



Dr Jason Lam
The Dance Doctor
www.thedancedr.com.au | www.drjasonlam.com.au



Perioperative Management of Patients with Hypermobility, Mast Cell Activation Syndromes and Dysautonomia (the “Trifecta”)

This document aims to provide a brief background and supportive information for patients who have one or more of the following commonly co-morbid conditions: Hypermobility Spectrum Disorder (HSD)/Hypermobile Ehlers-Danlos Syndrome (hEDS), Dysautonomia (most commonly: Orthostatic Intolerances (OI), Orthostatic Hypotension (OH) and Postural Orthostatic Tachycardia Syndrome (POTS) and Mast Cell Activation Syndrome (MCAS).¹⁻⁶

Patients with these conditions often have had unsatisfactory experiences with healthcare, surgery and anaesthesia⁷ highlighting the need for a careful, individualised, trauma-informed approach that prioritises their needs, safety and autonomy. We are grateful for your consideration and expertise to help them have a positive experience.

Pre-operative considerations

- The patients are often complex and benefit from a coordinated, interdisciplinary team approach throughout the perioperative and rehabilitation period.
- There is a high prevalence of neurodivergence in this population^{5,8} and consideration should be made to tailor the perioperative care strategies to the individual.⁹
- Patients are often prescribed Low Dose Naltrexone in the range of 0.5mg - 10mg for pain,¹⁰⁻¹³ energy-limiting conditions^{14,15} and MCAS. Each hospital's policy varies, and patients may need advice around washout periods (usually 72 hours) or potentially increased analgesia needs.¹⁶

Hypermobility Spectrum Disorder, Hypermobile Ehlers-Danlos syndrome and other Connective Tissue Disorders.

These conditions are characterised by fragility and laxity in connective tissue. They are often multisystemic, with degrees of orthostatic intolerance that might not make formal POTS criteria, pain, small fibre neuropathy and other autonomic dysfunction.¹⁷ Surgical stabilisation can be successful, but hypermobile patients have higher rates of recurrent instability and poor wound healing and should not be approached as a 'typical patient'.¹⁸⁻²¹

Transfers:

Patients with hypermobility are at substantially greater risk of musculoskeletal injuries, subluxation and dislocations, particularly when under general anaesthesia and have loss of protective muscle tone.

- Where possible, please consider allowing the patient to position themselves on the operating table.
- If not possible, please take extra care in transfers and, if relevant, consider using their braces intraoperatively.
- Due to skin fragility, please consider extra padding and particular attention to positioning and pressure areas. Nursing staff should be made aware of the diagnosis of hypermobility and the importance of protecting the joints during transfers and patient positioning.^{22,23}
- Any joint may be an issue for any given patient; however, shoulders, neck, ribs, hips and knees are commonly problematic.²¹
- Please consider supporting under the knees with a pillow when supine, or between the knees if side-lying.

Intubation and Intraoperative Care:

Temporomandibular joint subluxation/dysfunction and cervical spine instability (particularly C0-C1) are common in the hypermobile population.

- Patients may not be aware of these issues.
- Please consider working up similarly to a rheumatoid arthritis patient and consider a difficult airway.^{24–26}
- No consensus has been reached regarding imaging, but dynamic X-rays would not be an unreasonable initial investigation if concern,^{24,27} although they may not be sensitive enough to find small degrees of increased motion.
- Fibreoptic intubation should be considered.^{25,28}
- Excessive and/or prolonged cervical extension can result in significant injury and post-operative morbidity.
- Consider a soft or hard collar (Aspen Vista/Miami J) for patients with known upper cervical symptoms or at high risk intra- and post-operatively. The collar may provide a visual reminder to the surgical and anaesthetic team for altered handling/positioning and provide support during muscle inhibition.²⁹
- Consider using the collar in the post-operative period, especially during transport home, as travel can be very provocative.
- Patients may suffer from easy bleeding/bruising. Consider the use of tranexamic acid or DDAVP²⁶.

Local Anaesthetic:

Individuals with HSD or EDS frequently experience resistance to local anaesthetics, such as reduced effectiveness or shorter duration of anaesthesia during medical and dental procedures.^{30,31}

While the exact mechanisms are still being investigated, potential factors include altered connective tissue affecting anaesthetic diffusion, variations in nerve cell sodium channels, and altered drug pharmacokinetics.

- Articaine and Bupivacaine appear to be 3-4 times more likely than lidocaine to achieve adequate anaesthesia.³⁰
- Regional or general anaesthesia may be considered as alternatives when local anaesthesia is insufficient.

Skin Closure:

Patients with connective tissue disorders are notable for poor wound healing and late dehiscence.^{19,20}

- Consideration should be made for dual-layer closure (with a long-lasting absorbable suture like PDS or Maxon), leaving the skin sutures longer than usual, and consideration of suturing through adhesive strips to minimise train-tracking/cheese wiring.^{28,32}
- Consider keeping Steristrips or Hypafix on for 6 weeks.
If there is an adhesive allergy, silicone-based dressings are often better tolerated.

Pain Relief:

- Up to 90% of patients with EDS suffer from chronic pain with moderate to severe impairment of daily function, with many possible pain generators implicated, from small fibre neuropathy,¹⁷ Chiari malformation, neuralgia, dystonia, thoracic outlet syndrome, etc.^{33,34}
- There is a significant overlap between neurodivergence and hypermobility^{5,8} and it should be recognised that pain presentation and experience in neurodivergent individuals may differ from what might be typically expected.^{35–37}
- Pain management may therefore be challenging, and early involvement of the pain team should be considered.
- Recognising the challenges, a case series from an experienced hypermobility centre has described an opiate free protocol that showed improved analgesia postoperatively.³⁸

Rehabilitation:

Post-operative physiotherapy/rehabilitation in individuals with symptomatic hypermobility requires tailored planning and extended timelines.³⁹

- In the early post-operative period, changes in diet/hydration, medication, poorly controlled pain and the effects of anaesthesia can delay mobilisation and discharge.
- Emerging evidence suggests that post-exercise soreness is heightened and recovery is slower in this population,⁴⁰ and tissue healing is often slower and of poorer quality when compared to the general population.⁴¹
- Additionally, individuals with hypermobility are often starting from a lower baseline of strength compared to age-matched controls⁴¹, further underscoring the importance of a gradual and individualised rehabilitation approach.

Antibiotic Choice

Patients with HSD, EDS, and other forms of connective-tissue disorders should avoid fluoroquinolone antibiotics (e.g., ciprofloxacin, levofloxacin) due to the increased risk of serious complications, including aortic aneurysm and dissection, tendon rupture, nerve damage, and spontaneous cervical artery dissection.^{42–44} These medications can exacerbate connective tissue fragility, worsening joint hypermobility and increasing the risk of musculoskeletal injury.

Mast Cell Activation Syndrome

Mast Cell Activation Syndrome (MCAS) is a condition involving the inappropriate activation of mast cells (rather than the classical understanding of a clonal proliferation of mast cells as seen in mastocytosis) with a vast, heterogeneous range of clinical presentations.^{45,46} Patients with MCAS are often reactive to many medications and commonly have adverse experiences during surgery.

- Anxiety and pain can be significant triggers for mast cell degranulation, and judicious use of an anxiolytic in the benzodiazepine class may be considered.
- Large temperature changes can also trigger mast cell degranulation; warmed blankets and managing the operative room temperature are helpful.
- Intraoperatively, some of the first signs of impending anaphylaxis/degranulation may be hives and skin changes and require vigilant surveillance.⁴⁷
- Preservatives in IV fluids and local anaesthetics have been described as triggers, so preservative-free preparations are preferable where possible.
- Histamine-releasing benzylisoquinolines (eg Atracurium, Mivacurium) and Nefopam should be avoided.
- Administer the patient's usual dose of H1 and H2 antihistamines and mast cell stabilisers in the morning if possible.

Dysautonomia

Patients may have dysautonomia such as OH, POTS, neurocardiogenic syncope or inappropriate sinus tachycardia. These may present as unsteadiness, presyncope, shortness of breath, anxiety, and loss of balance.¹⁷ Some patients will be symptomatic with reduced cerebral blood flow despite not meeting the formal diagnostic threshold.¹⁷

- Please consider screening for orthostatic intolerance (if not already established) as there is a significant comorbidity (89-90%) between symptomatic hypermobility and orthostatic intolerance/dysautonomia^{3,48,49} and MCAS.⁵⁰
- Establishing pre-operative lying and standing observation (HR, BP and SpO2) is best practice in dysautonomia^{51,52} and may assist in understanding the baseline haemostatic presentation and subsequent postoperative rehabilitation course.
- Patients may benefit from extra IV fluid pre/intra/post-operatively, especially with decreased oral intake.⁵³ Please take extra care with the patient transitioning from lying to sitting to standing to reduce risk of presyncope/syncope.
- Full-length compression/surgical tights may help.^{52,54}

Gastrointestinal

There is recognition that these conditions often have co-morbid gastrointestinal manifestations, with the American Gastrointestinal Association releasing a Clinical Practice Update Expert Review⁶. Disorders of Gut-Brain Interaction (DGBI) are common, as are gastroparesis and other motility disorders and should be considered in the perioperative setting.

Thank you for your consideration, expertise and care.



Dr Jason Lam

BMBS, DCH, MSports Med, FRACGP, Sports and Exercise
Physician Registrar
www.thedancedr.com.au



Australian EDS and HSD network, an Ehlers-Danlos Society
CORE Network of Excellence www.edsaustralia.com



Sharon Hennessey

B Pty (Hons)
Principal Physiotherapist and Core Lead
Not Just Bendy Hypermobility Services



Not Just Bendy Hypermobility Services, an Ehlers-Danlos
Society CORE Centre of Excellence www.notjustbendy.com
<https://hypermobilityproject.com/>

This document will be updated periodically. Please check the websites for the latest version.

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