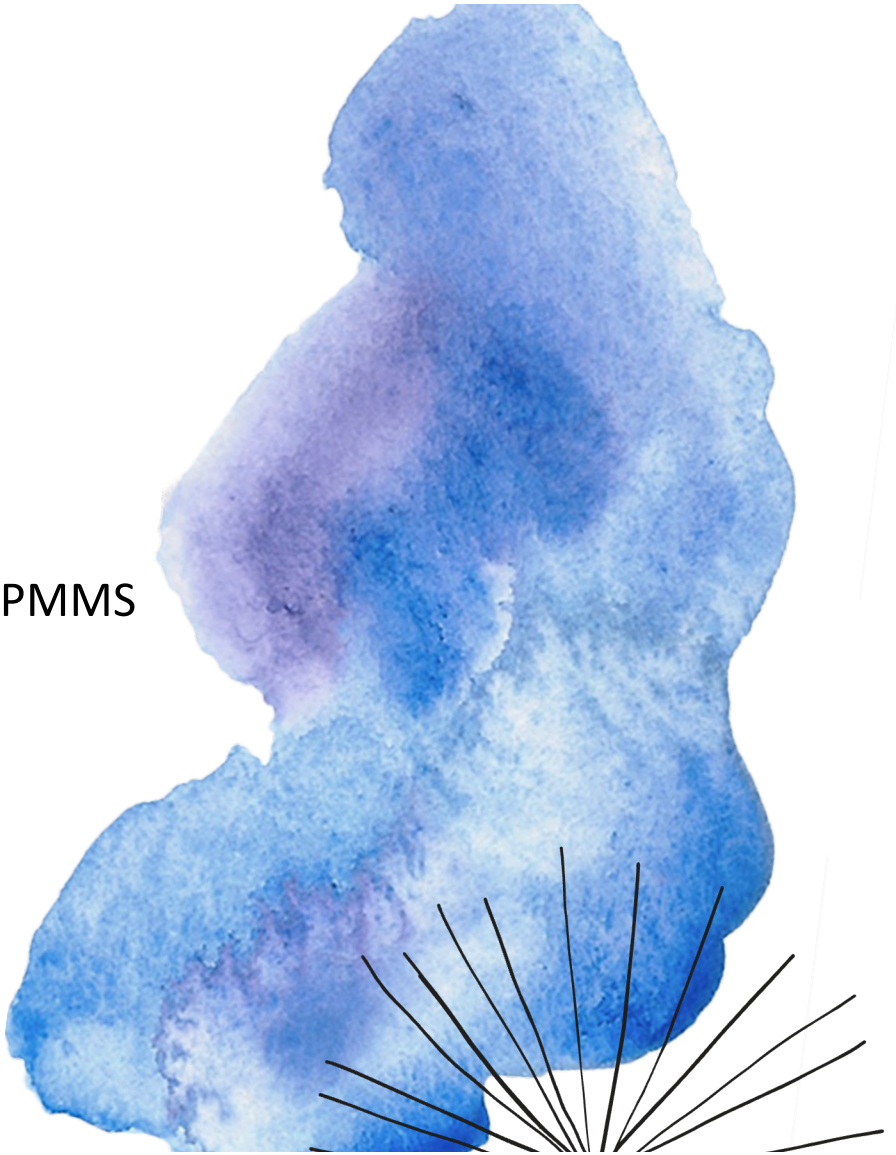
FLEXIBLE SOLUTIONS:

INTEGRATIVE HEALTH CARE IN CONNECTIVE TISSUE DISORDERS

LINDA BLUESTEIN, MD
BENDY BODIES, LLC

Outline

1. Why integrated health care?
2. My Integrative pain medicine approach – MENS PMMS
3. Conclusions



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Disclaimer and Disclosures

No conflicts of interest to declare

Information not advice

Off-label treatments will be discussed

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Why integrative health care?

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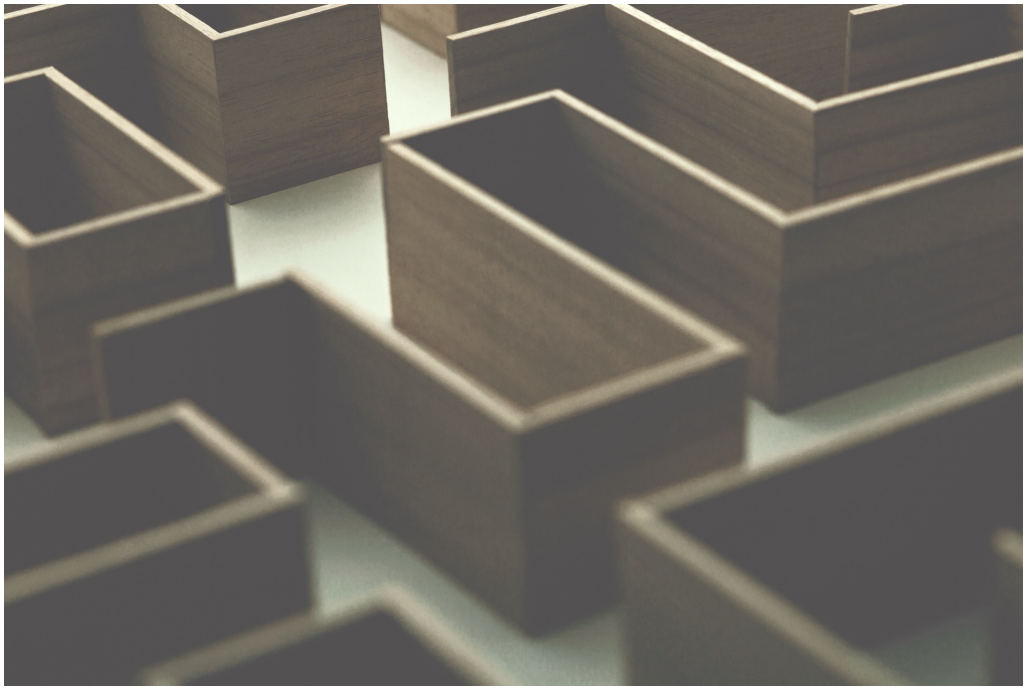
FANTASY ISLAND

- Every patient gets every consult they need
- Every clinician listens and takes as much time as the patient needs
- Every clinician speaks to the others and together they formulate a plan (ALA cancer conference)
- Advocates, nurse managers, social workers etc. facilitate and coordinate care
- No fragmented care – no dropped communication

REALITY - COMMON PATIENT PROBLEMS

- Extensive problem list – each complex on its own
- Diagnoses with overlapping symptoms – often managed by different specialists each of whom does not understand how the other would address the problem(s)
  - E.g.; surgeon lacks the skill set to evaluate movement patterns and see how they contribute to joint dysfunction. Proposes surgery because that is their “hammer” when perhaps non-surgical approach could significantly alleviate symptoms and improve function.
- Conflicting recommendations
- Overwhelming patient responsibilities – unfair burden
- Being labeled “non-compliant” because you could not carry out all responsibilities

REALITY - COMMON SYSTEM PROBLEMS



- Silos with each specialist understanding only their narrow scope
- Multiple clinicians and departments
- Poor to no communication
- Usually more than one health system
- Fragmented care – many balls dropped

PROBLEMS WITH TRADITIONAL (NON-INTEGRATED) HEALTH CARE DELIVERY MODELS

1) acute illness is the focus
2) lack of emphasis on prevention
3) volume-based (not quality)
4) lack of coordination/integration
5) inadequate access to primary care (unnecessary utilization of emergency department)
6) specialization is unnecessarily emphasized
7) care delivery is fragmented.

ROOT CAUSE MEDICINE

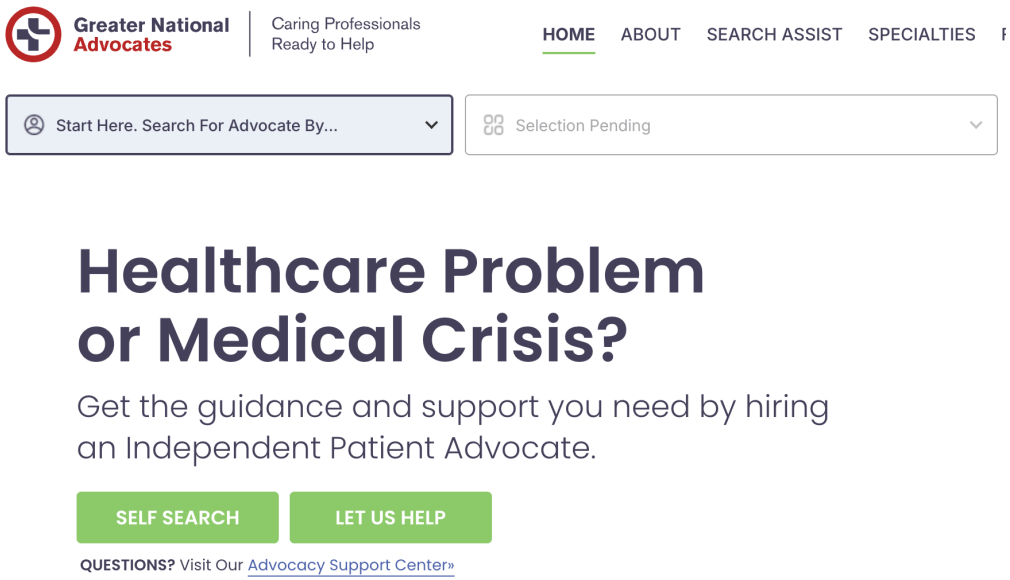
- Instead of usual strategies - respond to illness in patient presentation
- ie wait for dis-ease to develop
- Treat symptoms of disease: pain

Delia Chiaramonte and Shelley Adler, JACM, Sept 2020.

WHY IS IT PARTICULARLY IMPORTANT TO HAVE AN INTEGRATED DELIVERY SYSTEM WHEN CARING FOR INDIVIDUALS WITH CHRONIC CONDITIONS?

- 1% of ALL people have complex conditions and account for 20% of ALL health care spending
  - –EDS, POTS, MCAS, etc. common
- These patients need strategies for higher value care
- Coordinated mental health, physical health, social needs, and family caregiver involvement
- These patients need the most resources and have the potential for the most serious negative consequences.

GREATER NATIONAL ADVOCATES



Search by condition, specialty, credentials and more

Survivor Support

https://gnanow.org/

My Integrative Pain Medicine Approach

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TOPICS IN
PAIN MANAGEMENT

CONTINUING EDUCATION ACTIVITY

Hope for Hypermobility: Part 2—An Integrative Approach to Treating Symptomatic Joint Hypermobility

Daylor, Victoria BFA; Gensemer, Cortney PhD; Norris, Russell A. PhD; Bluestein, Linda MD

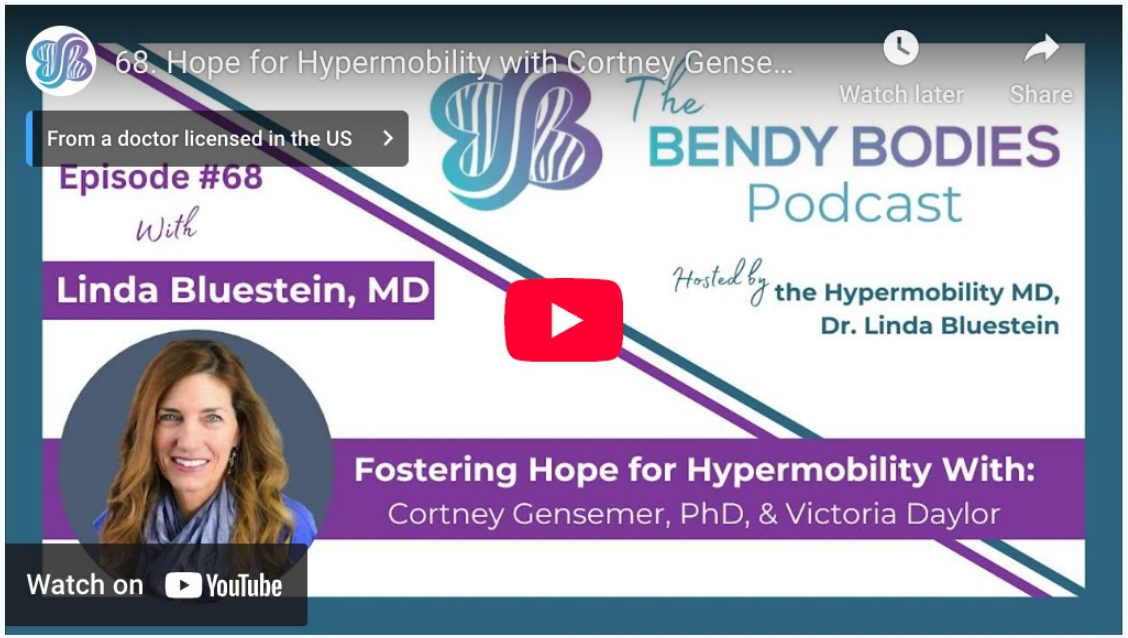
Author Information

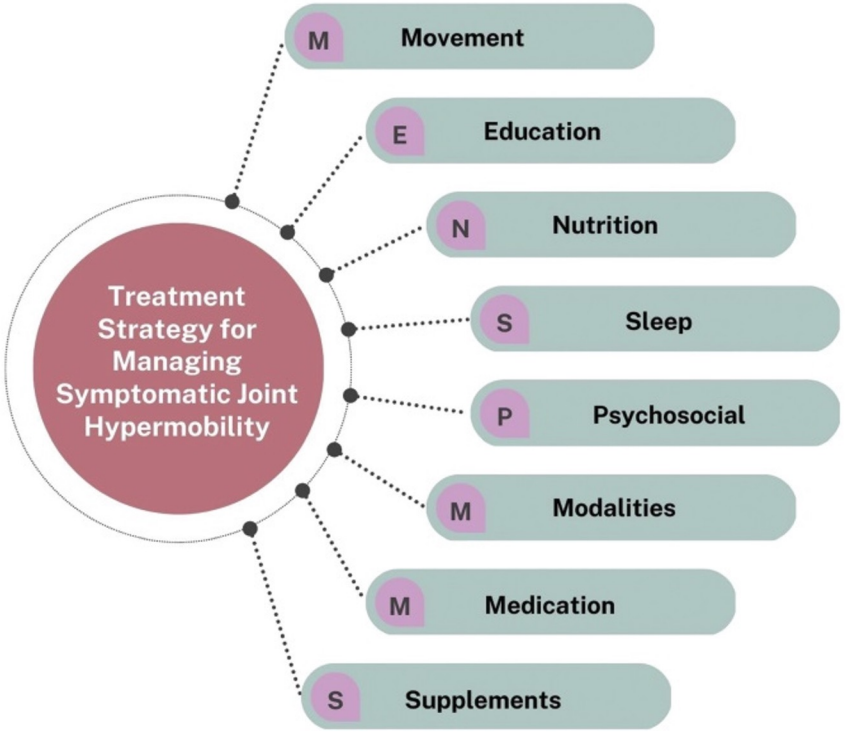
Topics in Pain Management 38(9):p 1-10, April 2023. | ***DOI:*** 10.1097/01.TPM.0000933968.28098.59

https://www.nursingcenter.com/cearticle?an=00587875-202304000-00001&Journal_ID=3402523&Issue_ID=6649307

MAY 25, 2023

68. FOSTERING HOPE FOR HYPERMOBILITY WITH CORTNEY GENSEMER, PHD, VICTORIA DAYLOR, AND LINDA BLUESTEIN, MD





MENS PMMS treatment strategy for managing SJH.

Figure 1.
MENS PMMS treatment strategy for managing SJH.
Source
Hope for Hypermobility: Part 2—An Integrative Approach to Treating Symptomatic Joint Hypermobility
Topics in Pain Management38(9):1-10, April 2023.

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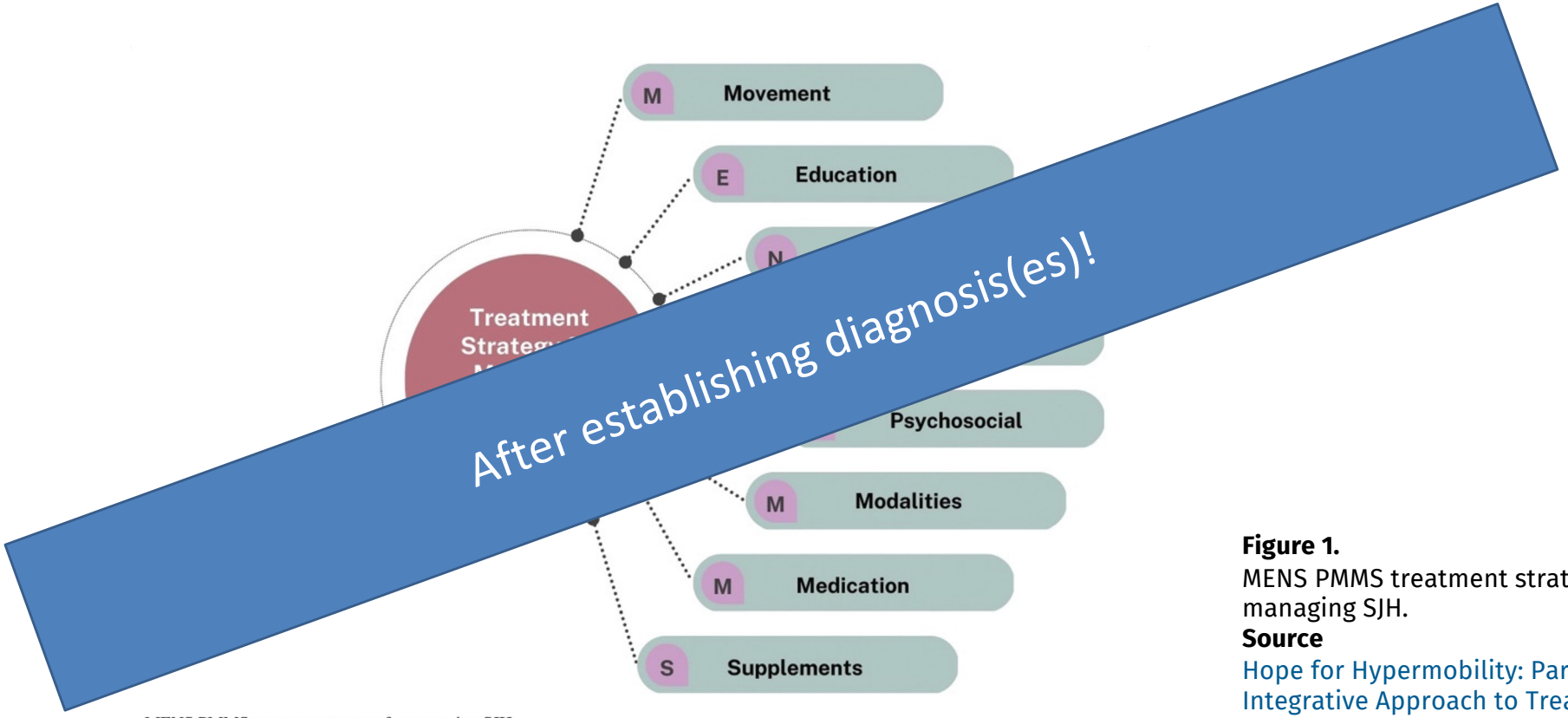

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Topics in Pain Management38(9):1-10, April 2023.

THE FIRST OF THREE ”M” STANDS FOR MOVEMENT

- Preferable term over “exercise”
- LOW and SLOW
- And STEADY
- AVOID boom and bust

Why Movement Matters in EDS and HSD

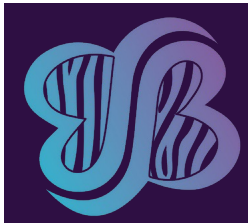
- **Movement is medicine. For people with hypermobility disorders, it's essential for:**
- **Joint Stability**
  Activating surrounding muscles provides dynamic support to loose joints, reducing subluxations and dislocations.
- **Proprioception & Body Awareness**
  Targeted movement retrains the nervous system, improving balance, coordination, and joint protection.
- **Circulation & Lymph Flow**
  Movement supports blood flow and reduces pooling, especially important for those with dysautonomia or POTS.

Movement as a Therapeutic Tool

- **Beyond joints and muscles, movement benefits multiple systems:**
- **Pain Modulation**
  Physical activity triggers endorphins, which can help reduce chronic pain.
- **Digestive Function**
  Gentle core work and upright movement can improve motility and reduce GI symptoms.
- **Sleep Regulation**
  Movement helps normalize circadian rhythms and improve sleep quality—often disrupted in EDS/HSD.

Psychological & Functional Benefits

- **Movement builds resilience—physically and mentally:**
- **Mental Health & Stress Relief**
  Activity helps regulate mood, reduce anxiety, and improve emotional well-being.
- **Bone Density & Muscle Preservation**
  Movement protects against deconditioning, sarcopenia, and osteoporosis risk.
- **Body Confidence & Empowerment**
  Regular, safe movement helps patients trust their bodies again—fostering independence and hope.



"When you have EDS, HSD, or any flavor of floppy collagen circus syndrome, your body is on constant high alert. Muscles around your joints tighten up—not because they're strong, but because they're panicking. They're trying to act like ligaments that don't show up to work anymore. This is called muscle guarding—an involuntary protective strategy your body uses when it senses instability or pain."

-Christie Cox, Zebras Underground on Substack

Movement Assessment

- Individualized whenever possible
- Major deficits in accessing biomechanics and movement
- Consider sensory, psychological, and motor processing factors
- Kinesiophobia is common and understandable
- Appropriate movement intervention(s) may require creativity
- NS pain processing and movement adaptations – dynamic relationship
- Optimize NS safety

Butera, K. A., Fox, E. J., & George, S. Z. (2016). Toward a transformed understanding: from pain and movement to pain with movement. Physical therapy, 96(10), 1503-1507.

Corbett DB, Simon CB, Manini TM, George SZ, Riley JL 3rd, Fillingim RB. Movement-evoked pain: transforming the way we understand and measure pain. Pain. 2019 Apr;160(4):757-761. doi: 10.1097/j.pain.0000000000001431. PMID: 30371555; PMCID: PMC6424644.

Proprioception

- Knowing where body is in space without looking
- Less good in JH = clumsy + increased injury risk (brain imaging study)
- Excellent balance and proprioception needed for control
- Those with JH need to work extra hard at proprioception (time, practice)
- Exercises / balances eyes closed = improves balance and proprioception

Movement

- Focus on stabilizing joints before strengthening
- Proprioception is often suboptimal and contributes to injury risk
- Multiple studies show Pilates very beneficial for persistent pain
- PT, OT, Tai Chi, Alexander Technique, Feldenkrais, aquatic therapy helpful for the right person done in the right way

Wells C,Kolt GS,Marshall P, Hill B, Bialocerkowski A.The effectiveness of Pilates exercise in people with chronic low back pain: a systematic review. PLoS One. 2014;9(7):e100402

Lin HT, Hung WC, Hung JL,Wu PS, Liaw LJ, Chang JH. Effects of Pilates on patients with chronic non-specific low back pain: a systematic review. J Phys Ther Sci. 2016;28(10):2961–2969.

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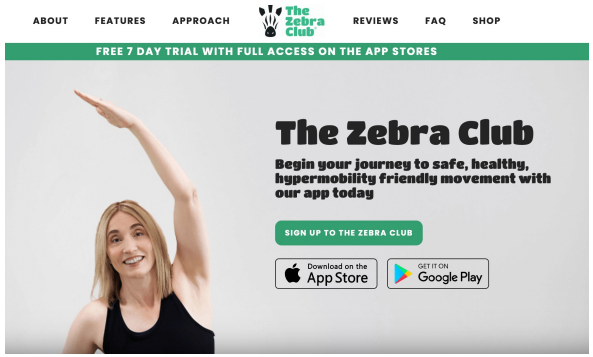

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“E” stands for Education – Pain Neuroscience Education and Education about EDS and Comorbitidites

Goals of Education – Pain Neuroscience Education (PNE)

- Understand neurophysiological-endocrine-immune changes that occur in CNS with chronic pain
- Optimize patient's and clinician's beliefs and perceptions to facilitate and encourage positive adaptive and effective coping strategies

Education – Pain Neuroscience Education (PNE)

- Decatastrophization
- Pain ≠ Damage
- No magic bullet
- 10% rule
- Non-pharmacologic approaches
- essential

Neuroscience Education

● In nociplastic and neuropathic pain = CNS overly responsive to afferent inputs due to

- central sensitization
- increased membrane excitability
- amplified synaptic activity
- reduced inhibitory mechanisms

MAST CELL MEDIATORS

Pergolizzi, J. V., Varrassi, G., Magnusson, P., Breve, F., Raffa, R. B., Christo, P. J., … Coluzzi, F. (2021). Pharmacologic agents directed at the treatment of pain associated with maladaptive neuronal plasticity. *Expert Opinion on Pharmacotherapy*, *23*(1), 105–116. https://doi.org/10.1080/14656566.2021.1970135

Neuroscience Education

- Mast cells catalyze/recruit numerous substances that initiate, amplify, or continue immunological and neuronal responses.
- There is complex bidirectional communication between immune and nervous systems.
- An imbalance between the ascending and descending pathways may underlie chronic pain syndromes. Ascending pathways become aberrantly amplified while inhibitory effects of descending pathways become diminished.

Pergolizzi, J. V., Varrassi, G., Magnusson, P., Breve, F., Raffa, R. B., Christo, P. J., ... Coluzzi, F. (2021). Pharmacologic agents directed at the treatment of pain associated with maladaptive neuronal plasticity. *Expert Opinion on Pharmacotherapy*, *23*(1), 105–116. https://doi.org/10.1080/14656566.2021.1970135

Neuroscience Education

- Altered threshold for microglial activation results in ‘priming’ maladaptively altering the homeostatic balance between the brain and the immune system resulting in sustained neuroinflammation, neuronal damage, and chronic pain.
- Activated microglia release an abundance of proinflammatory cytokines.

Pergolizzi, J. V., Varrassi, G., Magnusson, P., Breve, F., Raffa, R. B., Christo, P. J., … Coluzzi, F. (2021). Pharmacologic agents directed at the treatment of pain associated with maladaptive neuronal plasticity. *Expert Opinion on Pharmacotherapy*, *23*(1), 105–116. https://doi.org/10.1080/14656566.2021.1970135

Review Article | Published: 24 March 2025

How microglia contribute to the induction and maintenance of neuropathic pain

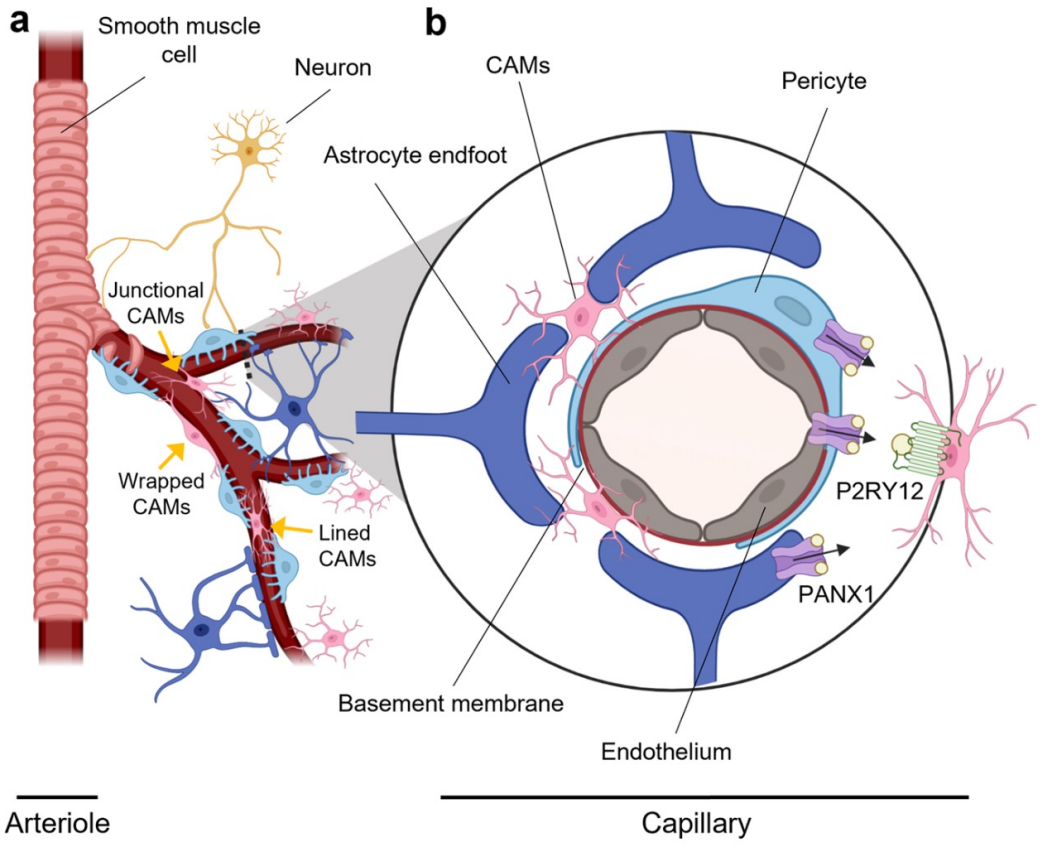
Marzia Malcangio & George Sideris-Lampretsas

Nature Reviews Neuroscience **26**, 263–275 (2025) | Cite this article

Microglia have a grip on brain microvasculature

Fig. 1: Microglia positioning in the neurovascular unit.

From: Microglia have a grip on brain microvasculature



Kisler, K., Nikolakopoulou, A.M. & Zlokovic, B.V. Microglia have a grip on brain microvasculature. *Nat Commun* **12**, 5290 (2021). https://doi.org/10.1038/s41467-021-25595-3

Two Top Priorities

Work To Make the Brain Feel Safe!

Work To Keep the Mind OPEN!

Nutrition

- Foods alter bodily chemistry (increase or decrease inflammation)
- Bi-directional relationship between CNS and gut microbiota
- Gut microbiome influences systemic inflammation + CNS inflammation = pain amplification and chronification.
- Nutritionist or dietitian recommended when possible
- Needs dictated by cellular needs of that particular patient (inflammatory pain, neurological pain, malabsorption, gastroparesis, mast cell activation, SIBO, etc.)

Elma, Ö., Yilmaz, S. T., Deliens, T., Coppieters, I., Clarys, P., Nijs, J., & Malfliet, A. (2020). Do nutritional factors interact with chronic musculoskeletal pain? A systematic review. Journal of Clinical Medicine, 9(3), 702.

Sleep

- Chronic pain leads to desynchronization of circadian and biological rhythms
- Painsomnia vicious cycle
- Positioning difficulties – subluxations, pressure points, allodynia etc.
- Melatonin has analgesic effects (B-endorphins, GABA receptors, opioid 1-receptors, and NO-arginine pathway)
- Melatonin may help improve migraines, fibromyalgia, irritable bowel syndrome, preoperative anxiety, and post-operative pain.

Yang, S., & Chang, M. C. (2019). Chronic pain: structural and functional changes in brain structures and associated negative affective states. International journal of molecular sciences, 20(13), 3130.


89. Conquering the Sleep Struggle with Roger Se...
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Roger Seheult, MD
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Hosted by the Hypermobility MD, Dr. Linda Bluestein
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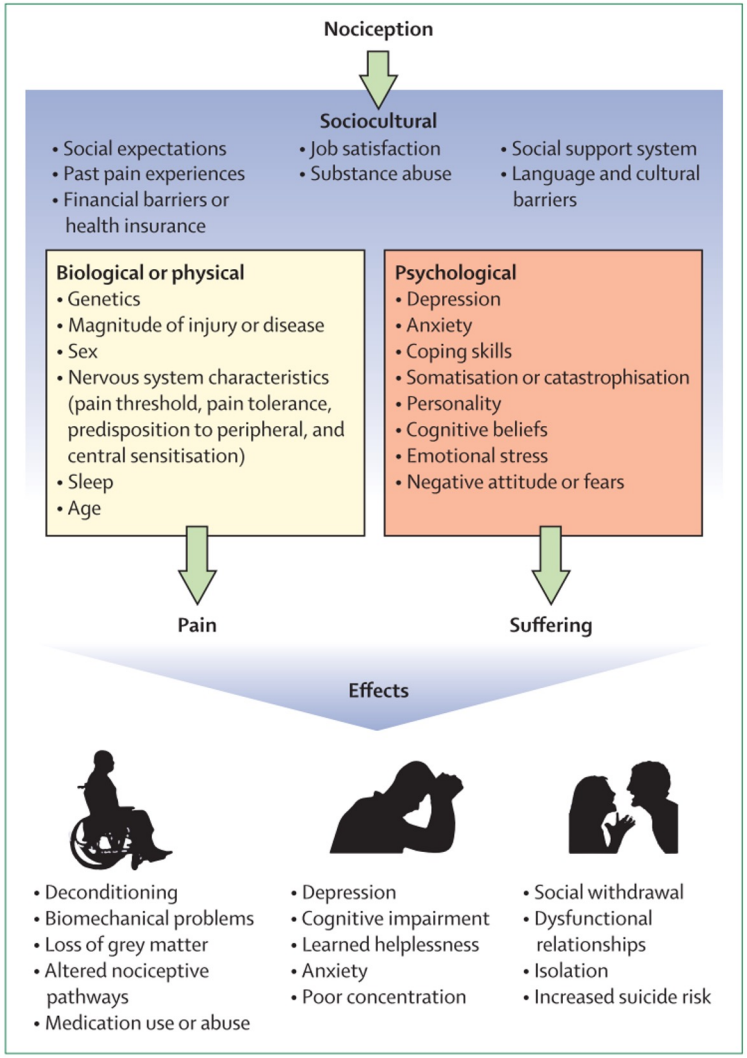
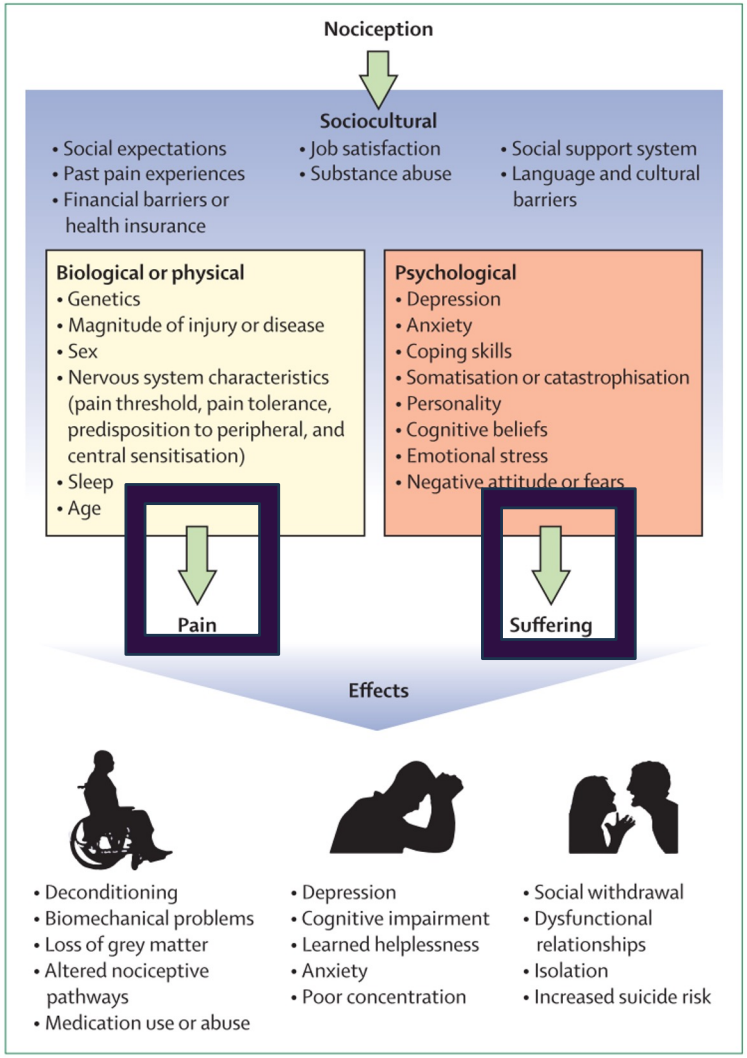


Figure 1: **Biopsychosocial model of pain showing the complex interaction between chronic pain and biological, psychological, and social factors**

Psychosocial - Factors influencing pain perception

Steven P Cohen, Lene Vase, William M Hooten, Chronic pain: an update on burden, best practices, and new advances, The Lancet, Volume 397, Issue 10289, 2021, Pages 2082-2097, ISSN 0140-6736, https://doi.org/10.1016/S0140-6736(21)00393-7.



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Psychosocial - Traumatic Experiences

- Traumatic experiences are common in people with chronic pain
- People with both chronic pain and PTSD report more PTSD symptoms, pain, disability, anxiety, depression, and opioid use than those with one condition.

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Kind S, Otis JD. The Interaction Between Chronic Pain and PTSD. Curr Pain Headache Rep. 2019 Nov 28;23(12):91. doi: 10.1007/s11916-019-0828-3. PMID: 31781875.

Psychosocial - Beliefs

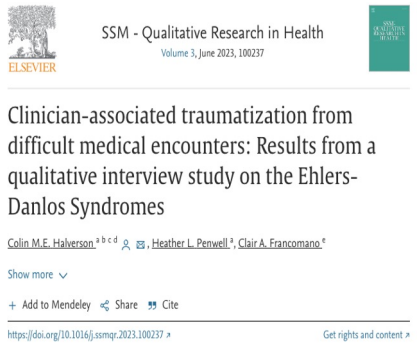
- Beliefs can predict chronic pain duration and disability
- Modifiable – therefore are an important target for treatment and prevention of persistent pain.
- Addressing unhelpful and erroneous beliefs on the part of the patient and clinician should be first line treatment.
- The transition from acute to chronic musculoskeletal pain can be facilitated by unhelpful pain beliefs.

HYPERMOBILITY MD

Caneiro JP, Bunzli S, O'Sullivan P. Beliefs about the body and pain: the critical role in musculoskeletal pain management. Braz J Phys Ther. 2021 Jan-Feb;25(1):17-29. doi: 10.1016/j.bjpt.2020.06.003. Epub 2020 Jun 20. PMID: 32616375; PMCID: PMC7817871.

Psychosocial - Clinician-associated trauma

- 85% of interviewees were immediately able to identify 1+ particularly stressful encounters with clinicians
- Perceived lack of empathy negatively impacted the relationship leading to a strong distrust of the medical institution
- Leads to worse - but preventable - outcomes!
- “A trusting relationship between a patient and a single clinician is not sufficient to repair the effects of institutional betrayal”



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Review > Pain Physician. 2017 Sep;20(6):E849-E861.

A Practical Guide for Treatment of Pain in Patients with Systemic Mast Cell Activation Disease

Stefan Wirz [1], Gerhard J Molderings [2]

Multi-disciplinary approach (Psychosocial)

- Essential for optimal analgesia in MCAD
- CBT co-treatment supports patients in mentally coping with the incurability of the disease
- Psychotherapy - strategies for dealing with the "***social environment that often reacts uncomprehendingly and adversely against the MCAD patient***"
- Psychological stress activates MC (e.g., via CRH). Psychotherapeutic approaches may successfully reduce stress. (2)

1. Wirz S, Molderings GJ. A Practical Guide for Treatment of Pain in Patients with Systemic Mast Cell Activation Disease. Pain Physician. 2017 Sep;20(6):E849-E861. PMID: 28934791.
2. Alysandratos et al.Neurotensin and CRH interactions augment human mast cell activation. PLoS One 2012; 7:e48934.

Suffering vs Pain

- Pain involves mind and body
- Suffering ≠ Pain or nociception
- Alleviate suffering

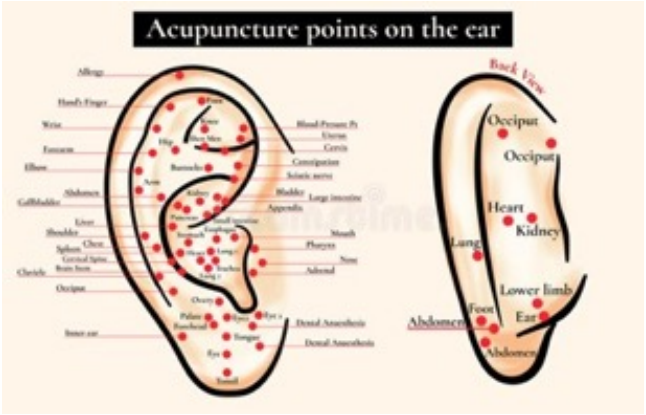
- “Just because psychology works doesn’t mean it is a psychological problem.”
  –Heather Tick, MD,

APRIL 11, 2024

95. PAIN CARE REDEFINED: NON-DRUG THERAPIES FOR PAIN RELIEF WITH HEATHER TICK, MD

Modalities

- Music Therapy
- Virtual Reality
- Acupuncture / Acupressure
- TENS
- Vagal Stimulation
- LASER
- Shockwave Therapy
- Red Light Therapy
- Sauna
- Hyperbaric Oxygen
- Regenerative Medicine
- Adaptive Tools



Medication

- Most treatments used are “off-label” (borrowed from other conditions)
- Details about “failed treatments” matter (dose, titration, excipients)
- Keep an open mind to new trials
- Patients and clinicians aware of the placebo (and nocebo) effect
- Pharmacogenomic testing can be beneficial but also has limitations

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Colloca, Luana, Barsky, Arthur. Placebo and Nocebo Effects. N Engl J Med. 2020;382(6):554-561. doi:10.1056/NEJMra1907805

https://doi.org/10.1080/14656566.2021.1970135

Medications studied for chronic pain

- BDNF agonists (Brain-derived Neurotrophic Factor)
- CGRP blockers (Calcitonin gene-related peptide)
- Complement inhibitors
- Disease-modifying antirheumatic drugs (DMARDs)
- Epidermal growth factor (EGF) blockers
- ‘Food for special medical purposes’
- Ion channel antagonists
- Ketamine
- Memantine
- Monoclonal antibodies
- Nerve growth factor (NGF) antagonists
- Nucleotide receptor antagonists
- Tumor-necrosis-factor-alpha (TNF-å) blockers

Pergolizzi JV Jr, Varrassi G, Magnusson P, Breve F, Raffa RB, Christo PJ, Chopra M, Paladini A, LeQuang JA, Mitchell K, Coluzzi F. Pharmacologic agents directed at the treatment of pain associated with maladaptive neuronal plasticity. Expert Opin Pharmacother. 2022 Jan;23(1):105-116. doi: 10.1080/14656566.2021.1970135. Epub 2021 Aug 30. PMID: 34461795.

Medication – Low Dose Naltrexone (LDN)

- Opioid antagonist originally developed for SUD
- At low dose, less affinity for μ-opioid receptor and instead binds to toll-like receptor 4 (TLR4)
- Breaks glial cell activation cycle and reduces cytokine release modulating inflammation
- Recent scoping review demonstrated improved pain severity, hyperalgesia, physical function, quality of life, and sleep in centralized pain conditions - variable time to benefits

Rupp A, Young E, Chadwick AL. Low Dose Naltrexone's Utility for Non-Cancer Centralized Pain Conditions - A Scoping Review. Pain Med. 2023 Jun 11:pnad074. doi: 10.1093/pm/pnad074. Epub ahead of print. PMID: 37302106.

Medication – Low Dose Naltrexone (LDN)

- Rare adverse effects usually dissipate with time or slower titration – vivid dreams, diarrhea, headache (consider BID or qam dosing)
- SE rarely required discontinuation
- Consider excipient issues
- Apparent increase in efficacy over time with large subset of patient seeing some benefit
- Discontinue prior to scheduled surgery or procedure where opioids might be used

1. Weinstock LB, Myers TL, Walters AS, et al. Identification and Treatment of New Inflammatory Triggers for Complex Regional Pain Syndrome: Small Intestinal Bacterial Overgrowth and Obstructive Sleep Apnea. A A Case Rep. May 1 2016;6(9):272-6. doi:10.1213/xaa.0000000000000292
2. Shannon A, Alkhouri N, Mayacy S, Kaplan B, Mahajan L. Low-dose naltrexone for treatment of duodenal Crohn's disease in a pediatric patient. Inflamm Bowel Dis. Sep 2010;16(9):1457. doi:10.1002/ibd.21185
3. Ghai B, Bansal D, Hota D, Shah CS. Off-label, low-dose naltrexone for refractory chronic low back pain. Pain Med. May 2014;15(5):883-4. doi:10.1111/pme.12345
4. Cruciani RA, Lussier D, Miller-Saultz D, Arbuck DM. Ultra-low dose oral naltrexone decreases side effects and potentiates the effect of methadone. J Pain Symptom Manage. Jun 2003;25(6):491-4. doi:10.1016/s0885-3924(03)00139-8
5. Rupp A, Young E, Chadwick AL. Low Dose Naltrexone's Utility for Non-Cancer Centralized Pain Conditions - A Scoping Review. Pain Med. 2023 Jun 11:pnad074. doi: 10.1093/pm/pnad074. Epub ahead of print. PMID: 37302106.

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Medication – Ketamine

- Dissociative anesthetic agent with analgesic, psychomimetic, anti-inflammatory and anti-depressant effects
- Blocks N-methyl-D-aspartate (NMDA) receptor which is crucial in neuroplastic changes (wind up and central sensitization)
- Can help reverse OIH (1)
- Formulations – nasal, IV, IM, SL
- Prolonged-release ketamine tablets may increase exposure to an active metabolite therefore be a safer and more efficient option in the future (2)

1. Guichard L, Hirve A, Demiri M, Martinez V. Opioid-induced Hyperalgesia in Patients With Chronic Pain: A Systematic Review of Published Cases. Clin J Pain. 2021 Oct 26;38(1):49-57. doi: 10.1097/AJP.0000000000000994. PMID: 34699405.
2. Hasan M, Modess C, Roustom T, Dokter A, Grube M, Link A, Rey H, Adler S, Meissner K, Siegmund W. Chiral Pharmacokinetics and Metabolite Profile of Prolonged-release Ketamine Tablets in Healthy Human Subjects. Anesthesiology. 2021 Aug 1;135(2):326-339. doi: 10.1097/ALN.0000000000003829. PMID: 34019627.

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- Prolonged-release ketam… exposure to an active metab… and more efficient option i…

Relative contraindications include pregnancy, active psychosis, cirrhosis, severe cardiovascular disease, and increased intracranial pressure.

…in M, Martinez V. Opioid-induced Hyperalgesia in Patients With Chronic Pain: A Systematic Review of … J Pain. 2021 Oct 26;38(1):49-57. doi: 10.1097/AJP.0000000000000994. PMID: 34699405.

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Medications - Ketotifen

- Antihistamine – first generation
- Stabilizes mast cells – anti-inflammatory
- Antianaphylactic properties
- Crosses BBB so may be sedating – can also help brain fog
- Indications – asthma, atopic dermatitis, urticaria, food allergy, MCAS
- Side effects – sedation, weight gain, dry mouth
- Consider topical application
- Must be compounded – not commercially available


The Bendy Bulletin

Ketotifen for Ehlers-Danlos Syndrome, Pain, and Mast Cell Activation: Dr. Linda Bluestein's Top Medication Picks (Part 2)

DR. LINDA BLUESTEIN, MD
JUN 03, 2025

7 8 4 Share

We're back with another edition of The Bendy Bulletin, your go-to resource for all things related to living with Ehlers-Danlos Syndromes (EDS). Whether you're navigating the daily challenges of hypermobility or exploring new tools for symptom management, we're here to bring you the latest research, resources, and hope for living well with EDS.

This is **Part 2** of our medication series focused on treatments that may help people with EDS better manage their symptoms.

(If you missed Part 1 on **Low-Dose Naltrexone** (**LDN**), you can catch up here.)

HYPERMOBILITY MD

Medications - Cromolyn

- Cromoglicic acid or cromolyn sodium introduced in 1969
- Stabilizes mast cells, anti-inflammatory
- Available as oral solution, nasal spray, inhaler, compounded
- Rare side effects and minimal drug interactions
- Difficult to obtain – may need to compound
- Can use topically or as douche
- Typical oral dose – 100-200mg QID (before meals and before bed)

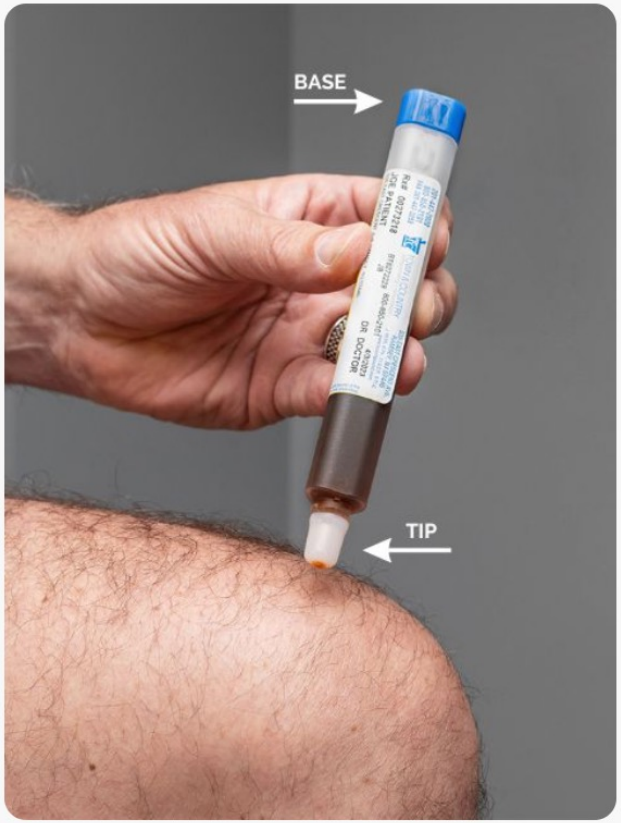
HYPERMOBILITY MD

Afrin LB, Dempsey TT, Rosenthal LS, Dorff SR. Successful mast-cell-targeted treatment of chronic dyspareunia, vaginitis, and dysfunctional uterine bleeding. J Obstet Gynaecol. 2019 Jul;39(5):664-669. doi: 10.1080/01443615.2018.1550475. Epub 2019 Apr 9. PMID: 30964355.

Journavx (suzetrigine)

- **Sodium channel blocker**
- **Off-Label Use in Chronic Pain**
- Variable response
- Costly and insurance coverage problematic
- **Contraindications & Drug Interactions**
- **P**otential interactions with **hormonal contraceptives**
- **Lab Monitoring & Safety Parameters**
- Treatment duration **no more than 14 days**, and longer-term dosing has **not been systematically studied**.

VASCEPTOR® 8.5% TOPICAL/TRANSDERMAL CURCUMIN GEL



- Developed to deliver the well-known anti-pain/inflammation benefits of curcumin.
- Patented delivery system enables >100X more curcumin solubility for deeper penetration into the skin
- Requires a prescription
- Topical or SL
- Possible staining
- Only available at Town & Country in NJ but they ship to many states in the US
- Active ingredient – curcumin 8.5%. Inactive ingredients: Myristic Acid; PEG.

Supplements

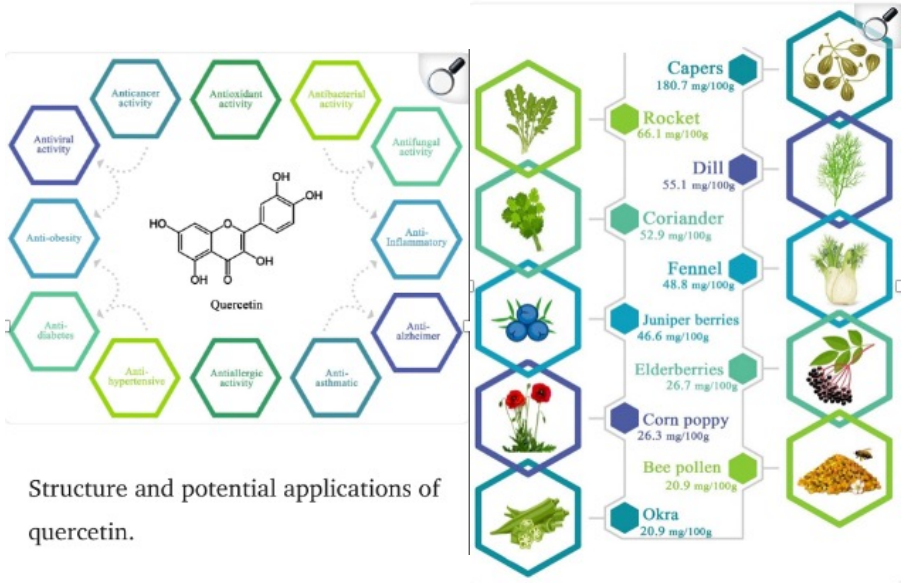
Supplements – Vitamin C

- Inhibits MC degranulation
- Inhibits histidine decarboxylase – enzyme produces histamine
- Increases DAO – which breaks down histamine
- Antioxidant
- Cofactor in college synthesis – important for CTD
- Decreases bronchial hypersensitivity
- Avoid large doses in renal insufficiency, hemodialysis, hemochromatosis, oxalate stone formers

Carr AC, Maggini S. Vitamin C and Immune Function. Nutrients. 2017 Nov 3;9(11):1211. doi: 10.3390/nu9111211. PMID: 29099763; PMCID: PMC5707683.

Supplements – Quercetin

- Flavonoid found in fruits and vegetables
- Antioxidant, antimicrobial, anti-inflammatory, anti-viral, anti-cancer
- Lowers BP & cholesterol, improves endothelial function
- Low toxicity profile
- Apples, berries, cilantro, onions, capers, vegetables, tea, wine
- Typical supplement dose 500mg BID
- Helpful in MCAD
- Brands matter – excipients, absorption, quality



Structure and potential applications of quercetin.

Aghababaei F, Hadidi M. Recent Advances in Potential Health Benefits of Quercetin. Pharmaceuticals (Basel). 2023 Jul 18;16(7):1020. doi: 10.3390/ph16071020. PMID: 37513932; PMCID: PMC10384403.

Supplements – Luteolin

- Yellow flavonoid pigment
- Found in plants
- Antioxidant, anti-inflammatory, neuroprotective, anti-cancer
- Abundant in celery, carrots, EVOO, olives, dandelion greens, parsley, spinach, blackberries, apples
- Inhibits release of histamine, tryptase, MMP-9, VEGF (more potent than cromolyn)
- Inhibits IL-1 beta, IL-6, IL-8 and TNF (cromolyn had no effect)
- Liposomal form increases oral absorption

Tsilioni I, Theoharides T. Luteolin Is More Potent than Cromolyn in Their Ability to Inhibit Mediator Release from Cultured Human Mast Cells. Int Arch Allergy Immunol. 2024;185(8):803-809. doi: 10.1159/000537752. Epub 2024 Apr 8. PMID: 38588651.

Supplements – Magnesium

- Second most common intracellular cation
- Physiologic functions include protein synthesis, signaling, and neurotransmission
- Magnesium sulfate (MgSO4) physiologically blocks N-methyl-D-aspartate (NMDA)-coupled channels
- Antinociceptive – inhibits central sensitization and decreases preexisting pain hypersensitivity
- Supplementation improves dysmenorrhea, fibromyalgia, and migraine.

Soleimanpour H, Imani F, Dolati S, Soleimanpour M, Shahsavarinia K. Management of pain using magnesium sulphate: a narrative review. Postgrad Med. 2022 Apr;134(3):260-266. doi: 10.1080/00325481.2022.2035092. Epub 2022 Feb 7. PMID: 35086408.

Supplements – Magnesium

- Deficiency difficult to detect, common, and contributes to many symptoms (fatigue, poor sleep + memory, muscle spasms, anxiety, constipation, menstrual cramps, migraines)
- Neuroinflammation results from Mg++ deficiency contributing to chronic pain hypersensitivity, memory and emotional deficits
- Animal studies demonstrate that Magnesium L-Threonate attenuates pain, allodynia, and depression

Chen JL et al. Correction to: Normalization of magnesium deficiency attenuated mechanical allodynia, depressive-like behaviors, and memory deficits associated with cyclophosphamide-induced cystitis by inhibiting TNF-α/NF-κB signaling in female rats. J Neuroinflammation. 2021 Nov 14;18(1):269. doi: 10.1186/s12974-021-02258-0. Erratum for: J Neuroinflammation. 2020 Apr 2;17(1):99. PMID: 34774073; PMCID: PMC8590763.
Zhang J et al. The Causal Role of Magnesium Deficiency in the Neuroinflammation, Pain Hypersensitivity and Memory/Emotional Deficits in Ovariectomized and Aged Female Mice. J Inflamm Res. 2021 Dec 7;14:6633-6656. doi: 10.2147/JIR.S330894. PMID: 34908863; PMCID: PMC8665878.

Supplements – Vitamin D

- Deficiency frequently observed in FM and CMP patients
- Hypovitaminosis D activates inflammatory cytokines influencing central and peripheral pain perception + contributes to sarcopenia and impaired muscle strength
- Low Vitamin D increases prostaglandin release and impairs immune cell responses

Lombardo M, Feraco A, Ottaviani M, Rizzo G, Camajani E, Caprio M, Armani A. The Efficacy of Vitamin D Supplementation in the Treatment of Fibromyalgia Syndrome and Chronic Musculoskeletal Pain. Nutrients. 2022 Jul 22;14(15):3010. doi: 10.3390/nu14153010. PMID: 35893864; PMCID: PMC9330000.

Supplements – Vitamin D

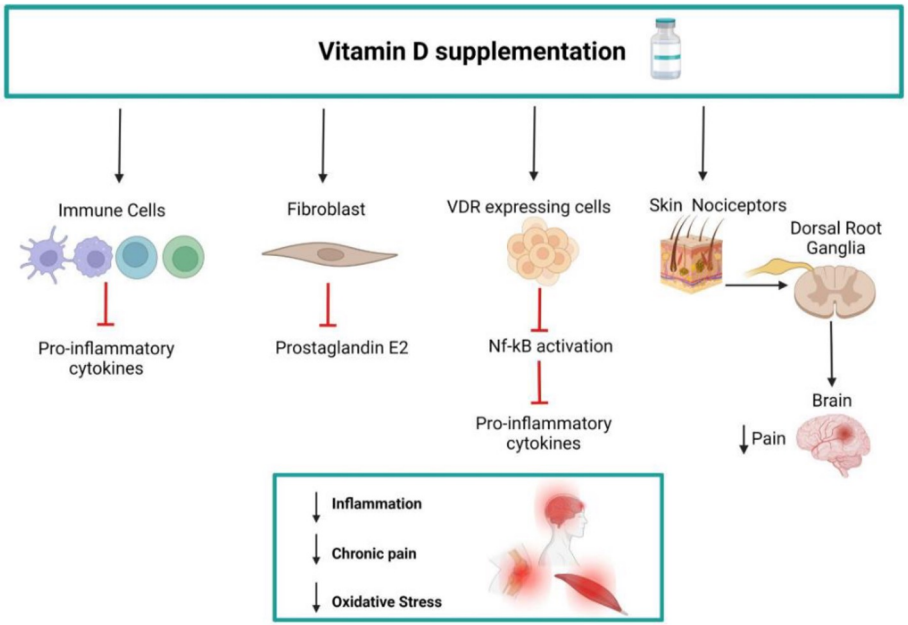


Figure 4. Possible mechanisms underlying the efficacy of vitamin D supplementation in chronic pain management include anti-inflammatory effects mediated by reduced cytokine and prostaglandin release and effects on immune cell responses. Furthermore, alterations in the somatosensory nervous system are observed in fibromyalgia. Pain signals are transmitted to the brain by pain receptors called nociceptors distributed also in the skin. Vitamin D and vitamin D receptor (VDR) activation has been described in several tissues, including skin, DRG neurons, and the brain, where the pain signal is perceived, thus contributing to ascending pathways that mediate chronic pain.

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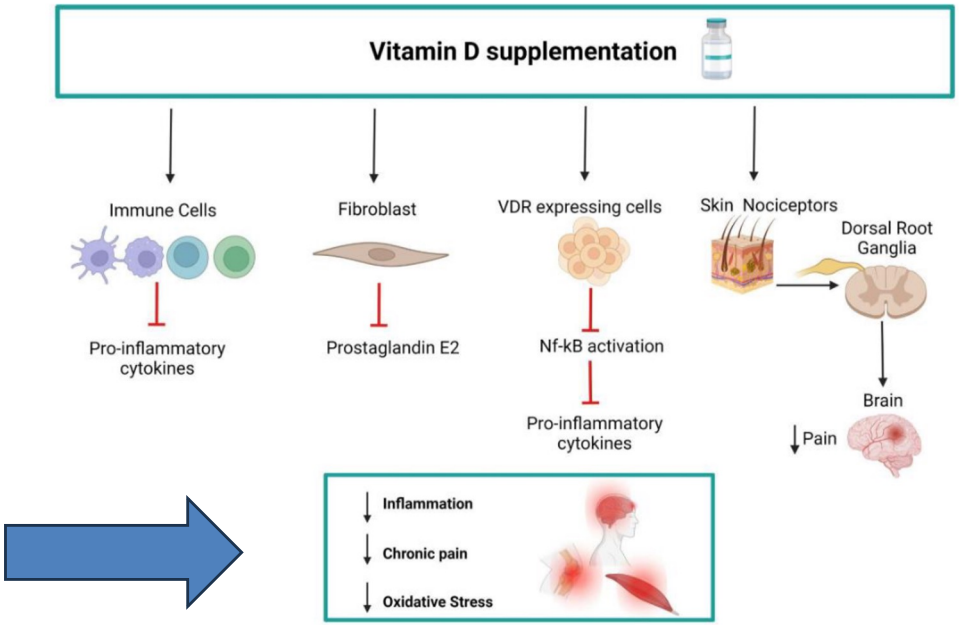

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Conclusions

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Concern for the trends in clinical medicine

“Medicine is a science of uncertainty and an art of probability.”

"Listen to your patient – he is telling you the diagnosis."

"The very first step towards success in any occupation is to become interested in it.”

---Sir William Osler

What can we do?

- Healthcare reform so that patients are always believed, and clinicians are better able to address complex patients
- Take steps to reduce ACEs and other forms of trauma
- Validation helps - Lessens mast cell activation – pain is a neuro-immune condition
- Accessible options to reduce nervous system danger and increase safety (via meditation, guided imagery, online programs like Empowered Relief™ etc)

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Take Home Points

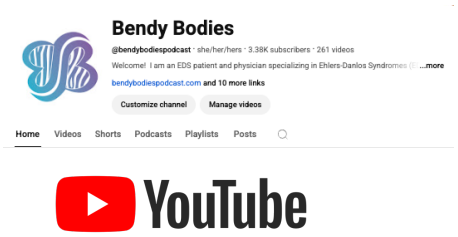
1. Adress the root cause whenever possible
2. The MENS PMMS method is one integrative pain treatment approach
3. YOU are the continuity piece
4. Access and keep all original documentation
   - Full encounter note
   - Full imaging reports
   - Full lab reports
5. Prepare your medical binder and “one sheet”
6. You often need just one HCP in your corner to start the ball rolling
7. Consider an advocate (GNA)
8. There are many reasons to be hopeful!

Where Can You Learn More and Help Spread Awareness?

- BendyBodiesPodcast.com
- HypermobilityMD.com
- hypermobilitymd.substack.com/
- bendybodies.threadless.com/
- Info@BendyBodies.org

You can help by subscribing to the Bendy Bodies Podcast, YouTube Channel, and Substack Newsletter, the Bendy Bulletin

The Bendy Bulletin



BENDY BODIES BOUTIQUE

External Gratitude to....

- To all my mentors, especially Dr. Pradeep Chopra
- All my Bendy Bodies Podcast guests – Ep 151 and counting
- My patients
- And my clients


Thank you, Bobby Jones Chiari &
Syringomyelia Foundation