recent study suggests that mitochondrial dysfunction, as measured by abnormal electron transport chain complex activity, may affect a significant portion of individuals with PMS.

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

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The pre-operative examination should be thoroughly conducted to take into consideration concomitant issues. Baseline neurological/mental status and facial deformities should be assessed. Considerations prior to initiation of anaesthesia care are collecting information about the best approach to deal with the behavioural and communication issues. Evaluation of the airway and the presence of gastroesophageal reflux should be done pre-operatively. Patients with Phelan-McDermid syndrome may have cardiac and respiratory issues, as well as immunological problems. Baseline brain imaging for the presence of arachnoid cysts and attention to symptoms of possible increased intracranial pressure with evaluation by a neurologist may be recommended. Lymphoedema may appear in adolescence or adulthood. The presence of renal problems should be determined. Pre-operative evaluation should include the evaluation of possible associated kidney/urinary abnormalities.

Type, frequency and severity of seizures should be documented and treatment should be optimised pre-operatively. The tolerance to pain should be assessed as much as possible by interviewing the family or by reviewing previous medical records. Tendency to overheat and

decreased perspiration should also be documented as much as possible by interviewing the family.

Patients with PMS may be affected by mitochondrial dysfunction and anesthesia should be planned accordingly.

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### **Particular preparation for airway management**

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Careful evaluation for difficult tracheal intubation secondary to dysmorphic features. The presence of facial, mandibular deformities and possible tracheal stenosis may result in difficulty in mask ventilation and airway maintenance.

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### **Particular preparation for transfusion or administration of blood products**

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None reported.

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### **Particular preparation for anticoagulation**

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None reported.

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### **Particular precautions for positioning, transportation and mobilisation**

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Developmental delay, autistic-like behaviour may require help with mobilisation and transport. Prevention of risk of injury from seizures and careful positioning is indicated secondary to hypotonia.

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### **Interactions of chronic disease and anaesthesia medications**

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There are no known interaction between anaesthetic agents and patient's long term medication. However, special pharmacological considerations for this syndrome are related to possible involvement of vital organs/urological tract that may alter the clearance of medications. Decreased perspiration and overheating may also affect cardiac output and hydration status. Concomitant use of antiepileptic medications may induce the metabolism of some anaesthetic medications. Decreased sensitivity to pain/increased sensitivity to anaesthetics has been documented in animal studies of Phelan-McDermid syndrome genetic model. Careful titration of pain medications is recommended secondary to decreased sensitivity to pain.

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### **Anaesthetic procedure**

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Consideration and preparation for a possible difficult airway. Possibility of seizures.

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### **Particular or additional monitoring**

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Special precautions to be taken in titrating administration of medications, especially pain medications in view of coexistence of decreased sensitivity to pain with possible agitation secondary to behavioural problems.

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### **Possible complications**

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Special attention to the following points: Potential difficult airway/injury from agitation/hyperthermia from overheating. CNS (seizures); urinary problems. Over- or under-estimation of pain secondary to decreased sensitivity to pain with possible agitation secondary to behavioural problems and inability to communicate secondary to cognitive/speech delay. Possible mitochondrial dysfunction.

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### **Post-operative care**

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Documentation and stabilisation: Airway patency, haemodynamic stability.

Management of seizures, management of agitation and pain as described above.

Positioning secondary to hypotonia or agitation.

Prevention of thermal perturbations and hydration status secondary to decreased perspiration.

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

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Differential diagnosis includes syndromes associated with hypotonia, developmental delay, speech delay and/or autistic-like behavior (Prader-Willi, Angelman, Williams, Smith-Magenis, Fragile X, Sotos, FG syndrome, trichorhinophalangeal and velocardiofacial syndromes, autism spectrum disorders and cerebral palsy.

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### **Ambulatory anaesthesia**

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Each patient must be evaluated carefully for co-morbidity and/or airway issues. Anaesthesia and surgery have to be performed in a medical facility with capacity of taking care of potential complications.

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### **Obstetrical anaesthesia**

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No fertility studies that would exclude the possibility of reproduction have been performed. Females with Phelan-McDermid syndrome go through puberty and begin menstruation at the normal age. Anaesthesia and surgery have to be performed in a medical facility with capacity of taking care of potential challenges and complications.

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## Further information

- <https://omim.org/entry/606232>
- [https://www.orpha.net/consor/cgi-bin/Disease\\_Search.php?lng=EN&data\\_id=10630&Disease\\_Disease\\_Search\\_diseaseGroup=PhelanMcDermidsyndrome&Disease\\_Disease\\_Search\\_diseaseType=Pat&Disease\(s\)/group%20of%20diseases=Monosomy22q133&title=Monosomy%2022q13.3&search=Disease\\_Search\\_Simple](https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=10630&Disease_Disease_Search_diseaseGroup=PhelanMcDermidsyndrome&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group%20of%20diseases=Monosomy22q133&title=Monosomy%2022q13.3&search=Disease_Search_Simple)
- <https://rarediseases.org/rare-diseases/phelan-mcdermid-syndrome>
- Phelan-McDermid Syndrome Foundation (PMSF). [www.pmsf.org](http://www.pmsf.org)
- Asociación Española Phelan-McDermid. [www.22q13.org.es](http://www.22q13.org.es).

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

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