The Trifecta in Neurodivergence

EDS, MCAS and PoTS

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What we are going to cover

- Who am I and how did I come to be here?
- Introducing the Trifecta
- Other comorbidities
- The link to neurodivergence
- Specific challenges for neurodivergent patients
- Case studies
- Links and further information

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How did a dietitian with a long and eclectic career including renal, eating disorders, community and diabetes become a specialist in the Trifecta and neurodivergence?

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This is my daughter age 12…

We are waiting to see the psychologist because most of her ‘care’ was psychology based. She can’t stay awake or sit up anymore.

Early signs starting with severe gastro symptoms and exercise intolerance.

- No friends
- No school
- Housebound
- Mainly bedbound
- For years…

But there were lots of missed opportunities before this…

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- M.E/CFS
- Hypermobility
- PoTS
- MCAS
- Autistic (waiting on ADHD diagnosis)
- And more…

The right diagnoses and professionals who listened and noticed symptom patterns (plus lots of research and help from other mums) led us to where we are today.

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Just for fun these are some of the diets professionals have recommended over the years – ages 6-18

- Milk free
- Dairy free
- Low lactose
- Low fibre
- High fibre
- Migraine diet
- Low histamine
- Low FODMAP
- High energy/nutritional support
- Low carbohydrate
- Gluten free
- High salt
- Low salt
- High fluid
- Low fluid

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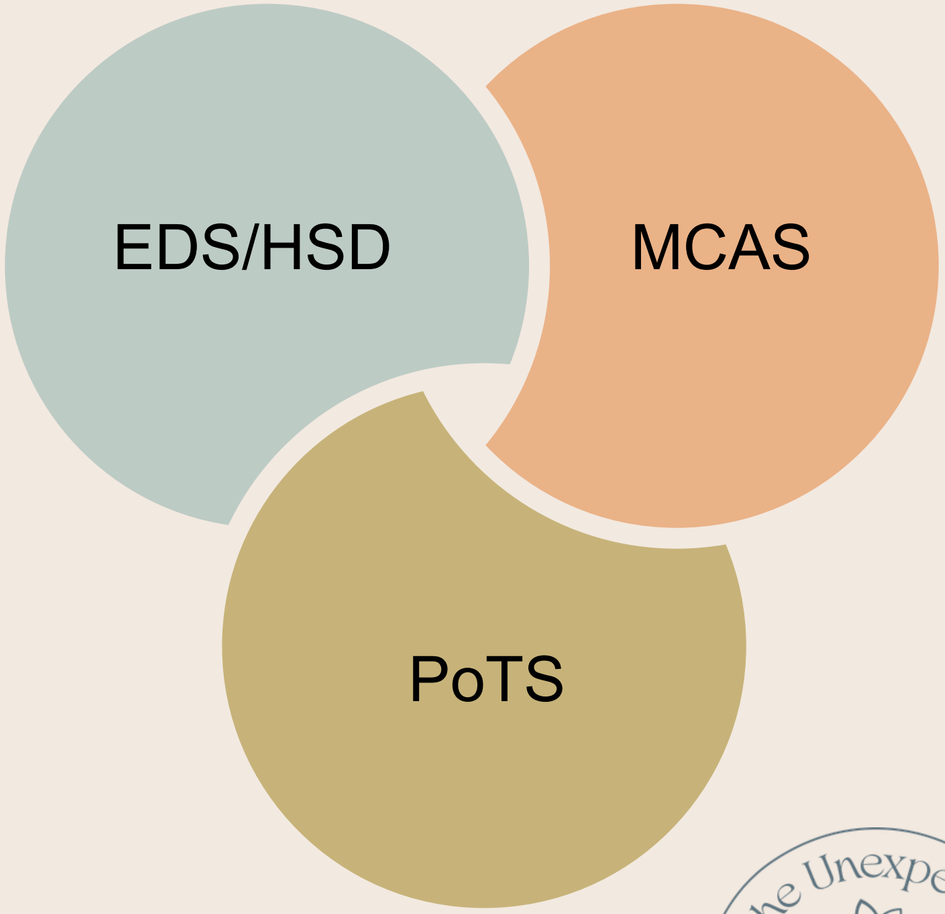
What is ‘The Trifecta’?

- Ehlers Danlos Syndrome/ Hypermobility Spectrum Disorder (EDS/HSD)
- Mast Cell Activation Syndrome (MCAS)
- Postural Tachycardia Syndrome (PoTS) and other dysautonomias



Frequently co-occurring and frequently delayed diagnosis.

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The Trifecta

Prevalence data varies widely due to poor recognition and poor access to services for diagnosis. Data for MCAS in particular remains unclear due to evolving diagnostic criteria (Afrin L et al, 2020)

~50% of adults with hypermobile Ehlers–Danlos syndrome (hEDS) or hypermobility spectrum disorder (HSD) were found to also have PoTS (Celletti C et al, 2020)

Around 31% of patients with both PoTS and hEDS were also diagnosed with mast cell activation syndrome (MCAS), compared with about 2% in patients without PoTS or hEDS (Wang E et al, 2021)

! In practice prevalence is much greater

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Ehlers Danlos Syndrome (EDS) / Hypermobility Spectrum Disorder (HSD)

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Ehlers Danlos Syndromes

- EDS are a group of heritable connective tissue disorders
- There are 13 recognised subtypes. The most common is hypermobile EDS (hEDS)
- Hypermobility spectrum disorder (HSD) describes symptomatic joint hypermobility that does not meet full diagnostic criteria for hEDS but may have similar clinical impact
- Each subtype has specific clinical features
- All, except hEDS/HSD are diagnosed via genetic testing
- hEDS/HSD is the type linked with neurodivergence
- New diagnostic criteria due December 2026

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What Might Suggest Ehlers Danlos Syndrome in Clinic?

- Long history of “unexplained” gastrointestinal symptoms labelled as IBS. In one cross-sectional survey study of over 600 with hEDS/HDS, almost all (98%) patients met diagnostic criteria for disorders of gut brain interaction (DGBI) (Lam CY et al, 2021)
- Pelvic floor issues, urinary symptoms or prolapse
- Dental issues like early decay, poor enamel, gum disease
- Lots of symptoms in multiple organ systems
- Family history – genetics!
- History of joint pain, frequent sprains or dislocations
- You may visibly see hypermobile features – bendy fingers for example
- Patient reports being told “everything is normal” despite significant symptoms

Clinical pattern:
Multisystem symptoms with connective tissue features and long diagnostic journeys

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Dietitian Summary - EDS/HSD

Foundation

- Is their diet nutritionally balanced and supportive of ongoing connective tissue, joint and gut health? Energy, protein, fibre.
- Do they have nutritional deficiencies or risks? *Ferritin over 50
- Is there any unnecessary restriction to address?
- Review supplement use.

*Al-Naseem A et al (2021)

Symptom Specific

- Are they being medically supported and do they need additional therapy/ medications to help broaden their diet?
- Any symptoms of comorbid conditions – MCAS, PoTS and more
- How can we adjust diet to manage individual symptoms?

Personalised

- Any additional risks such as neurodivergence, food fear, eating disorder, refeeding syndrome?
- Any adaptations needed for disability? - hand strength, difficulty standing
- Do social circumstances impact nutrition and care?

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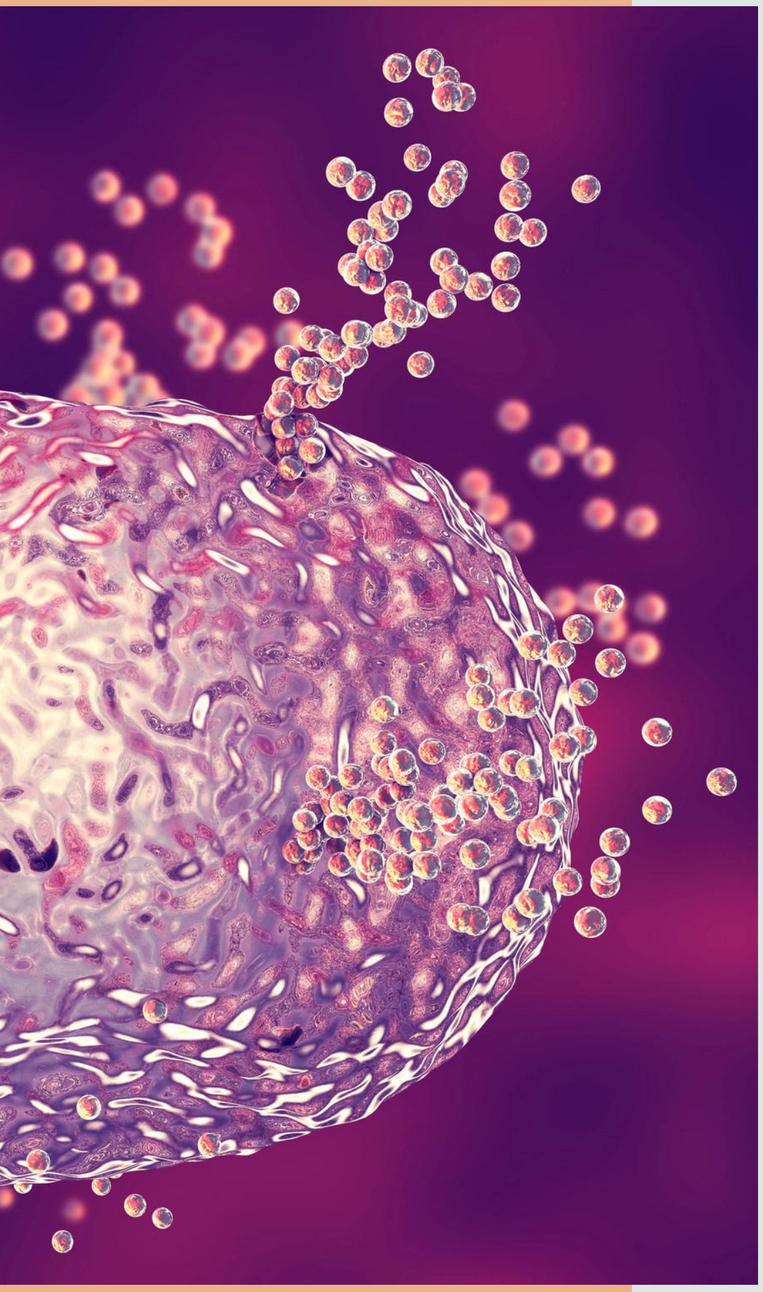

Mast Cell Activation Syndrome (MCAS)

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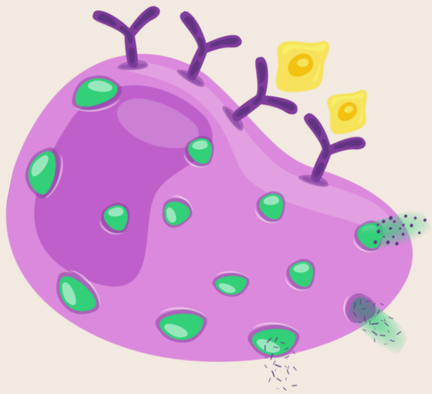
Mast Cell Activation Syndrome



- An immune disorder in which mast cells are inappropriately activated by triggers such as food or chemicals in the environment
- Mast cells are a type of blood cell found in all parts of the body
- Part of the immune system – detect triggers and signal for other immune cells to respond
- In response to triggers – release mast cell mediators – there are hundreds of different mediators that can be released in large amounts symptoms relate to specific mediators

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Symptoms/Pathology Mediator(s) Potentially Involved

Histamine, Cytokines, PAF, PGE2, PGD2, Bradykinin

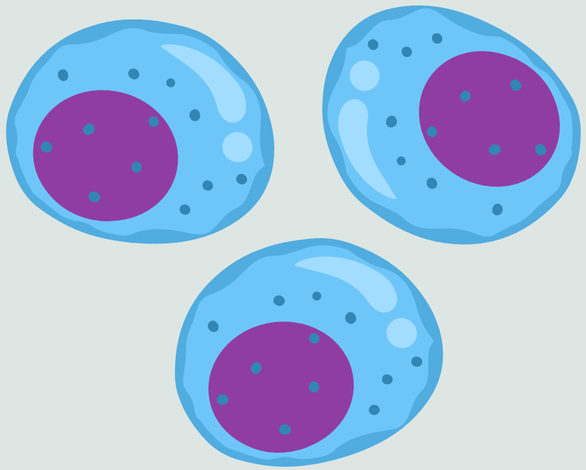
Skin

- Pruritus
- Urticaria
- Angioedema
- Flushing

Skeletal

- Bone remodeling
- Osteoporosis

Proteases, Cytokines, Heparin



Histamine, LTC4, LTE4, PGD2, PAF, VEGF, LTC4, Cytokines, Proteases (Tryptase, Chymase), Heparin, Tissue Type Plasminogen Activator, Tumor Necrosis Factor, Chemokines

Systemic

- Vascular instability
- Edema formation
- Tissue remodeling
- Bleeding tendency
- Fever and cachexia
- Eosinophilia, eosinophil infiltration
- Lymphocyte infiltration

Neurological

- Fatigue
- Headache and nausea

Cytokines, Histamine

Respiratory

- Nasal congestion, wheezing
- Bronchoconstriction
- Secretion of mucus
- Pulmonary edema

Histamine, PGD2, LTC4, LTD4, PAF, Endothelin, Proteases

GI-Tract

- Gastric hypersecretion
- Peptic ulcer disease
- Cramping, abdominal pain
- Diarrhea

Histamine, LTC4, PAF

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(Valent P et al, 2020)

Triggers

Food and drinks

Hormones – menstruation and menopause

Weather/temperature

Fragrances and chemicals

Stress

Bites and stings

Medications and supplements

Hayfever/pollen

Illness

And more…

The effect is cumulative – If reacting to food, also need to work to reduce other triggers

(Arun s et al, 2022)

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What Might Suggest Mast Cell Activation Syndrome in Clinic?

- Reports of reacting to “many foods” without clear IgE allergy
- Fluctuating tolerance to foods
- Reactions that are multisystem such as flushing, itching, abdominal pain, diarrhoea, palpitations
- Symptoms triggered by non food factors such as heat, stress, hormones or fragrances
- Improvement with antihistamines
- Fear of new foods due to unpredictable reactions
- Patient already following a highly restrictive low histamine, Low FODMAP or multiple exclusion diets (Harris et al, 2024)

Clinical pattern:
Variable, trigger based, multisystem reactions with cumulative effect

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Summary of things to consider as a dietitian seeing patients with MCAS

Foundation

- Is their diet nutritionally balanced? Energy, protein, fibre.
- Do they have nutritional deficiencies or risks? *Ferritin over 50
- Is there any unnecessary restriction to address?
- Review supplement use.
- Can we support with reducing non diet triggers?
- How can we identify their dietary triggers?

*Al-Naseem A et al (2021)

Symptom Specific

- Are they being medically supported and do they need additional medications to help broaden their diet?
- Any symptoms of other comorbidities? Primary allergy, EDS, PoTS
- Is there a way we can broaden their diet without de-stabilising symptoms? Reintroductions after elimination?

Personalised

- Any additional risks such as neurodivergence, food fear, eating disorder, refeeding syndrome?
- Any adaptations needed for disability? - hand strength, difficulty standing
- Do social circumstances impact nutrition and care?

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Dysautonomia / Postural Tachycardia Syndrome (PoTS)

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Dysautonomia / PoTS

Dysautonomia is an umbrella term for disorders of the autonomic nervous system, includes PoTS, orthostatic hypotension and more.

The autonomic nervous system regulates automatic body functions such as:

- Heart rate
- Blood pressure
- Gastrointestinal motility
- Temperature regulation
- Sweating
- Bladder function
- When this system does not regulate effectively, multiple body systems can be affected

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Postural Tachycardia Syndrome

PoTS is defined by:

- Sustained increase in heart rate of 30 (40 for under 18) beats per minute or more within 10 minutes of standing
- In the absence of orthostatic hypotension

Other causes should be ruled out e.g anaemias, addisons' disease

Common symptoms:

- Palpitations
- Dizziness or presyncope
- Fatigue
- Brain fog
- Nausea
- Migraine
- Exercise intolerance

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What might suggest Dysautonomia / PoTS in clinic?

- Reports of dizziness, light headedness or “almost fainting”
- Symptoms worse on standing, activity or heat
- Marked fatigue or “crashing” after activity
- Palpitations or racing heart, particularly when upright or after meals
- Nausea, early satiety or poor appetite
- Large fluid intake or salt cravings
- Symptoms worse in hot environments, showers, illness or dehydration
- Patient reports brain fog or difficulty concentrating

Clinical pattern:
Orthostatic symptoms with fatigue, nausea and poor appetite that fluctuate with hydration, heat and activity

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Summary of things to consider as a dietitian seeing patients with PoTS

Foundation

- Is their diet nutritionally balanced? Energy, protein, fibre.
- Do they have nutritional deficiencies or risks? *Ferritin over 50
- Review supplement use.
- Are they drinking enough fluids?
- Review caffeine intake.

*Al-Naseem A et al (2021)

Symptom Specific

- Are they being medically supported and do they need additional medications to help broaden their diet?
- Any symptoms of other comorbidities? EDS, MCAS, *Coeliac, reactive hypoglycaemia
- Adjust diet to manage symptoms? CHO balance/low GI, little and often.
- Are they having enough salt for their needs?
- Consider electrolytes?

*(Penny HA et al , 2016; Laszkowska M et al, 2016)

Personalised

- Any additional risks such as neurodivergence, food fear, eating disorder?
- Any adaptations needed for disability? - hand strength, difficulty standing
- Do social circumstances impact nutrition and care?

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The Trifecta doesn't come alone...

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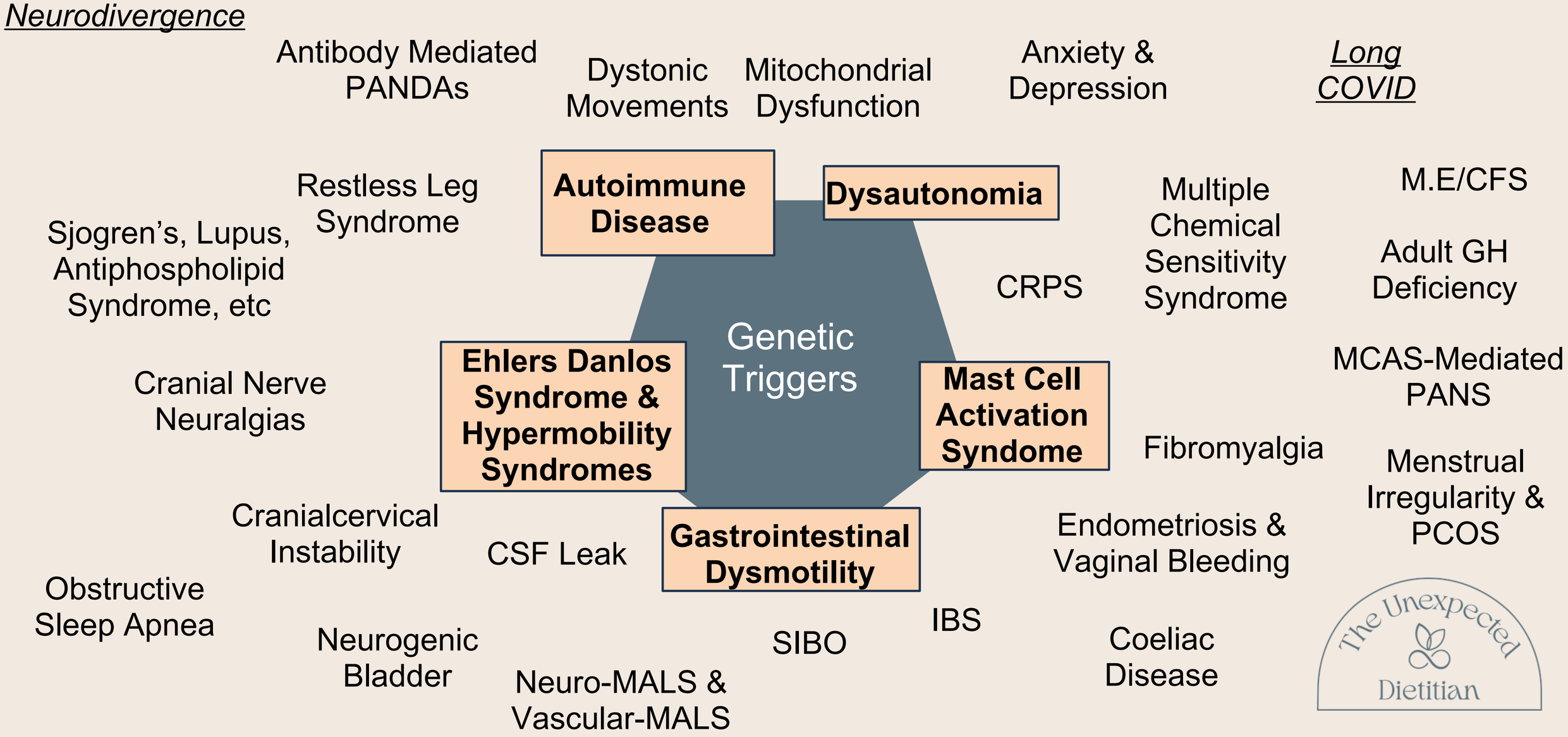
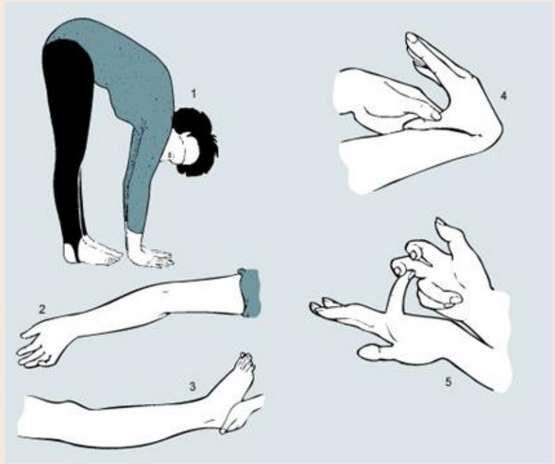
Dr. J Andrew Maxwell's Pentad



Summary of Signs to Look For

Migraine

Fatigue



Weak pelvic floor, prolapses

Poor healing, stretchy skin, easy bruising

Family history

IBS-like symptoms, indigestion

Chronic pain

Allergies, autoimmunity

Hypermobile joints, dislocations and sprains

Anxiety, poor sleep

Low BP, palpitations

Symptoms in multiple organ systems

“Medically unexplained symptoms”

Dizziness, fainting

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Why does this matter for our neurodivergent patients?

- Higher incidence of the trifecta with neurodivergence
- Diagnostic overshadowing is common
- Symptom recognition and communication differences impact diagnosis and care
- Nutrition interventions may need adaptation
- Significant nutritional risk when unmanaged or mismanaged

The Link to Neurodivergence

Autism and ADHD are more common in hypermobility disorders:

- In people with EDS, Autism was around 7 times more common, and ADHD around 5 times more common than in matched controls (Cederlöf et al, 2016)

- Orthostatic intolerance symptoms were also significantly higher in people who are Autistic (Csecs et al, 2022)

Hypermobility is also more common in people who are Autistic:

- 22 to 31% of people who are Autistic have joint hypermobility
- 28 to 39% have HSD or EDS when clinically assessed (compared to 0.1-0.2% in the general population)
- (Baeza-Velasco et al, 2025)

Clinical Implication:

Dietitians working with neurodivergent patients are more likely to encounter hEDS/HSD, dysautonomia and related conditions even when these have not yet been recognised or diagnosed.

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Dietetic specialities where patients are most likely to present?

- Gastro - Gi Disorders including disorders of gut brain interaction (DGBI)
- Neurodevelopmental – Neurodivergence
- Allergy/Immunology – Food based reactions – allergies and intolerances
- Nutritional support – Restricted diets, gastroparesis
- Eating disorders – ARFID, Food fear, misdiagnosis/diagnostic over shadowing
- M.E/CFS/ Fibromyalgia, Long Covid clinics
- Community - catch all!

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Diagnostic Overshadowing

Neurodivergent patients are at increased risk of diagnostic overshadowing, particularly when symptoms are complex, multisystem or difficult to describe.

Eating and gastrointestinal symptoms:

- Food avoidance or reduced intake assumed to be driven by disordered eating rather than attempts to manage symptoms
- Appetite loss attributed to anxiety/ depression or burnout
- Severe bloating, nausea or abdominal pain labelled as functional without consideration of further diagnoses

Autonomic symptoms:

- Palpitations, dizziness and tremor attributed to anxiety or panic disorders
- Fatigue and cognitive symptoms attributed to stress or burnout

Why this matters for dietitians:
Patients may arrive after years of being told symptoms are psychological and significant nutritional risk may develop before underlying conditions are recognised

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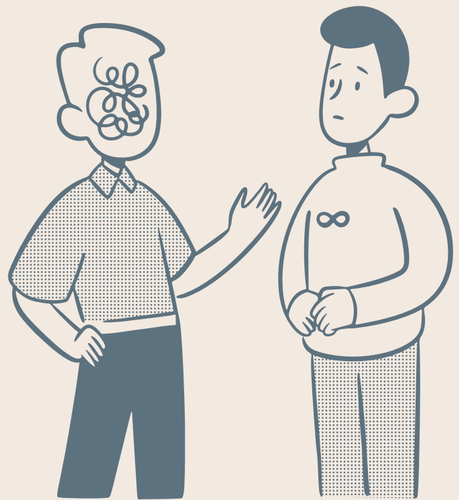
Symptom Recognition and Communication

- Interoceptive differences can mean that symptoms are difficult to notice until they are severe
- Sensory differences may make symptoms more or less intense or feel different from the ‘norm’



- Time blindness may make it difficult to give a clear timeline of symptom development or when tracking triggers
- Being non speaking affecting direct communication
- Interrupting, questioning, lateness, missed appointments - affecting relationships with professionals

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Symptom Recognition and Communication

For professionals who don't recognise these differences, it can seem like:

- Over exaggerating symptoms
- Experiencing/describing the 'wrong' symptoms for the condition
- The wrong timeline or order of symptoms for the development of a condition
- Inconsistent story telling
- Non 'compliance'
- Rudeness or questioning 'authority'

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I TAKE THINGS LITERALLY

Why nutrition advice may need adapting?

- Executive function differences
- Interoceptive differences
- Sensory needs
- Safe foods
- Hyperfocus
- Rule following/ difficulty with inconsistent rules
- Communication differences
- Physical disability

Seeing the world differently

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Specific Risks in Neurodivergence

- Restriction stacking
- ARFID and other eating disorders
- Diet rules

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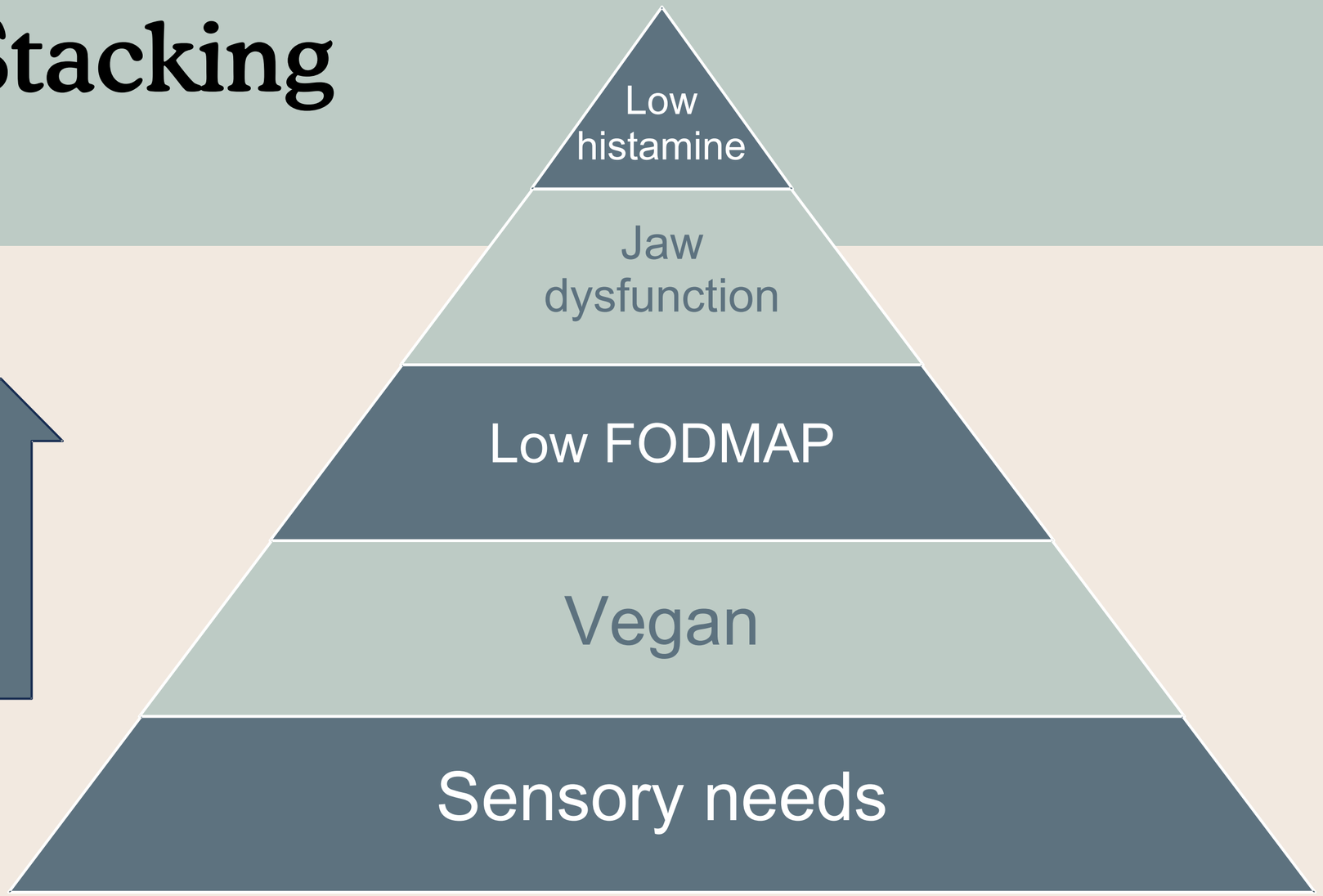
Restriction Stacking



Decreasing food intake and variety

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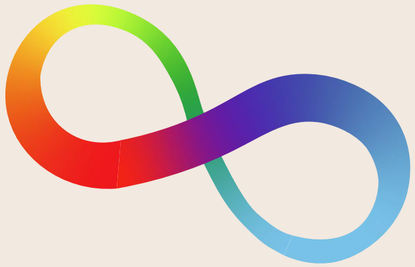
Diet Rules



- Strong rule following tendencies
- Clear rules can feel safer than uncertainty
- Patients may follow elimination diets extremely strictly, even when advice was intended to be flexible or temporary
- Ambiguous guidance creates confusion
- Online dietary information is often inconsistent
- Unclear rules can increase overwhelm and lead to over-restriction “just in case” or inability to start
- Difficulty with change once a rule is established
- After foods are removed it can be hard to reintroduce them
- Patients may experience significant anxiety about testing foods again, even when clinically appropriate

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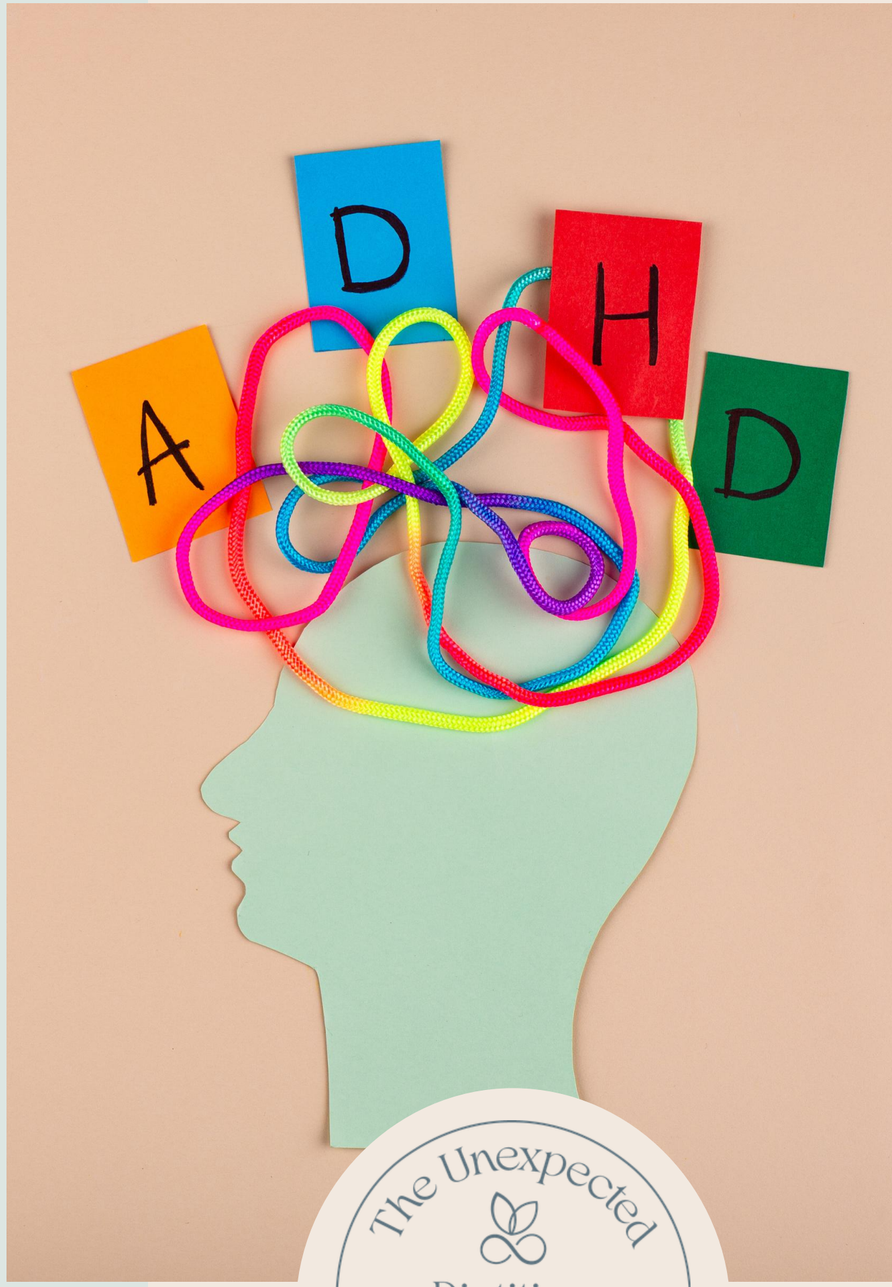
Diet Rules

For ADHD in particular:

- Tracking, experimenting and “working out the diet” can provide novelty and dopamine reward
- The process of optimisation can become a hyperfocus in itself, sometimes leading to increasingly restrictive patterns

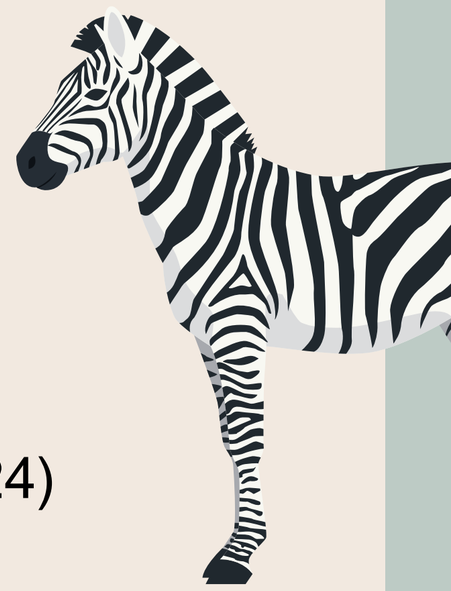
Clinical implications:

- Provide clear rationale, flexible language and planned reintroduction steps from the start.
- Focus on nourishment and stability before restriction, and support gradual, structured food reintroduction



Eating Disorders Including ARFID

- In women with Ehlers-Danlos syndromes, 30.3% screened positive on SCOFF, compared with 12.8% of controls
- (Baeza-Velasco et al, 2021)
- In hEDS/HSD, ARFID was strongly linked with gastrointestinal symptom burden and those with ARFID (fear based) had a 4x increased risk of needing nutrition support
- (Topan et al, 2024)
- Additional vulnerability - Neurodivergent populations (Inal-Kaleli I et al, 2024)
- Additional vulnerability – GI conditions (Peters JE et al, 2022)



Clinical implications:
Restrictive eating in hEDS/HSD may reflect multiple aetiologies so assessment needs to stay broad and curious

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Case Studies

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Case Study: Tom age 42

"My diet is very limited and I want to improve my health."

Current diet (very consistent routine):

Breakfast	Lunch	Evening Meal	Supper	Fluids
4 hash browns and 2 fried eggs	4 slices toast with butter and cheese. Apple, crisps.	Large pasta with tomato sauce and cheese. Sometimes chicken and fries.	KitKat	1.5 litres Pepsi Max

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Case Study: Tom

Symptoms and observations:

- Tom reported feeling unwell after meals, particularly lunch and evening meals

Symptoms included:

- Shakiness
- Nausea
- “body and head feel separated”
- Sometimes nauseous in the morning

During the video consultation I noticed:

- Finger hypermobility

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Case Study: Tom

Dietetic Thinking

Initial concerns:

- Limited food variety
- Risk of micronutrient insufficiency
- Low fluid intake and high caffeine

But the symptom pattern raised additional questions:

? Hypermobility

? Dysautonomia

? Reactive hypoglycaemia

Key clinical point
Symptoms in hypermobile or neurodivergent patients are sometimes interpreted as ARFID when underlying physiology may be contributing – however start with the basics – nutritional adequacy

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Case Study: Tom

Initial Dietetic Plan: Focus on optimising nutrition, exploring possible contributors to symptoms, and ensuring appropriate medical follow up

Nutrition support:

- Maintain regular meals and safe foods
- Add protein, fat and fibre to carbohydrate based meals where possible
- Introduce a small number of additional foods gradually to improve nutrient variety, particularly sources of fruit and vegetables
- Review intake and supplement nutrients that may currently be low, particularly: Vit C, Iron, Folate, Calcium, Vit D

Fluid and caffeine:

- Support adequate hydration
- Gradually reduce Pepsi Max intake to lower caffeine intake

Further investigation:

- Given the observation of hypermobility and symptom pattern, suggest that dysautonomia may be worth exploring with the GP and point to safe online resources

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Case Study: Aisha age 19

Autistic, non-speaking, seen with mum

- Previously diagnosed with IBS and advised to try a low FODMAP diet

Main concerns:

- Increasing distress around meals
- Vomiting after eating on some occasions
- Food refusal and very limited diet

Background:

- Longstanding sensory food differences
- Mum reports Aisha is very hypermobile
- Low BMI 16/ nutritional risk

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Case Study: Aisha

Why this needed a pause

At first glance this could look like:

- IBS
- Sensory food restriction
- ARFID

But there were red flags:

- Vomiting after meals
- Meal-related distress and food refusal linked to symptoms
- Low BMI / nutritional risk
- Background of hypermobility
- Advice likely to increase restriction further

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Case Study: Aisha

Dietetic Thinking

Consider:

- Sensory and interoceptive differences affecting symptom expression
- Constipation and low food intake contributing to upper GI symptoms
- Reflux or gut dysmotility associated with hypermobility
- Dysautonomia / post-prandial symptom worsening
- Compression syndromes in hypermobility

Clinical question:

Is this really IBS, or is neurodivergence plus hypermobility changing the presentation?

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Case Study: Aisha

Dietetic Plan

- Avoid unnecessary further restriction
- Protect nutritional status using safe foods and supplementation
- Explore symptom pattern carefully with mum and patient
- Consider constipation, meal size, texture, timing and volume
- Liaise with GP / medical team about further assessment

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“Recognising the overlap between neurodivergence, connective tissue disorders, dysautonomia and mast cell disorders can help dietitians understand complex symptom patterns and support safer, more sustainable nutrition strategies, reducing the symptom burden for their patients.”

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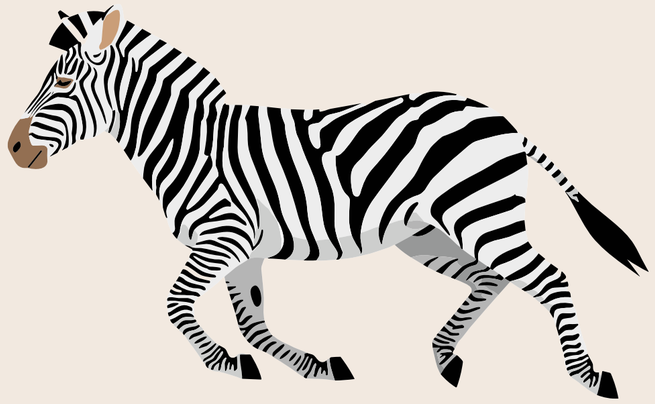
Links



- The Ehlers-Danlos syndromes (EDS) GP Toolkit
- GP Guide: PoTS on a Page - PoTS UK
- How can a dietitian help support those with Mast Cell Activation Syndrome? - British Dietetic Association (BDA)
- Health professionals | Mast Cell Action
- Supporting someone with MCAS as a Dietitian
- The PENTAD
- SEDSConnective | Hypermobility, EDS & Neurodivergence Charity

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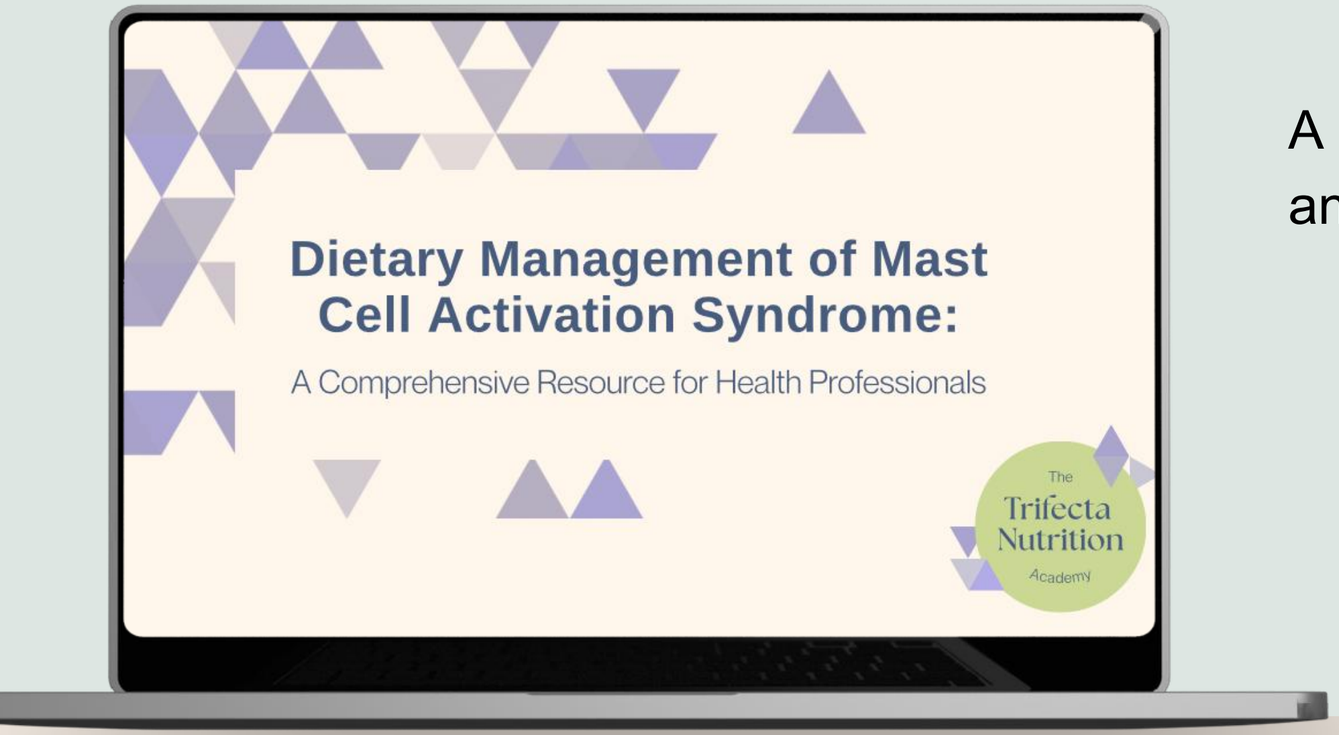
Access via my website www.theunexpecteddietitian.co.uk or instagram bio @theunexpecteddietitian



A paid course created by myself, Alison Holloway and Chloe Hall @The Calm Gut Dietitian

Dietary Management of Mast Cell Activation Syndrome

- Learn the essential dietary strategies for managing Mast Cell Activation Syndrome
- Enhance your professional knowledge with up-to-date, science-backed content
- Access at your own pace, anytime, anywhere

References 1

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