**Food Allergies, Intolerances and Sensitivities:**

**Link to Chronic Pain**

Approximately 15-20% of adults have a food intolerances or sensitivity.[[1]](#endnote-1) These patients report a wide range of symptoms, including gastrointestinal distress including abdominal pain, gas/belching/burping, IBS, Crohn’s, ulcerative colitis, peptic ulcer, migraines, chronic fatigue, arthritis, rashes, respiratory distress, skin issues, weight gain, increased illnesses/immune imbalances, and chronic pain issues.[**1**](https://www.liebertpub.com/doi/full/10.1089/acm.2018.0310#B1).[**3**](https://www.liebertpub.com/doi/full/10.1089/acm.2018.0310#B3).[**6**](https://www.liebertpub.com/doi/full/10.1089/acm.2018.0310#B6),[**7**](https://www.liebertpub.com/doi/full/10.1089/acm.2018.0310#B7)

Current literature supports the fact that food allergies, intolerances and sensitivities are directly tied to metainflammatory sequelae and the release of GUT mucosal IgE and IgG type antibodies.[[2]](#endnote-2),[[3]](#endnote-3),[[4]](#endnote-4) This inflammatory signaling “drives” pain perception. How you deal with this metaflammation dictates patients health outcomes and their ability to overcome pain.

One of the main culprits of metainflammatory signaling is the GUT, including mucosal integrity and microbiome issues.[[5]](#endnote-5) As we know, food allergies/sensitivities and intolerances are closely related to GUT health integrity.

**Background**

Globally, it is estimated that 1 in 5 individuals suffer from chronic pain, with prevalence increasing with age, nutrient status, and stress level.[[6]](#endnote-6) The pathophysiology of chronic pain encompasses multifaceted sensory, immune, and inflammatory signaling interactions within both the central and peripheral nervous systems. Microglia, the resident macrophages of the central nervous system (CNS), are critically involved in the initiation and persistence of chronic pain.

A picture containing basket star

Description automatically generatedBriefly, under steady-state conditions, microglia serve as the sole immune cells of the central nervous system (CNS). As macrophages, these myeloid cells have been implicated in a wide array of CNS processes such as mediating inflammation, directly combating infection, and clearing cellular debris via phagocytosis.[[7]](#endnote-7) While some features of closely regulated pro-inflammatory activity are necessary for healthy neurodevelopment, unrestrained early-life inflammation may alter programming of the microglial population itself, leading for a lower baseline required for reactivation, thereby perpetuating inflammatory damage to the neuronal compartment later in life.[[8]](#endnote-8)

Microglia respond to local signals from the CNS but are also modulated by signals from the gastrointestinal tract. Emerging data from preclinical and clinical studies suggest that communication between the gut microbiome, the community of bacteria residing within the gut, and microglia is involved in producing chronic pain.[[9]](#endnote-9),[[10]](#endnote-10),[[11]](#endnote-11) Targeted strategies that manipulate or restore the gut microbiome have been reported to reduce microglial activation and alleviate symptoms associated with inflammation.[[12]](#endnote-12) This data indicates that concern for the gut microbiome in chronic pain patients is a high impact choice that improves pain outcomes and overall quality of life.

The microbiome is linked to the CNS via different proposed communication pathways:[[13]](#endnote-13)

* Bacterial metabolic products including tryptophan metabolites and short chain fatty acids (SCFA)
* Innervation of the gut by the vagus nerve
* Microbe-associated molecular patterns (MAMPs) that drive inflammation

The mechanism by which bacterial products or MAMPs trigger an inflammatory response in the brain may include entry to the circumventricular organs, areas in the brain where the BBB is less tightly regulated as in leaky gut syndrome.[[14]](#endnote-14)

Diagram

Description automatically generatedRecent evidence suggests that gut microbiota may also play a critical role in many other types of chronic pain, including inflammatory pain, headache, neuropathic pain, and opioid tolerance.  Patients with various pain “conditions”, including visceral pain, chronic pelvic pain, fibromyalgia, and osteoarthritis-related knee pain all display changes in microbiome diversity and abundance compared to healthy individuals.[[15]](#endnote-15),[[16]](#endnote-16) Restoring the gut microbiome following dysbiosis improves pain responses in animal studies of visceral, inflammatory and neuropathic pain.[[17]](#endnote-17)

Gut Microbes and microglia influence chronic pain by:[[18]](#endnote-18)

* Vagal nerve signaling
* GUT permeability issues
* Signaling mechanisms – TLR-4-mediated, cytokines, BDNF

Communication between gut microbes and the CNS is mediated by a combination of immune, enteric, and neural pathways that provide physical and chemical connections between the CNS and the periphery, and several experimental paradigms have been used to demonstrate that gut microbes influence many facets of CNS physiology.[[19]](#endnote-19)

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| The GUT microbiome is reportedly involved in several types of pain:   * Visceral pain – dyshomeostasis of GUT microbiota; internal pain generally caused by IBDs including IBS, Crohn’s, ulcerative colitis, dyspepsia, abdominal pain syndrome, infantile colic and interstitial cystitis, antibiotic use[[20]](#endnote-20),[[21]](#endnote-21) * Inflammatory pain – i.e., arthritic pain[[22]](#endnote-22) * Neuropathic pain – caused by damage from nerve trauma, chemotherapy, nutrient deficiencies, cancer, diabetes[[23]](#endnote-23) * Headache – studies report direct relationship of migraine headaches to GI disorders[[24]](#endnote-24) * Opioid tolerance - recent studies report long-term use of opioids is associated with microbial dysbiosis in humans[[25]](#endnote-25); long-term use of morphine can lead to disruption of the intestinal epithelial barrier and cause leaky gut and also cause enhanced bacterial translocation, leading to chronic inflammatory upregulation and immune disorders [[26]](#endnote-26) |

**Sympathetic pain**

GUT microbiome disruption can also lead to sympathetic dominance, which is reported to lead to many adverse health effects including PAIN as well.

In some chronic pain states, activity in sympathetic efferent neurons can exacerbate the pain and sympathectomies relieve it- these patients are said to have sympathetically maintained pain (SMP).[[27]](#endnote-27) An example is fibromyalgia (FM) – fibromyalgia is a syndrome characterized by chronic musculoskeletal pain, hyperalgesia on specific areas of tenderness (tender points) and by an autonomic nervous system dysfunction consistent with sympathetic overactivity.[[28]](#endnote-28)

GUT microbiota individualized diversity is critical to keep the inflammatory cytokines released by an inflamed GUT from leading to sympathetic nervous system dominance.[[29]](#endnote-29)

**Opioids**

The last decade has exposed the harsh realities of using opioids for pain control – it is not a great idea to use them. Besides the tolerance and dependency, opioids also lead to GUT dysbiosis which can initiate a host of debilitating and deteriorating chronic health conditions – metainflammation, type 2 diabetes, cardiovascular issues, sex and thyroid hormone dysregulation, immune issues, mood disorders, and yes even chronic pain.[[30]](#endnote-30) In conjunction with the issues of addiction and dependency, opioids are reported to:[[31]](#endnote-31)

* Modulate intestinal function
* Impair GUT Epithelial Integrity
* Lead to GUT microbial dysbiosis and bile dysregulation – alters xenobiotic metabolism
* Modulate immunity – Th1/Th2 imbalances
* Deplete Melatonin, DHEA and testosterone

**Conclusion**

Testing for IgE, IgG, IgG4 and complement vs. a food panel is very important for clinicians with patients experiencing PAIN. Certain foods may trigger GUT microbiome issues that then disrupt GUT-Brain signaling, thereby leading to increased pain issues.

Also, recommending a diet that minimizes foods that provoke these responses will decrease many types of inflammation and symptoms and is foundational to wellness. When we are recommending eating a personalized anti-inflammatory diet, we are optimizing patient’s chance for success and improved health and vitality. Remember that HPA axis dysregulation due to chronic stress and imbalanced cortisol levels is directly related to GUT issues, so take that into consideration when issuing a treatment plan. Proper diet, stress control and sleeping 7-8 hours a night results in stronger immunity and better protection for the body from many factors including foods that irritate the GUT and lead to increasing levels of inflammation and pain.

1. Lomer MC. Review article: the aetiology, diagnosis, mechanisms and clinical evidence for food intolerance. Aliment Pharmacol Ther. 2015;41(3):262-275. [↑](#endnote-ref-1)
2. Ohtsuka Y. Food intolerance and mucosal inflammation. Pediatr Int. 2015;57(1):22-9. [↑](#endnote-ref-2)
3. Chahine BG, et al. The role of the GUT mucosal immunity in the development of tolerance versus development of allergy to food. Curr Opin Allergy Clin Immunol. 2010;10(4):394-9. [↑](#endnote-ref-3)
4. Berlin MC. Mucosal antibodies in the regulation of tolerance and allergy to foods. Semin Immunopathol. 2012;34(5):633-42. [↑](#endnote-ref-4)
5. Lobionda S, et al. The role of gut microbiota in intestinal inflammation with respect to diet and extrinsic stressors. Microorganisms. 2019;7(8):271. [↑](#endnote-ref-5)
6. Centers for Disease Control CDC. [www.cdc.gov](http://www.cdc.gov). Accessed January 2021. [↑](#endnote-ref-6)
7. Salter MW, Stevens B. Microglia emerge as central players in brain disease. Nature Med. 2017;23:1018–27. [↑](#endnote-ref-7)
8. Bilbo SD, et al. A lifespan approach to neuroinflammatory and cognitive disorders: a critical role for glia. J Neuroimmun Pharmacol.  2012;7:24–41. [↑](#endnote-ref-8)
9. Lin B, et al. Gut microbiota regulates neuropathic pain: potential mechanisms and therapeutic strategy. J Headache Pain. 2020. [↑](#endnote-ref-9)
10. Guo R, et al. Pain regulation by gut microbiota: molecular mechanisms and therapeutic potential. Br J Anaeasth. 2019;1233(5):737-54. [↑](#endnote-ref-10)
11. Abdel0-Haq R, et al. Microbiome-microglia connections via the gut-brain axis. JEM. 2018;216(1):41-59. [↑](#endnote-ref-11)
12. Dworsky-Fried Z, et al. Microbes, microglia, and pain. Neurobiol. 2020;7(100045):1-8. [↑](#endnote-ref-12)
13. Erny D, et al. Communicating systems in the body: how microbiota and microglia cooperate. Immunology. 2017;150:7–15. [↑](#endnote-ref-13)
14. Cowan M, et al. Microglia: immune regulators of neurodevelopment. Front Immunol. 2018;9:2576. [↑](#endnote-ref-14)
15. Boer CG, et al. Intestinal microbiome composition and its relation to joint pain and inflammation. Nature Comm. 2019;10:4881. [↑](#endnote-ref-15)
16. Minerbi A, et al. Altered microbiome composition in individuals with fibromyalgia. Pain 1. 2019;160(11):2589-2602. [↑](#endnote-ref-16)
17. Dworsky-fried, Z et al. Microbes, microglia and pain. Neurobiol Pain 7. 2020;100045. [↑](#endnote-ref-17)
18. Dworsky-fried, Z et al. Microbes, microglia and pain. Neurobiol Pain 7. 2020;100045. [↑](#endnote-ref-18)
19. Mayer, E.A., K. Tillisch, and A. Gupta. 2015. Gut/brain axis and the microbiota. J. Clin. Invest. 125:926–938. [↑](#endnote-ref-19)
20. Grundy L,. et al. Visceral pain. Annu Rev Physiol. 2019;81:261-84. [↑](#endnote-ref-20)
21. O’Mahony SM ,. Et al. The gut microbiota as a key regulator of visceral pain. Pain. 2017;158:”S19-S28. [↑](#endnote-ref-21)
22. Xu ZZ, et al. Resolvins RvE1 and RvD1 attenuate inflammatory pain via central and peripheral activity. Nat Med. 2010;16:592-97. [↑](#endnote-ref-22)
23. Costigan M, et al. Neuropathic pain: a maladaptive respoinse of the nervous system to damage. Annu Rev Neurosci. 2009;32:1-32. [↑](#endnote-ref-23)
24. Camara-Lemarroy CR, et al. Gastrointestinal disorders associated with migraine: a comprehensive review. World J Gastroenterol. 2016;22:8149-60. [↑](#endnote-ref-24)
25. Xu Y, et al. Bacterial diversity of intestinal microbiota in patients with substance use disorders revealed by 165 mRNA gene deep sequencing. Sci Rep. 2017;7:3628. [↑](#endnote-ref-25)
26. Wang F, et al. Gut homeostasis, microbial dysbiosis and opioids. Toxicol Pathol. 2017;45(1):150-56. [↑](#endnote-ref-26)
27. McMahon SB. Mechanisms of sympathetic pain. Br Med Bull. 1991;47(3):584-600. [↑](#endnote-ref-27)
28. Zamuner AR, et al. Relationship between sympathetic activity and pain intensity in fibromyalgia. Clin Exp Rheumatol. 2015;33(Suppl 88):S53-7. [↑](#endnote-ref-28)
29. Toral M, et al. Critical role of the interaction GUT microbiota – sympathetic nervous system in the regulation of blood pressure. Front Physiol. 2019;10:231. [↑](#endnote-ref-29)
30. Wang F, et al. Gut homeostasis, microbial dysbiosis and opioids. Toxicol Pathol. 2017;45(1):150-56. [↑](#endnote-ref-30)
31. Schulzke J D, et al. Epithelial tight junctions in intestinal inflammation. Ann N Y Acad Sci. 2009;1165:294–300.

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