MCAS - Considerations for Anesthesia / Surgery

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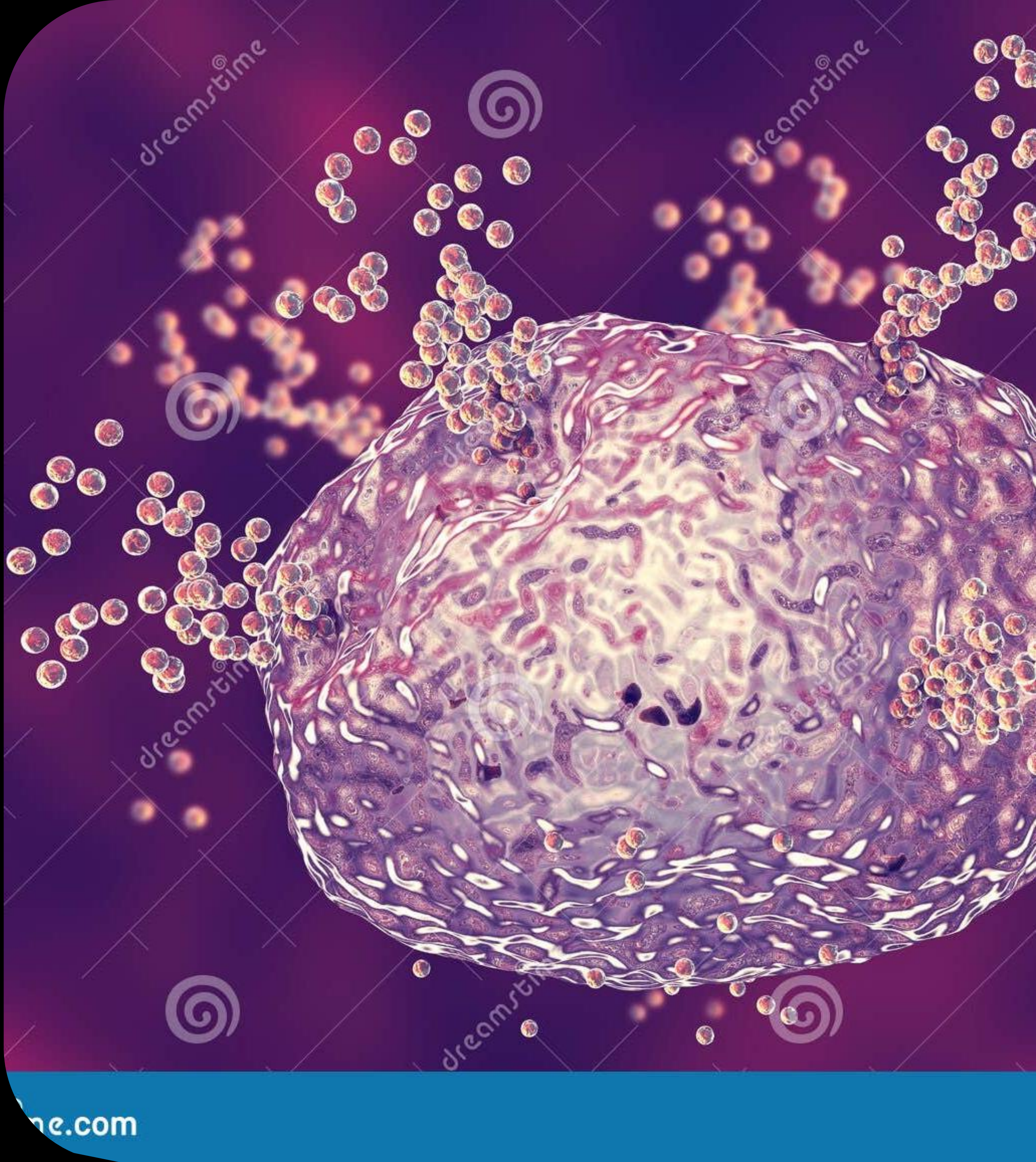
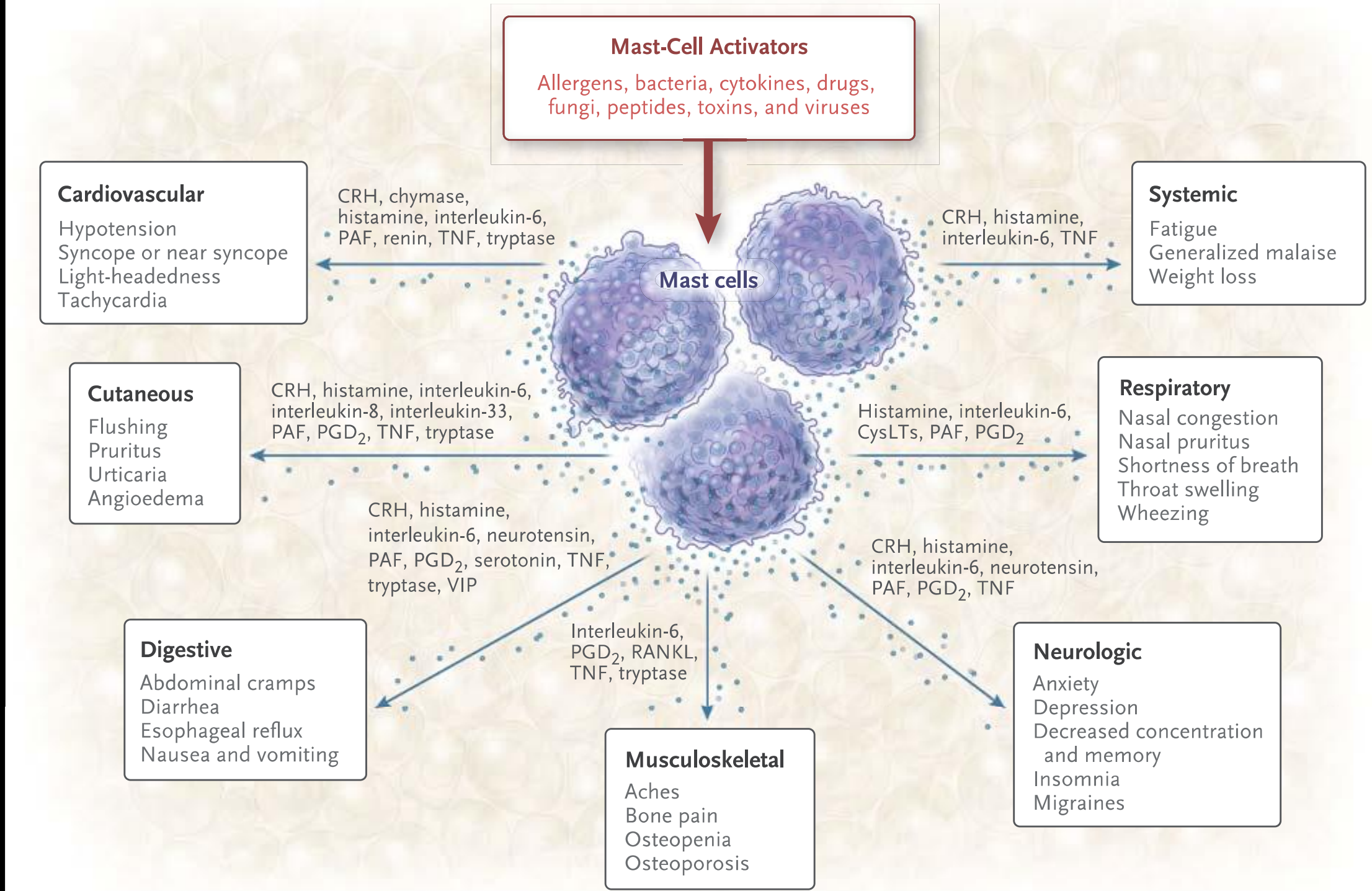
June 2025



Mast Cell Biology

- Mast Cells are Heterogeneous
  + No single mast cell produces all identified mediators, but each mast cell can release some or all of the mediators that it produces.
  + Somatic mutations drive activation (but not proliferation).
- Mast Cells are found in most tissues/organs in the body
  + They are found in higher concentrations in areas where they are in close contact with the environment (skin, airways, GI tract).
  + They are ideally placed to participate in the early recognition of pathogens and environmental toxins.


Mast-Cell Activators
Allergens, bacteria, cytokines, drugs, fungi, peptides, toxins, and viruses
Mast cells
Cardiovascular
Hypotension
Syncope or near syncope
Light-headedness
Tachycardia
CRH, chymase, histamine, interleukin-6, PAF, renin, TNF, tryptase
CRH, histamine, interleukin-6, TNF
Systemic
Fatigue
Generalized malaise
Weight loss
Cutaneous
Flushing
Pruritus
Urticaria
Angioedema
CRH, histamine, interleukin-6, interleukin-8, interleukin-33, PAF, PGD2, TNF, tryptase
Histamine, interleukin-6, CysLTs, PAF, PGD2
Respiratory
Nasal congestion
Nasal pruritus
Shortness of breath
Throat swelling
Wheezing
CRH, histamine, interleukin-6, neurotensin, PAF, PGD2, serotonin, TNF, tryptase, VIP
CRH, histamine, interleukin-6, neurotensin, PAF, PGD2, TNF
Digestive
Abdominal cramps
Diarrhea
Esophageal reflux
Nausea and vomiting
Interleukin-6, PGD2, RANKL, TNF, tryptase
Neurologic
Anxiety
Depression
Decreased concentration and memory
Insomnia
Migraines
Musculoskeletal
Aches
Bone pain
Osteopenia
Osteoporosis

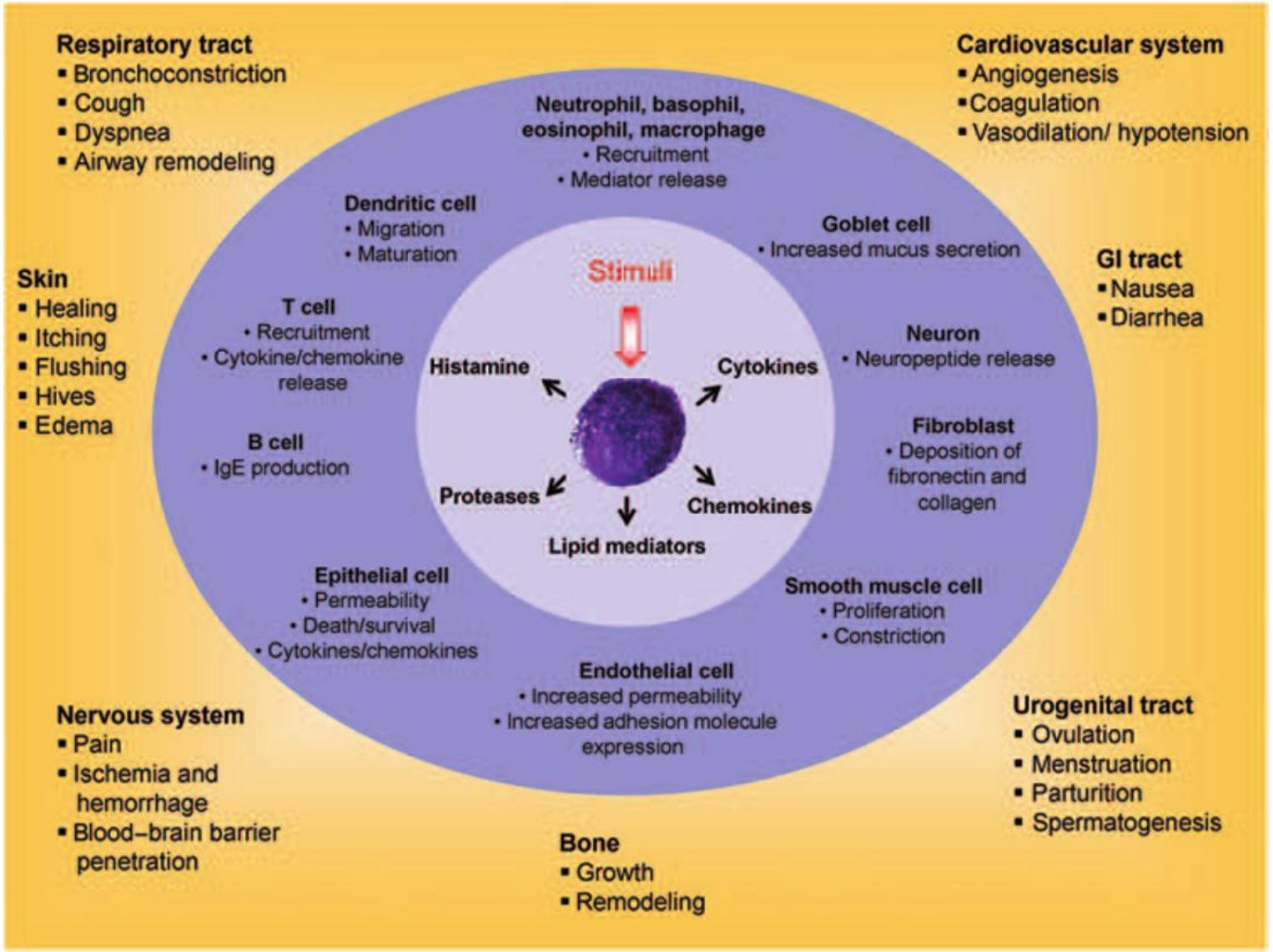


Figure 2 Mast cells (MCs) as effectors in homeostasis and disease. MCs in various tissue microenvironments are poised to respond to an array of stimuli by releasing numerous mediators. These regulate both physiological (e.g., wound healing, hair follicle cycling, angiogenesis, bone remodeling) and pathological process (e.g., allergic reactions) by influencing various cell types. Mechanisms of action of certain MC mediators on their targets maybe similar, but the outcome can differ depending on circumstances and site (e.g., wound healing vs. airway remodeling, or bronchoconstriction in airway vs. motility disturbances in intestine).

MCAS Presentation

- Age of onset: Usually under the age of 20, may be unrecognized for decades.
- Symptoms often are:
  - Inflammatory
  - Waxing/ waning vs. chronic vs. episodic
  - Inconsistent - different symptoms at different times of day or changing symptoms.
  - Provoked with/without identifiable trigger.

General Characteristics of MCAS Patients

An MCAS patient must have symptoms consistent with chronic MCA, which is abnormal at baseline and/ or reactive to triggers

An MCAS patient must have signs/ symptoms of aberrant MCA in at least two organ systems.

An MCAS patient must not have some other disease that better accounts for the full range of the observed symptoms/ signs.

International Archives of Allergy and Immunology

Original Paper

Int Arch Allergy Immunol 2015;167:47–56
DOI: 10.1159/000436969

Received: January 28, 2015
Accepted after revision: June 11, 2015
Published online: July 9, 2015

Management of Anesthesia in Adult and Pediatric Mastocytosis: A Study of the Spanish Network on Mastocytosis (REMA) Based on 726 Anesthetic Procedures

- MC mediator-related symptoms in adults 2%
- Anaphylaxis in adults 0.4%
- MC mediator-related symptoms in children 4%
- Anaphylaxis in children 2%
- Adult frequency significantly higher in those:
  + previously presented with anaphylaxis,
  + underwent major surgeries & GA,
  + not given prophylactic antimediator therapy (PAT) 1 h before the anaesthesia (H1/H2 antihistamines and benzodiazepines)

Conclusion: The frequency of perioperative anaphylaxis appears to be higher in mastocytosis patients than in the general population. Mastocytosis should not be a contraindication for anaesthesia since PAT and adequate anaesthetic management using the drugs with the safest profile appears to be effective in preventing/controlling MC mediator-associated symptoms.

Perioperative Management Goal = Prevention of Mast Cell Mediator Release

Pre-operative Considerations

- Consultant Anaesthetist Preoperative Assessment Clinic +/- Allergy/Immunology Clinci Advice
- Careful history taking of MCAS symptoms and triggers
- Anaesthetic logbook
- Excellent communication between the anaesthesia and surgical staff
- Identify potential operating room/anaesthesia/surgery triggers
- Continuation of regular MCAS medications up to the day of surgery
- Consideration of preoperative intravenous hydration.

Category	Medication	Purpose	Primary Care Prescribable?
H1 blockers	Cetirizine	Reduce histamine effects	Yes
H2 blockers	Famotidine	Manage gastric symptoms	Yes
Leukotriene blockers	Montelukast	Address leukotriene effects	Yes
Mast cell stabilisers	Sodium cromoglicate	Prevent mediator release	Yes
Mast cell stabilisers	Ketotifen	Prevent mediator release	Yes
Corticosteroids	Prednisolone	Reduce inflammation symptoms	Yes
Bioflavonoids	Quercetin	Natural mast cell stabilisers	OTC
Vitamins	Vitamin C, Vitamin D, Probiotics, Magnesium	Support stabilising mast cells, control histamine levels & histamine production	OTC
Emergency medication	Adrenaline	Anaphylaxis management	Yes
	Low Dose Naltrexone	Mast cell stabilisers	No *

Mast Cell
Activation Syndrome

Intra-operative Considerations

- Suggested premedication regimes: H1 and H2 receptor antagonists (12 hrs and 1 hour before procedure), leukotriene blockers, corticosteroids and benzodiazepines for anxiety reduction.
- Maintenance of a steady environmental temperature
- Minimizing friction & mechanical trauma (i.e. tape, tourniquet use, etc.)
- Careful positioning of the patient - possible osteoporosis or osteolysis
- Consider invasive haemodynamic monitoring intra-operatively and remain vigilant for signs of mast cell degranulation or anaphylaxis.
- Epinephrine should be immediately available.
- Regional techniques may be associated with a lower risk of MCAS symptoms.
- Surgical Safety Checklist Team Brief

Intra-operative Considerations - Drugs

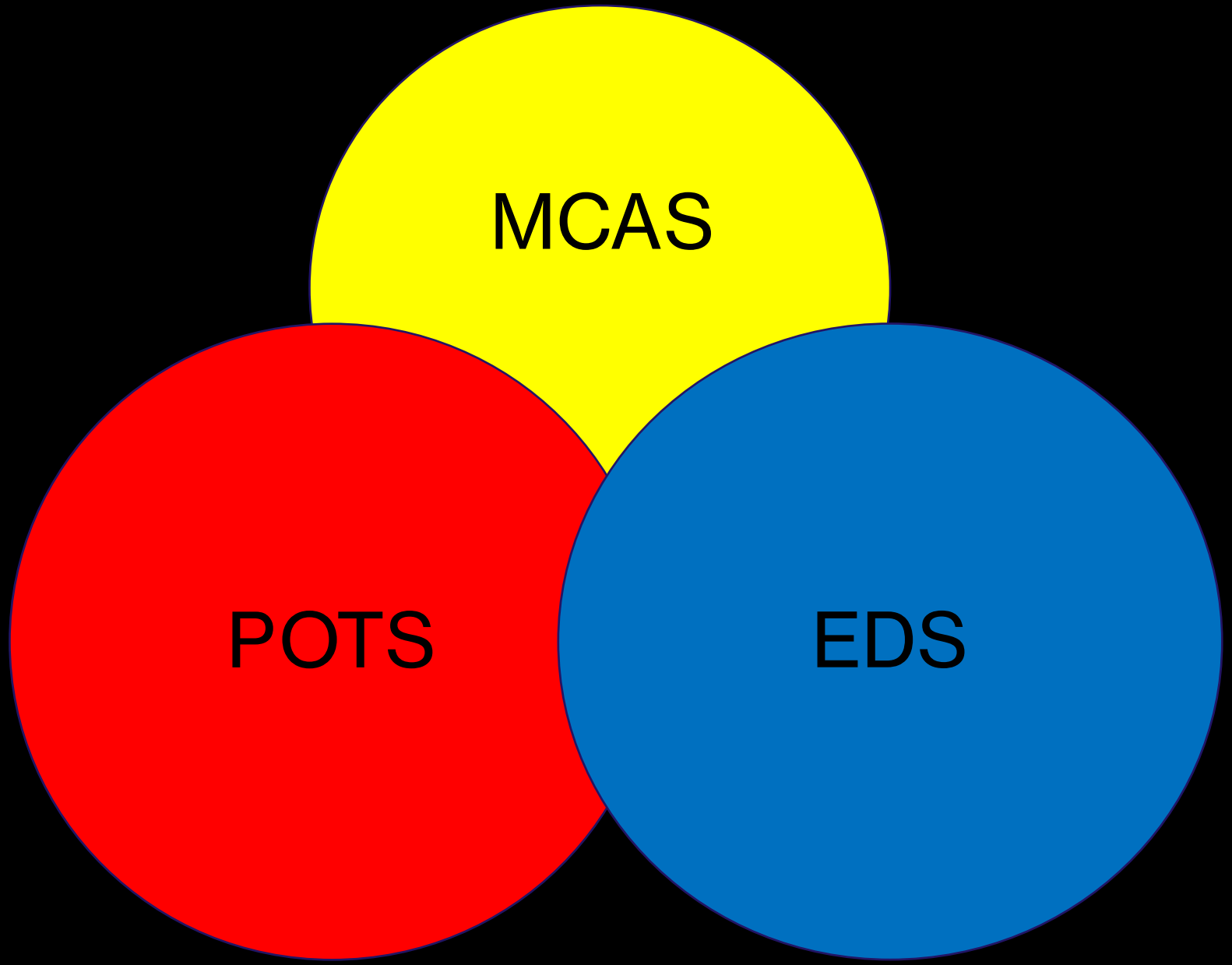
- Intravenous induction agents are generally considered safe (Propofol, Ketamine), except for thiopentone.
- Volatile anaesthetics appear well tolerated.
- Rocuronium, vecuronium and cisatracurium have shown the least mast cell activation, while mivacurium and atracurium generate the greatest mast cell activation. Suxamethonium does not generate histamine release, but is the primary cause of anaphylaxis, so best avoided in this group
- Synthetic opioids like fentanyl (PCA can be used postop) and remifentanil are preferred over morphine, pethidine, buprenorphine and codeine.

Intra-operative Considerations - Drugs

- No evidence to avoid amide-type LA: lidocaine, bupivacaine, ropivacaine, prilocaine. EMLA preferred to Ametop
- Paracetamol is safe, but NSAIDS/aspirin are variable.
- Anti-emetics safe
- Skin antiseptics: reactions are more common to Chlorhexidine than povidone iodine
- Penicillin's and cephalosporins carry the highest risk of anaphylaxis, followed by beta-lactams, vancomycin and quinolones.

Postoperative Considerations

- Extended post-operative monitoring
- Aggressive pain & PONV treatment
- Avoidance of known environmental triggers


MCAS
POTS
EDS

Authors: Wang, Edwin; Ganti, Tej; Vaou, Eleni; Hohler, Anna
Source: Allergy and Asthma Proceedings, Volume 42, Number 3, 1 May 2021, pp. 243-246(4)
Publisher: OceanSide Publications, Inc
DOI: https://doi.org/10.2500/aap.2021.42.210022

The relationship between mast cell activation syndrome, postural tachycardia syndrome, and Ehlers-Danlos syndrome

Results:

The percentage of MCAS within the group of POTS and EDS was 31% in comparison with 2% within the non-POTS and EDS group. The 95% confidence interval calculated for the MCAS in the POTS and EDS group did not overlap with 2%, which showed a statistically significant result. The odds ratio between the two groups was found to be 32.46.

Conclusion:

There was a marked percentage of MCAS among the patients with diagnoses of POTS and EDS.

ME/CFS GUIDE FOR PRIMARY CARE

INTRODUCTION

ME/CFS IS A COMPLEX MULTISYSTEM DISEASE THAT INVOLVES THE BRAIN, MUSCLE AND IMMUNE SYSTEM.

- It affects at least **250,000 people in the UK** and often has a significant impact on functional ability and quality of life.
- Around 25% of people are severely or very severely affected - meaning they are housebound and in some cases bedbound.
- This provides an overview of what to do in primary care and when to refer to secondary care - the information is based on the new NICE guideline on ME/CFS.

SUSPECT ME/CFS

- When a patient is failing to return to normal health after a viral infection - the commonest triggering factor.
- ME/CFS can also be triggered by vaccinations and other immune system stressors.
- In a minority there is no clear triggering event and symptoms develop gradually.

DIAGNOS

When the follo fluctuate in se or more and t

- Debilitating by minimal
- Post exertio exacerbatio exacerbatio or cognitive recovery pe
- Unrefreshing

CO-MORBID CONDITIONS

May include:

- Endometriosis
- Hypermobility
- Interstitial cystitis
- Irritable bowel syndrome
- Mast cell activation syndrome
- Migraine type headaches
- PoTS

IAGNOSIS

mples:
ddison's disease
romyalgia
ypothyroidism
epatitis C
fection
me disease
ultiple sclerosis
imary biliary
rrhosis
eep apnoea

ASSOCIATED SYMPTOMS

May include:

Central nervous system

- Alcohol intolerance
- Dysautonomia - postural orthostatic tachycardia syndrome/PoTS, cold hands and feet
- Fasciculations and myoclonic jerks
- Headaches
- Hypersensitivity to light, sound, touch and some medications
- Poor temperature control
- Pain - which can affect muscles, nerves or joints

Ear, nose and throat

- Tinnitus

Gastrointestinal

- Irritable bowel type symptoms

CO-MORBID CONDITIONS

May include:

- Endometriosis
- Hypermobility
- Interstitial cystitis
- Irritable bowel syndrome
- Mast cell activation syndrome
- Migraine type headaches
- PoTS

INVESTIGATIONS

The following investigations should always be checked, and reported as normal, before confirming the diagnosis:

- C-reactive protein and/or ESR
- Calcium and phosphate
- Coeliac screening
- Creatine kinase
- Full blood count
- HbA1C
- Liver, renal and thyroid function
- Serum ferritin
- Urea and electrolytes
- Urinalysis for blood, protein and glucose

Further investigation required in selected cases. Examples:

- **NASA lean test - if PoTS is suspected**
- **Vitamin B12**
- **9am serum cortisol for adrenal insufficiency**

CARE TEAM DO?

- Make an accurate and early diagnosis
- Believe and empathise with the way in which ME/CFS is impacting on all aspects of normal life
- Provide information and guidance on activity and symptom management in line with the updated NICE guidance on ME/CFS
- Help with benefits, disability aids, education, employment, social care
- Carry out regular monitoring and review.

ERVICES

- The NICE guideline on ME/CFS recommends that GPs should refer people with ME/CFS to a specialist ME/CFS service to confirm the diagnosis and provide a care and management programme.
- This should include a domiciliary service for people with severe or very severe ME/CFS.
- People with severe ME/CFS often experience difficulties with eating, swallowing and digestion and require expert guidance on nutritional support.
- The MEA website has a directory of all the UK ME/CFS referral services.

INFORMATION AND SUPPORT

The ME Association is one of the leading charities that provides information and support to people with ME/CFS and their carers – through the website, social media channels and ME Connect helpline and message service.

We provide a range of literature that is available as free downloads and using our medical education budget, we can supply free resources for healthcare professionals. Please scan the QR code for more information.

meassociation.org.uk

Helpline: 0800 538 5200

Registered UK Charity 801279

RCOA
Royal College of Anaesthetists

FACULTY OF PAIN MEDICINE

THE ME ASSOCIATION
me

Trusted Information Creator
Patient Information Forum

ME/CFS and anaesthesia

(myalgic encephalomyelitis or encephalopathy/ chronic fatigue syndrome)

Will my history of sensitivity to medications, chemicals and anaesthetic drugs be considered?

Canadian Journal of Cardiology 36 (2020) 357–372

Society Position Statement

Canadian Cardiovascular Society Position Statement on Postural Orthostatic Tachycardia Syndrome (POTS) and Related Disorders of Chronic Orthostatic Intolerance

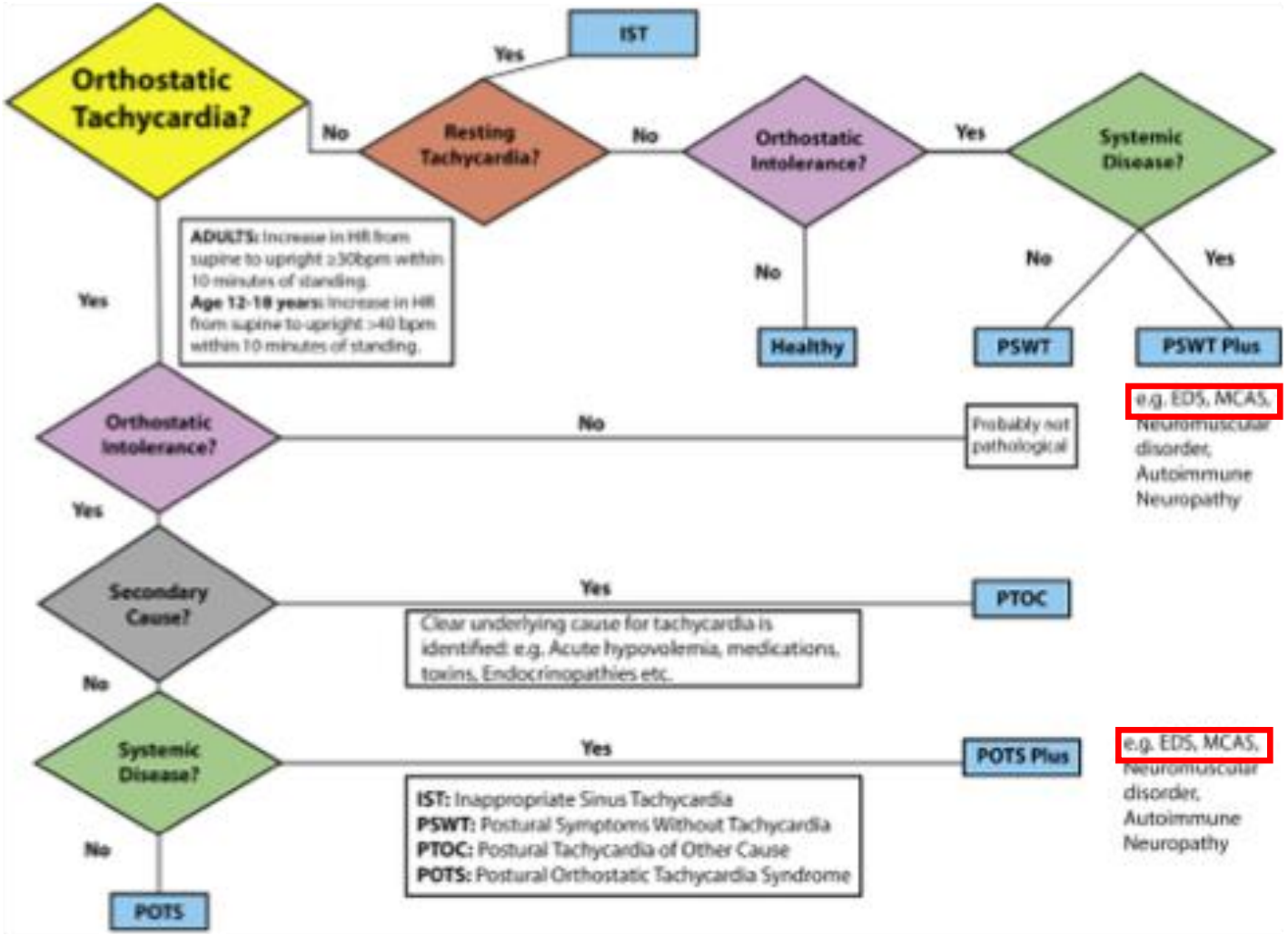
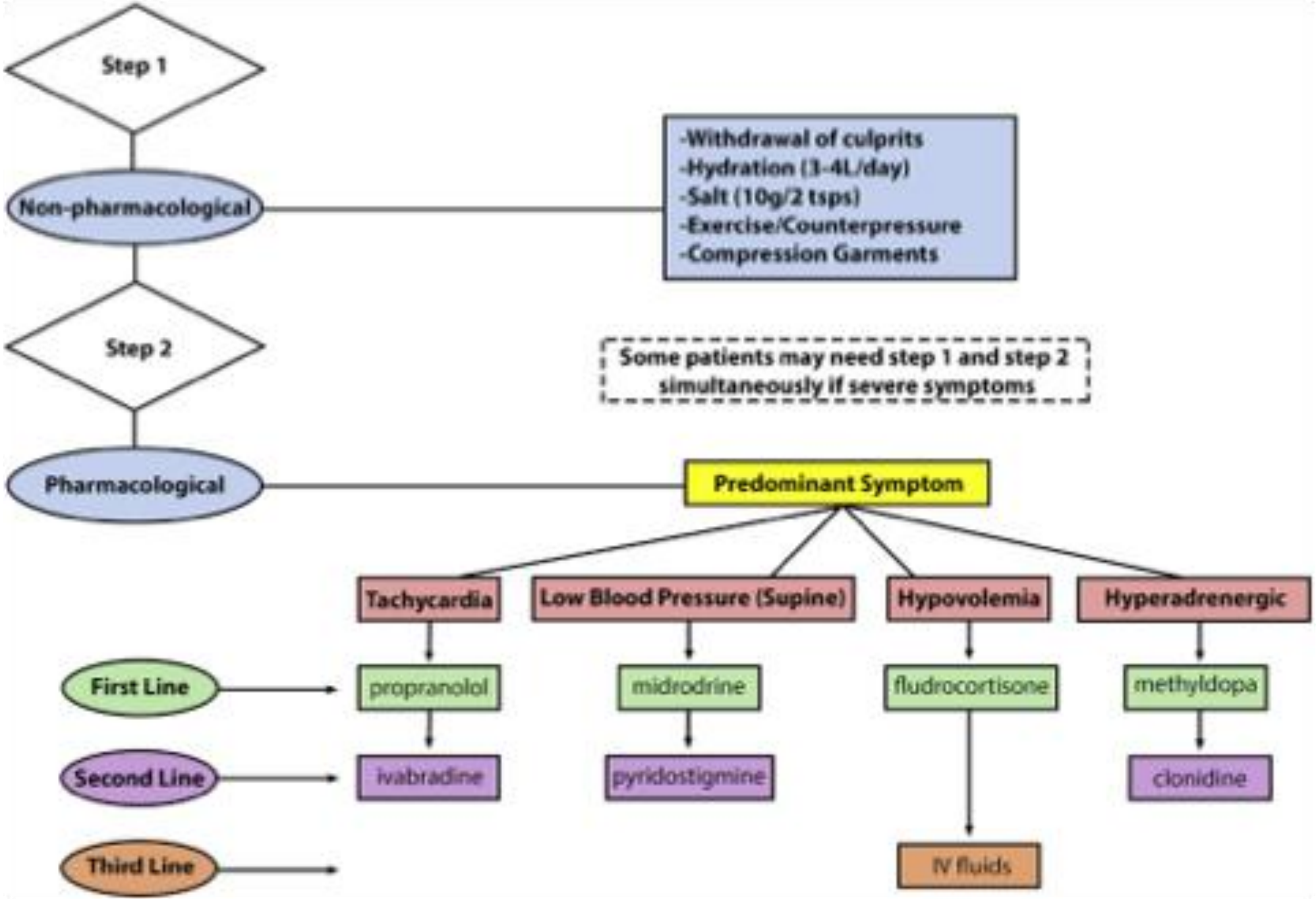


Table 4. Associated comorbid conditions seen in POTS plus

Comorbid condition	Prevalence
Chronic migraine/cerebrospinal fluid leak	40%
Hypermobile Ehlers-Danlos syndrome and hypermobile spectrum	25%
Chronic fatigue syndrome/myalgic encephalomyelitis	21%
Fibromyalgia	20%
Autoimmune disorders	16%
Mast cell activation disorder	9%
Celiac disease	3%

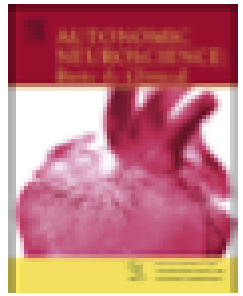

Step 1
Non-pharmacological
-Withdrawal of culprits
-Hydration (3-4L/day)
-Salt (10g/2 tsps)
-Exercise/Counterpressure
-Compression Garments
Step 2
Some patients may need step 1 and step 2 simultaneously if severe symptoms
Pharmacological
Predominant Symptom
Tachycardia
Low Blood Pressure (Supine)
Hypovolemia
Hyperadrenergic
First Line
Second Line
Third Line
propranolol
midrodrine
fludrocortisone
methyldopa
ivabradine
pyridostigmine
clonidine
IV fluids

Autonomic Neuroscience: Basic and Clinical 215 (2018) 119–120

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

journal homepage: www.elsevier.com/locate/autneu



Surgical and dental considerations in patients with postural tachycardia syndrome

Mohammed Ruzieh[a], Mark Dziuba[b], James P. Hofmann[c], Blair P. Grubb[c,*]

[a] Penn State Heart and Vascular Institute, Hershey, PA, USA
[b] University of Toledo, Toledo, OH, USA
[c] University of Toledo Medical Center, Toledo, OH, USA

Perioperative Management POTS

- Continue baseline POTS medication morning of surgery
- Monitor signs of adrenal insufficiency if on chronic Fludrocortisone
- Highly symptomatic patients with significant orthostatic BP changes - midodrine can be given while supine - takes about > 30 min to have any effect on BP
- Prevent prolonged hypotension – uncomplicated surgery 2- 3L fluid
- Persistent hypotension 1st line selective alpha 1 agonists – Phenylephrine/Metaraminol
- Avoid combined alpha-beta agonists
- Alternative is vasopressin analogues

Perioperative Management POTS

- No evidence to support 1 anaesthetic agent over another & no form of anaesthesia found superior
- Caution epinephrine in LA's
- Post-operatively, causes of tachycardia such as hypovolemia, anaemia, hyperthermia, pain, anxiety, or pulmonary embolism should be considered and treated in the appropriate clinical settings – DO NOT ASSUME IT IS ONLY DYSAUTONOMIA
- Orthostatic checks in PACU
- No need for routine hospitalisation or ICU admission unless deemed necessary by the overall surgical risk prediction
- More prone to deconditioning with prolonged immobilisation - early physio & rehabilitation are necessary to prevent deconditioning in patients with complicated post-operative courses who require prolonged hospitalisation.

Perioperative Care in Patients with Ehlers Danlos Syndromes

Pradeep Chopra[1*], Linda Bluestein[2]

Open Journal of Anesthesiology, 2020, 10, 13-29
https://www.scirp.org/journal/ojanes
ISSN Online: 2164-5558
ISSN Print: 2164-5531

- Laxity of the ligaments and the weakness of the connective tissue
- Multiple co-existing conditions: Chiari malformation, Tethered Cord Syndrome, spinal instability, abdominal pain, Dysautonomia and MCAS
- Relevant to anaesthesia may present with: Dysautonomia, MCAS, Chiari Malformation, Tethered Cord Syndrome, Craniocervical instability, Gastroparesis, altered sensitivity to local anaesthetics.
- Anaesthetic techniques are modified according to the presentation.

Perioperative Management

- Preoperative considerations:
  + note which joints subluxate most often, craniocervical instability.
  + prone to temporomandibular joint subluxation, obstructive sleep apnoea and tracheomalacia, spontaneous pneumothorax, POTS, MCAS, insensitivity to local anaesthetics and coagulation disorders.
- Intraoperative considerations:
  + possible fibreoptic intubation, IV fluid loading for POTS, avoid drugs that release histamine, unpredictable response to opioids, precautions for gastroparesis.
  + positioned to avoid joint subluxation & overstretching nerves.
- Postoperative considerations:
  + maintaining haemodynamic stability,
  + avoid exacerbation of symptoms of MCAS,
  + high suspicion of occult bleeding,
  + high risk of post-dural puncture headache in patients undergoing spinal procedure or neuraxial block.