COMPLEX PAIN: IDENTIFYING AND OVERCOMING COMMON SOURCES OF TREATMENT FAILURE

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When standard conventional and integrative therapies fail or have limited efficacy in managing chronic pain, patients are left with limited options. These complex cases require a broader, and sometimes unorthodox, approach.

In most circles, chronic pain is defined as persistent or recurrent pain lasting longer than three to six months. However, it is important to appreciate that beyond the temporal aspect, pain of this nature lasts longer than the expected time of healing, serves no biological purpose (i.e., defense mechanism), and adversely affects one's physical, cognitive, and emotional well-being due to pathophysiological changes within the central nervous system.

The multifactorial and dynamic nature of chronic pain often makes it a moving target. As a result, practitioners need to consider the various identified drivers of chronic pain, which include:[1]

- Adaptive movement disorders (somatosensory cortex)
- Chronic inflammation
- Chronic stress, isolation, and trauma
- Descending inhibitory pathways augment pain microglia
- Peripheral/central sensitization
- Persistent nociceptive sensitization

From a conventional/allopathic perspective, drug-therapy is used to reduce inflammation or immune system activity, and/or block/modulate pain pathway transduction, transmission, and perception. Great strides have been made in the ability to manage acute pain with drug-therapy, but these strategies often fail to provide adequate relief in chronic cases due to tolerance, dependency, side effects, and the fact that they often do not address the multifactorial underlying root cause of the condition.

From an integrative/naturopathic perspective, assessment of the physical, biochemical, and mind-body factors that underpin the pathophysiology of chronic pain opens the door for comprehensive management of complex, treatment-refractory cases.

Physical Factors Involved in Chronic Pain
Structural
• Skeletal structure such as fractures, joint fusion, osteomalacia, osteophytes, osteoporosis, scoliosis, etc.
Functional
• Myofascial adhesions contributing to hypoxia, nerve impingement, dysfunctional movement patterns from impaired transmission of local and remote kinetic forces, etc.
• Joint dysfunction contributing to hypoxia and nerve impingement from impaired neuromuscular activity, etc.
• Muscle (strength/tonicity) imbalances resulting from poor posture, repetitive stress, sedentarism, etc.
• Visceral pain from congestion/hypoxia, infections, lack of nutrients, tissue damage, etc.

Biochemical Factors Involved in Chronic Pain
• Dysbiosis and/or intestinal hyperpermeability and subsequent endotoxin-mediated inflammatory gene expression
• Extracellular matrix congestion and subsequent impaired neuroendocrine communication and circulation from deposition of toxins
• Immune dysregulation from chemical/environmental/food antigens, chronic infections, chronic immune activation, impaired production of resolution mediators, mycotoxin-induced inflammation, etc.
• Impaired enzyme activity (e.g., nutrient deficiencies, pH imbalances, etc.).
• Mitochondrial dysfunction from impaired cellular respiration due to infection, nutrient deficiency, toxins, etc.
• Neuroendocrine dysregulation (e.g., hypothalamic-pituitary-adrenal-thyroid (HPAT) axis dysregulation).
• Redox imbalance from glutathione system dysfunction, poor diet, etc.

Mind-Body Factors Involved in Chronic Pain
Psycho-neuro-endo-immunology (PNEI)
• Deviant brainwave activity
• Gut-brain axis
• HPAT-axis
• Vagal tone

Mind-Body Factors Involved in Chronic Pain *continued*
Biopsychosocial
• Physical functioning
• Mental health
• Social and family functioning
Bioenergetic
• Biophotons
• Chakras
• Consciousness
• Miasms
• Prana/Qi

It is common for NDs to assess and successfully treat chronic pain by addressing the common drivers of non-resolving inflammation, gut dysbiosis, HPAT-axis dysregulation, heavy metals, and mitochondrial dysfunction, amongst other breakdowns in normal physiology. However, despite comprehensive and effective treatments aimed at addressing the underlying root cause of illness, a handful of patients will experience little to no benefit. There are various factors that may contribute to treatment failure, including but not limited to: biofilm, electromagnetic frequency/radio frequency (EMF/RF) exposure, mycotoxins, oral health, and scars. These factors will be explored in more detail throughout this article.

BIOFILM

It is well known that pathogens prompt inflammation. When gut dysbiosis is present, gastrointestinal epithelial cells produce NFkB that drives inflammation and tissue destruction.[2] Systemically, and on other mucosal surfaces, recognition of pathogen-associated molecular patterns (PAMPs) by immune cells prompt fibroblasts and macrophages to release TNF-a, IL-1B, IL-6, and IL-10, triggering inflammation.[3] In addition, various pathogens have been implicated in rheumatologic conditions.[4-8] The ensuing pain results from immune-mediated inflammation as well as nociceptor activation and sensitization.[9]

Under optimal conditions, the immune system can identify and eradicate microbes. However, bacteria and other pathogens have developed the ability to evade immune surveillance and eradication via biofilm: adhesive extracellular matrix formations that act as a barrier to efficient management of microbial burden.[10] Biofilm can form anywhere in the body where water is present, with a common and well-known example being dental plaque. These multicellular structures are highly resistant to standard antimicrobial therapies, contributing to antibiotic resistance, chronic immune activation, and non-resolving inflammation.[11]

In order to alter the course of non-resolving inflammation related to the presence of chronic infections, biofilm disruption might need to be considered based on the chronicity/persistence of the biofilm and the vitality of the patient. The absence of

feasible laboratory testing means practitioners must use sound clinical judgment and implement empirical trials when warranted.

For milder cases, agents such as phenolics, proteolytic enzymes, xylitol, stevia, and black cumin are used. In more advanced cases, stronger agents such as nanoparticle silver, EDTA, and bismuth may need to be considered.[12] Note that it can take upwards of 12 weeks or longer to see clinical outcomes, and patients may experience aggravation of symptoms as the immune system activates and targets newly-exposed pathogens. This can be mitigated by eradicating what is present/exposed before disrupting biofilm, as well as supporting the body with agents that provide immunomodulatory, anti-inflammatory, and detoxification effects such as Astragalus, Reishi, Curcumin, and Milk Thistle. Further, it may be beneficial to pulse and/or rotate biofilm-disrupting agents (e.g., 3-5 days on and 3-5 days off and/or alternate between 2-3 agents on a weekly-biweekly basis). Successful eradication of chronic infections through the disruption of biofilm can counteract chronic immune activation and break the cycle of non-resolving inflammation.

EMF/RF

There is ongoing debate as to the theoretical and real health concerns associated with EMF/RF exposure. Although human research is limited, animal models have demonstrated altered energy metabolism,[13] attenuated analgesic response,[14-16] immunosuppression,[17-19] modulation of the nitric oxide/peroxynitrite ($NO\text{-}ONOO^-$) pathway,[20,21] and potentiation of pathogens.[22-24] With so many uncertainties regarding the impact of EMF/RF on human health, and the ever-expanding reach of wireless technology, NDs can become educated on herbs and nutrients that show promise in reducing these potentially harmful effects. These substances include:

- B-glucan[25]
- Garlic, onion, ginger[26]
- EGCG[27]
- Melatonin[28]
- N-acetyl cysteine[29]
- Propolis[30]
- Rosmarinus[31]
- Selenium, L-carnitine[32]

More research is needed to understand the health implications of EMF/RF exposure in humans, and how Naturopathic treatments can be utilized successfully. However, for the time being the priority is to avoid exposure when ever possible (i.e., hardwire the home).

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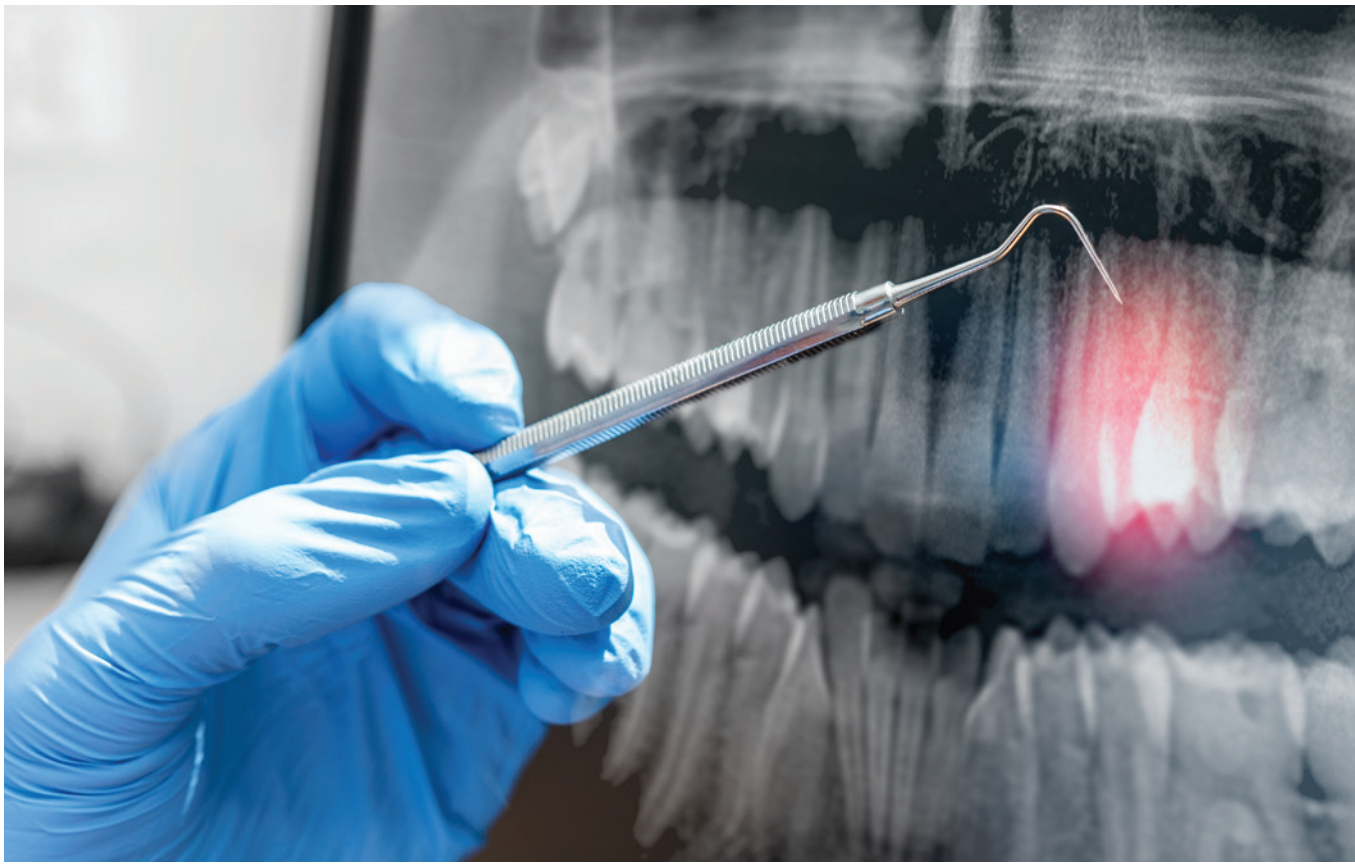
MYCOTOXINS

Mycotoxins (i.e., mould biotoxins) act as significant triggers of chronic immune activation via direct microbial effects, as well as dysregulation of host immune response mechanisms. Individuals often become exposed to mycotoxins following contact with a water-damaged building (i.e., flooding). It is postulated that the ensuing systemic chronic inflammation may relate to abnormalities of neuropeptides MSH and VIP, pro-inflammatory cytokines, complement activation, VEGF, erythropoietin, TGF-B1, and cellular immunity.[33] It is the experience of the author that regulation of chronic inflammation, and its subsequent influence on pain,



is very difficult to achieve when ongoing mycotoxin exposure is present. Management strategies are often quite drastic, ranging from remediation of the affected living space to moving to a new home/climate. When these options are not feasible, detoxification and glutathione system support (i.e., liposomal/IV glutathione, N-acetyl cysteine, alpha-lipoic acid, Gotu Kola, cordyceps, L-glutamine, Milk Thistle, selenium, vitamins A/C/E, etc.) may be indicated. Binders, such as bentonite clay, activated charcoal, and diatomaceous earth, are often used to assist in the elimination of mycotoxins.

ORAL HEALTH

Periodontitis, a dysbiotic chronic inflammatory disease involving the gingiva, periodontal ligaments, and alveolar bone, has been associated with a range of systemic diseases including cardiovascular disease, rheumatoid arthritis, and several forms of cancer.[34] Several mechanisms have been postulated to explain these connections. Firstly, that periodontitis-associated pro-inflammatory cytokines travel systemically, contributing to inflammation. Secondly, oral tissue ulceration can facilitate systemic dissemination of periodontal bacteria, prompting immune-mediated inflammatory responses. Lastly, one can only imagine the volume of periodontal bacteria introduced to the distal regions of the gastrointestinal tract via swallowing. The ensuing dysbiosis can contribute to local epithelial inflammation, intestinal hyperpermeability, and subsequent endotoxemia, further compounding systemic inflammation.[34]

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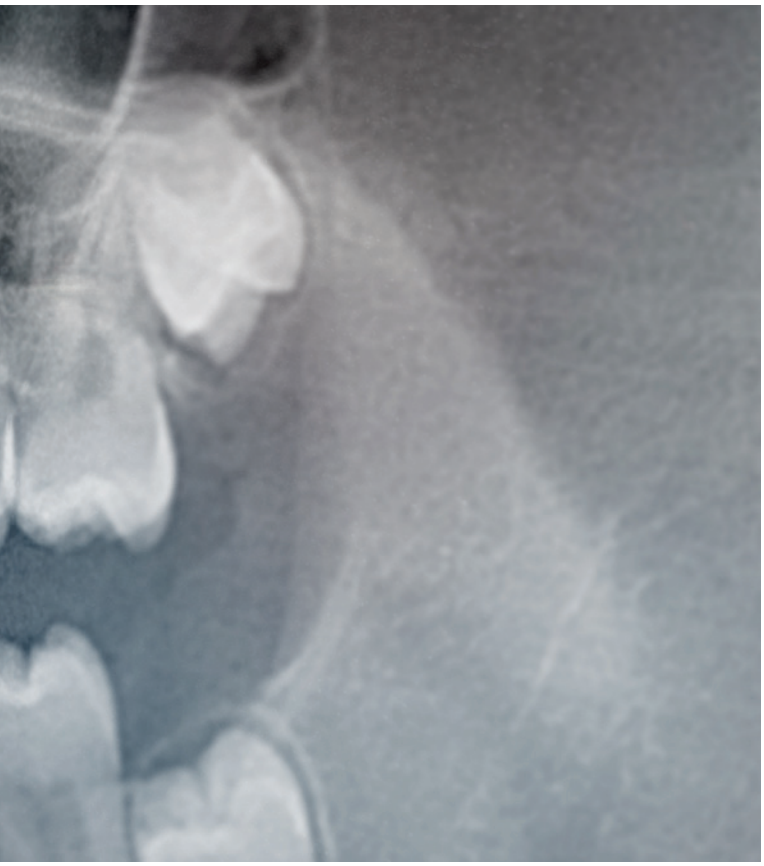
Much like periodontitis, though controversial, is jaw osteonecrosis (JON; sometimes termed cavitations). Defects of the jaw were identified in research as early as the 1860s, though were largely overlooked until the 1970s at which time JON was incorporated into oral pathology textbooks. The controversy lies in the dispute between whether or not osteonecrosis can occur in alveolar processes of the human mandible and maxilla, despite the fact that this can be seen in almost all other human bones.

JON is believed to occur for various reasons, one of which being persistence of pathogens or necrotic tissue following root canal procedures, with either scenario contributing to local inflammation.



The general consideration for those that identify JON as a legitimate pathology is that JON lesions contain abundant pro-inflammatory cytokines, particularly "regulated upon activation, normal T-cell expressed and secreted" (RANTES) and fibroblast growth factor (FGF-2). Given the role of RANTES and FGF-2 in the pathogenesis of various systemic diseases, such as arthritis, cancers, colitis, and nephritis, it is suspected that JON acts as a low-grade inflammatory signal that contributes to the upregulation of these inflammatory messengers and subsequent illness.[35]

Intestinal anti-dysbiotic protocols, a focal point of many Naturopathic chronic pain management protocols, may yield limited efficacy when oral health is not addressed appropriately. Though these conditions require the involvement of a regulated oral/dental health professional, NDs can screen for oral heath medical history, routine dental cleanings, and visual indications of dental involvement during the intake process. In addition to referring patients to regulated oral/dental health professionals, NDs can implement strategies to support oral hygiene such as an antimicrobial oral rinse containing cetylpyridinium, hydrogen peroxide, and/or essential oils, as well as oral probiotic therapy such as Streptococcus salivarius.[36]

SCARS

Fascia is the connective tissue that unifies the musculoskeletal and visceral systems, and coordinates neuroendocrine function via its continuity with the extracellular matrix. This long underappreciated anatomical feature is gradually gaining more widespread attention for its pivotal role in the maintenance of biomechanical function, as well as overall health.

Fascia facilitates the transmission of kinetic forces that support appropriate locomotion and movement patterns. Moreover, research into the act of grounding is elucidating the role of fascia in redox balance. It is understood that fascia, through its extension into the extracellular matrix, is a liquid-crystalline semiconductor which can deliver mobile electrons (drawn from the earth during grounding) throughout the body, subsequently protecting cells, tissues, and organs from oxidative stress or following an injury.[37]

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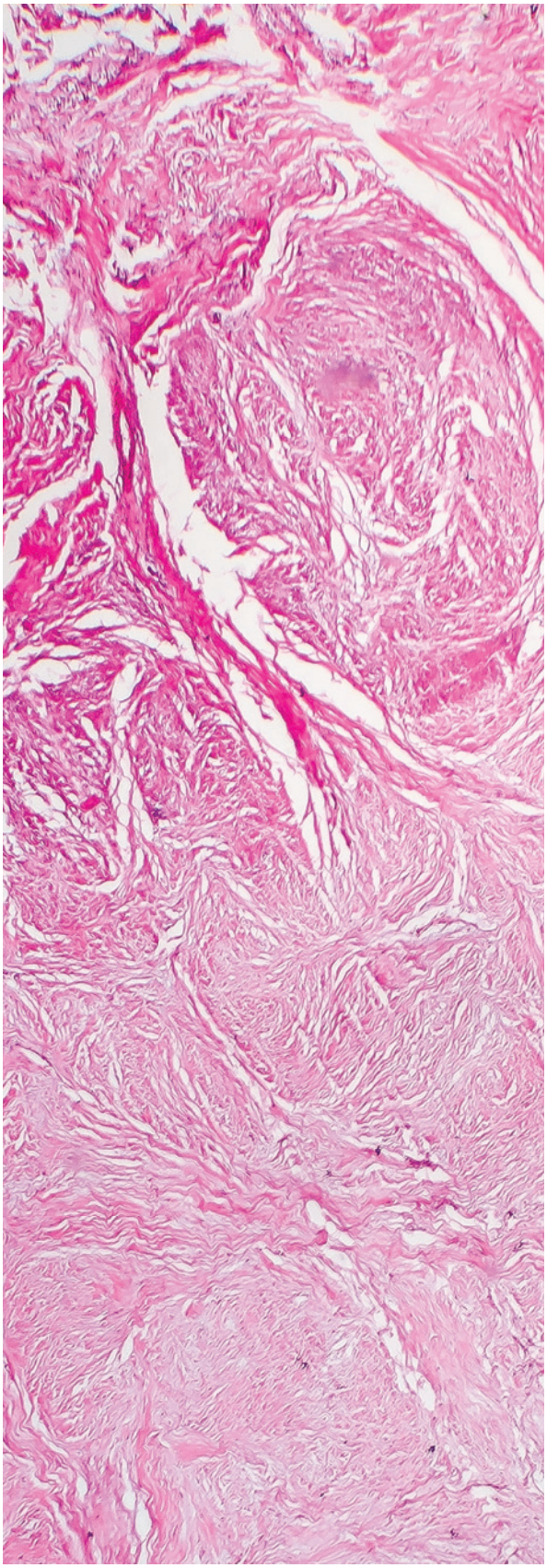
Scars attained through physical trauma compromise tensegrity (tensional integrity) of connective tissue, influencing autonomic regulation and nociception, contributing to treatment failure.[38,39]

Various techniques are used to address scar tissue, including manual therapy (including instrument-assisted soft tissue mobilization), injection-based therapy (including Neural Therapy), and microcurrent devices (including Frequency Specific Microcurrent). Due to limitations in scope of practice in Ontario, local NDs will generally rely on manual therapies. Thankfully, these therapies have the potential to be quite effective, and can be paired with oral systemic/proteolytic enzyme therapy such as serratiopeptidase, bromelain, papain, trypsin, and rutin, for further benefit.

CONCLUSION

Within the context of complex chronic pain, it is important to appreciate the concept of total body burden. In many cases of persistent and treatment-refractory pain, there are a multitude of factors that exert a cumulative pathophysiological effect. One can consider the analogy of the human body as a bucket; various factors contribute to the bucket filling up and when the bucket overflows, symptoms present. If the water level of one's bucket is already near the brim, it will not take much for the bucket to overflow and seemingly insignificant stimuli can become quite problematic. If, however, a buffer can be established by reducing the water level of the bucket by addressing several offending factors, the patient's resilience increases. There has never been, and probably never will be, a silver bullet to cure chronic pain. As NDs, we have the knowledge, skill, and treatment strategies to think outside of the box while applying sound science and traditional systems of medicine to support the body's ability to heal.



REFERENCES

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