

# A&I

## ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

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**Systemic mastocytosis**

**Systemic onset juvenile idiopathic  
arthritis**

orphan**a**nesthesia

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

**SUPPLEMENT NR. 13 | 2021**

## 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](http://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](http://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:**

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# orphananesthesia

## Anaesthesia recommendations for Systemic onset juvenile idiopathic arthritis

**Disease name:** Systemic onset juvenile idiopathic arthritis

**ICD 10:** M08.2

**Synonyms:** SOJIA, systemic juvenile idiopathic arthritis, adolescent Still's disease, systemic JIA (juvenile idiopathic arthritis)

**Disease summary:** Systemic onset juvenile idiopathic arthritis is a rare form of JIA (juvenile idiopathic arthritis) with an incidence of 0.4–0.8 per 100,000 [1]. Juvenile idiopathic arthritis (JIA), as defined by the International League of Associations of Rheumatologists, comprises various childhood arthritides of unknown cause in children less than 16 years of age and lasting for at least 6 weeks. Systemic onset JIA is a disease characterised by repetitive disease flares, with remissions in the interim.

The usual age at presentation is between 1–6 years with equal sex incidence. Systemic symptoms like fever, rash and lymphadenopathy could precede the development of arthritis. Other extra-articular manifestations [3] include anaemia, and inflammation of the pleura, pericardium or the peritoneum. One quarter of the cases develop severe destructive arthritis with time. The rash is typically transient, blanching macular or maculopapular; it occurs during the fever peaks.

It is classified as a subtype of juvenile idiopathic arthritis, with no sex bias or peak age at onset. Extraarticular features include daily spiking fevers, fleeting salmon-coloured macular rash, lymphadenopathy, hepatosplenomegaly and polyserositis. Persistent disease leads to severe growth impairment, in addition to the damage caused by steroid therapy. The main concern is the precipitation of macrophage activation syndrome (MAS) [4] by triggers like viral infections, drugs and external stresses. A systemic onset juvenile idiopathic arthritis is unique among childhood arthritides due to the association with the macrophage activation syndrome (MAS).

Both an infectious-pathogen-triggered and an auto-inflammatory aetiology have been proposed for SOJIA. Even though the disease triggers are unknown, SOJIA is driven by innate pro-inflammatory cytokines, perpetuated by synergy with endogenous ligands like S-100 proteins. The most important cytokine involved is interleukin-1 (IL1). Other cytokines involved include IL-6, M-CSF (macrophage colony-stimulating factor), tumour necrosis factor (TNF) and IL-18. Interleukin-1 has pleiotropic effects, with upregulation of its own transcription and other cytokines, stimulation of cartilage and bone destruction, as well as elevation of plasma proteins during SOJIA flare. Treatment with IL-1 and IL-6 inhibitors has been shown to be highly effective. Another pathogenetic explanation of SOJIA involves the alternative activation of monocytes and macrophages, with probable deficiencies of IL-10 and regulatory T cells.

► **Citation:** Hariharan U, Garg R: Systemic onset juvenile idiopathic arthritis. AnästH Intensivmed 2021;62:S283–S290. DOI: 10.19224/ai2021.S283

Mortality in SOJIA is related to complications of systemic inflammation (e.g., MAS and amyloidosis) and those due to immunosuppressive medications. In addition, SOJIA is complicated by limitations in functional outcome due to arthritis and long-term damage due to chronic inflammation.

Nearly 10 % of patients with active SOJIA are diagnosed with MAS, an acquired form of haemophagocytic lymphohistiocytosis (HLH). It is characterised by well-differentiated macrophages with haemophagocytic activity. It is a life-threatening condition presenting with persistent fever, pancytopenias, liver abnormalities, coagulopathy and central nervous system dysfunction. MAS resembles multi-organ dysfunction and shock. Laboratory features consist of liver function derangement (hepatobiliary dysfunction), abnormal coagulation profile, pancytopenia, hyperferritinaemia, and elevation of acute phase reactants.

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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

These patients can present for any kind of elective or emergency surgeries. Some common procedures include FESS (functional endoscopic sinus surgery) [5], adenotonsillectomy, septoplasty, ear grommet insertions, arthroscopies, biopsies and lymph node excisions. They can also present for emergency procedures like appendectomy, I&D (incision and drainage), trauma surgery and LSCS (lower segment caesarean section). The literature is sparse regarding anaesthesia and surgery for patients with SOJIA.

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### Type of anaesthesia

Usually, general anaesthesia is given for the common ENT (ear, nose and throat) procedures in these patients. Regional anaesthesia can also be given wherever indicated. There is no known contraindication for either general or regional anaesthesia, provided proper precautions are taken.

Anaesthesia should always be given when the child is in disease remission for elective surgeries. Pre-operative evaluation must be thorough, especially if the child also has a reactive airway disease and is on chronic steroid therapy. Intra-operatively, certain drugs like NSAID's (non-steroidal anti-inflammatory agents), atracurium and morphine (histamine releasers) must be avoided [6]. Post-operatively, care needs to be taken to prevent disease flare. Adequate corticosteroid coverage needs to be continued, along with humidified oxygen and patient warmer. Pain management needs to be effective with the judicious use of regional blocks, short-acting opioids like fentanyl or remifentanyl (if available) and paracetamol.

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

Laboratory investigations [7] in SOJIA reveal raised ESR (erythrocyte sedimentation rate), leukocytosis, thrombocytosis, raised serum ferritin levels and erythroid precursors in peripheral smears. When in remission, only the ESR may be raised. In contrast, the onset of MAS is associated with a sudden fall in ESR, elevated liver enzymes, hypofibrinogenaemia, hyperferritinaemia, raised triglyceride levels and pancytopenia (dramatic fall in platelet, erythrocyte and leukocyte counts). Bone marrow examination reveals haemophagocytosis. In suspected cases, CECT (contrast enhanced computed tomogram) of the abdomen may be done to evaluate the degree of hepatosplenomegaly and lymphadenopathy. Other pre-operative investigations are as for routine pre-anaesthetic evaluation.

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### Particular preparation for airway management

Patients with SOJIA may have cervical spine ankylosis with a fusion of both atlas and axis. They are prone to develop osteopenia [8] either because of the disease process or due to long-term steroid therapy. Special precautions must be taken during airway management to limit cervical spine extension. Pre-operative cervical spine X-ray (anteroposterior and lateral views) may be done in indicated patients. Use of advanced airway tools like intubating LMA (laryngeal mask airway) and videolaryngoscope is recommended for intubation in neutral head position. There is a possibility of laryngeal involvement in long-standing arthritis patients, as laryngeal cartilages are affected in both rheumatoid and osteoarthritis.

Laryngoscopy and patient positioning must also be gentle in these patients to avoid injury. The difficult airway cart must be checked and kept ready prior to airway manipulation.

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

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No specific preparation for transfusion or administration of blood products is required for patients with SOJIA. Nevertheless, allergy during transfusions has to be prevented at all costs, as they can trigger a flare of SOJIA during remission. Antihistaminics may be administered upon the slightest sign of an allergic reaction. In the event of coagulopathy complicating SOJIA, fresh frozen plasma (FFP) can be administered to tide over the crisis. In MAS, platelet transfusions may be required if the platelet counts drop below 20,000/microlitre. Whenever blood transfusions are required, leukocyte-poor blood is preferred.

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#### **Particular preparation for anticoagulation**

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Precautions for anticoagulation in SOJIA are the same as for other patients. The baseline coagulation profile must be done before initiation of treatment as coagulopathy can complicate SOJIA syndrome. For emergency surgeries, fresh frozen plasma (FFP) must be kept ready. Regional anaesthesia must be given cautiously in patients on anticoagulation. Standard ASRA (American Society of Regional Anaesthesia) guidelines [9] need to be followed during neuraxial blocks in patients on anticoagulants.

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

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The presence of arthritis in patients of SOJIA mandates that positioning during surgery is gentle and meticulous attention is paid to avoid neurovascular damage. Extremes of positioning required for certain surgeries (e.g. robotic surgery) [10] can cause neural impingement and musculoskeletal damage. Pressure points and bony prominences must always be padded during positioning and transport. Early mobilisation in the post-operative period is recommended. Pain relief must be good to facilitate mobility.

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

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Most of the SOJIA patients would be on NSAIDs or steroids or both. Immunosuppressants and biologics may be required for severe SOJIA or MAS. Anakinra (interleukin-1 receptor antagonist) is a promising drug for resistant cases [11]; tocilizumab (monoclonal anti-IL-6 antibody) is approved [12]. Long-term NSAID usage can lead to renal dysfunction and erosion of the gastric mucosa. It is preferable to avoid anaesthetic drugs which are solely dependent on the kidneys for excretion. Cis-atracurium [12] is the ideal muscle relaxant for these patients as it undergoes spontaneous Hoffman degradation in plasma and it does not cause histamine release. Vecuronium bromide may be administered if kidney function is normal. Anti-ulcer prophylaxis must be given in the perioperative period. Another important consideration in SOJIA patients subjected to the stress of anaesthesia and surgery is the chronic use of steroids. Corticosteroid supplementation [13] is mandatory in the perioperative period and its dose depends on the dose taken pre-operatively. If a patient is on immunosuppressants, then particular attention must be paid to complete asepsis. Serial

checks of blood counts may be done to exclude pancytopenia. Antibiotic coverage for surgery must be adequate to prevent nosocomial and other concurrent infections.

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#### Anaesthetic procedure

The anaesthetic procedure is standard as for any other patient apart from the avoidance of histamine releasers and diligent monitoring for complications. Strict asepsis must be followed during all anaesthesia procedures. Any airway handling (intubation and extubation) must be gentle. Care must be taken to avoid excessive cervical spine movements. Regional blocks can be given after ruling out coagulopathy. For epidural infusions, it is better to avoid morphine in view of histamine release. During general anaesthesia, atracurium as a muscle relaxant is avoided for the same reason.

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#### Particular or additional monitoring

In monitoring, special attention must be paid to temperature measurement, airway pressures and neuromuscular monitoring. To reduce anaesthesia awareness and to regulate the dose of inhalational agents, BIS (bispectral index) monitoring may be instituted. Otherwise, standard ASA monitors must be utilised in all cases, including those under MAC (monitored anaesthesia care). Patients need to be monitored for possible post-operative complications, especially MAS. Serial blood counts and ESR (erythrocyte sedimentation rate) may be done when indicated. Musculoskeletal injury must be prevented.

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#### Possible complications

Macrophage activation syndrome (MAS) is a life-threatening complication of SOJIA [14], characterised by persistent fever, hepatosplenomegaly, generalised lymphadenopathy, DIC (disseminated intravascular coagulation), central nervous system dysfunction and pancytopenia. The bone marrow typically shows haemophagocytic cells. The mainstay of treatment includes avoidance of triggers, institution of supportive measures, high-dose corticosteroid therapy and immunosuppressants (cyclosporine A). The major causes of death include acute respiratory distress syndrome and multi-organ failure. Its early recognition and treatment is indispensable for reducing morbidity and mortality. Some of the other rare complications [15] of SOJIA include pericarditis, pericardial effusion, myocarditis, endocarditis, vasculitis, hepatomegaly and coagulopathy.

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#### Post-operative care

Humidified oxygen must be provided to all patients in the post-operative period after recovery from general anaesthesia. Hypothermia and shivering must be prevented at all costs. Warm intravenous fluids and an external patient warmer must be utilised, apart from maintaining a warm ambient temperature. PONV (post-operative nausea vomiting) prophylaxis should be given. Early mobility is encouraged wherever possible and mechanical thromboprophylaxis can be utilised in all cases. Pain management is of great importance. Multimodal analgesia is preferred and intravenous morphine should be avoided. NSAIDs (non-steroidal anti-inflammatory agents) may be avoided in the presence of a reactive airway disease. Systemic paracetamol is sufficient analgesia for minor surgeries. Regional blocks, especially under

ultrasound guidance must be utilised whenever possible. Monitoring must be meticulous to look out for complications of SOJIA, especially MAS.

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

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Complications of SOJIA can present an emergency situation requiring prompt action. Of particular importance is the occurrence of MAS, which can have a downhill course if not detected and managed timely. Differential diagnosis [16] includes Still's disease, Samter's syndrome and other connective tissue disorders.

Other causes of chronic arthropathy must be excluded. These include systemic diseases that can mimic JIA (e.g. tuberculosis and neoplastic diseases), autoimmune diseases (e.g. systemic lupus erythematosus/SLE) and non-inflammatory disorders associated with chronic pain syndromes.

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#### **Ambulatory anaesthesia**

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Ambulatory surgery is possible in patients with SOJIA, provided there are no surgical contraindications and the procedure is done during the remission phase. The caregiver attending to the patient should be educated regarding the possible complications of SOJIA and immediately report to the health-care facility whenever necessary.

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#### **Obstetrical anaesthesia**

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There have been no reports of obstetric anaesthesia in patients with SOJIA in the literature. Nevertheless, both labour analgesia and anaesthesia for caesarean delivery can be safely administered, provided histamine releasers and triggers of SOJIA flare are avoided. Proper care must be taken in the post-operative period to look for possible complications, as the onset of MAS in these patients can be devastating. Other precautions taken for obstetric anaesthesia, like aspiration prophylaxis and avoidance of supine hypotension syndrome must be routinely followed.



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Date / Signature

Please contact me for further information

I would like to participate in the project

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