“Somatovisceral Pain”

Let’s talk about pain related to thoracic structures:
- Neurophysiological
- Musculoskeletal
- Visceral
- Cellular
- Molecular

Timeline Today

- 5 minutes: Introduction
- 45 minutes: Thoracic Pain Mechanisms
- 10-minute: Break
- 45 minutes: Other Considerations and Questions
- 10 minutes: Summary and Wrap Up

Goal of this lecture series: share clinical experience, enhanced by evidence, built on the structured foundation of IAOM Knowledge of anatomy, precise clinical diagnosis and specific treatment.

Goal for today: Peek into a potentially unfamiliar world of understanding neurophysiology as recently researched

Objectives: Together:
- Let’s go down the rabbit hole of new discoveries and directions in pain, as related to the complex region of the trunk
- Then let’s climb out again – not necessarily with a perfect understanding, but – with a better understanding and perhaps some new clinical tools for the complex patient
Basics of referred pain in the thoracic spine

Central Neurophysiology

Receptive Field

• Receptive Field - receptive field of an individual sensory neuron is the region in which a stimulus will trigger the firing of that neuron
  - Peripheral
  - Central
    - Projection neurons and interneurons

• Size of field can change due to excitability and inhibitory segmental processes

Basics of referred pain in the thoracic spine

Receptive Field

Influencers

- Increase in Size
  - Sympathetic overactivation
  - Sleep, diet, stress, fear
  - Loss of central inhibition
  - Ongoing nociception or neurogenic inflammation
  - Substance P
  - Silent nociceptors
  - Nerve growth

- Decrease in Size
  - Dampen sympathetic nervous system
  - Improve central inhibition
  - Reassurance
  - Treat painful structure
  - Change pH
  - Movement, sleep, nutrition

Visceral Pain: Somatic Consequences

Transferred to the body wall (somatic): Area is dependent on:

- Organ involved
- Level of innervation

Heart: C8 - T8
Lungs: T3 - T10
Stomach: T5 - T9
Spleen: T6 - T10
Caecum & Duodenum: T6 - T10
Pancreas: T7 - T9
Liver & Gall Bladder: T7 - T10
Appendix: T9 - T11
Kidney: T9 - T12

Visceral pain, involving thoracic, abdominal, and pelvic organs, is the most common type of chronic pain

- Poor understanding of its pathogenesis makes it difficult to manage
  - Organ(s) in the thoracic and abdominal cavities may be innervated by both the vagal and spinal nerves with central terminals in the brainstem and spinal cord, respectively.
  - Other pelvic organs are innervated by the pelvic nerves, which terminate in the lumbosacral spinal cord
  - As a result, visceral pain is diffuse and often referred to a distal superficial location.
  - Branching of C-nociceptor axons contribute to cutaneous hypersensitivity in visceral inflammation.

Viscero-somatic Pain

Basics of referred pain in the thoracic spine

- Referred hyperalgesia from viscera is also often accompanied by trophic changes, typically a thickening of the subcutaneous tissue and some degree of local muscle atrophy.
- Both findings presumably result from viscerosomatic reflexes activated by the massive afferent visceral barrage, and both may persist long after the primary visceral problem is in remission.
- Visceral pain can affect the somatic tissues in the referred area for months or even years.

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Viscero-somatic and Central Sensitization

- Visceral nociception readily sensitizes the central nervous system, causing referred somatic pain and hyperalgesia via somato-visceral convergence.
- Chronic pain after cardiac surgery:
  - Hyperalgesia in the perioperative period increases vulnerability to development of chronic pain.
  - Other predictive factors include acute postoperative pain and younger age.
- Previous evidence shows that gastrointestinal, biliary, renal, hepatic, heart, and pulmonary disorders may evoke referred pain to the upper quadrant of the body, including the neck region.
- Visceral disorders may evoke referred altered sensitivity, e.g., hyperalgesia or allodynia.
  - For instance, the radiation of pain to the neck and/or upper extremity that occurs during acute coronary syndromes is experienced in more than 65% of cases.
  - Neural hernias and gastrointestinal reflux disease (GERD) may involve referred pain to the neck.
- Discrimination between visceral and somatic sources of pain is not always evident, and if it is not achieved, it may lead to extensive diagnostic procedures and ineffective treatment approaches.
- In a systematic search of trials about neck pain:
  - Visceral etiology was not considered in 80% of the trials on neck pain, showing a low level of suspicion both in research and clinical settings.

Examples:
- Irritable bowel syndrome
- Fibromyalgia
- Chronic fatigue syndrome
- TMJ disorder
- Idiopathic LBP
- Multiple chemical sensitivity
- Tension-type HA
- Interstitial cystitis
- Chronic pelvic pain
- Myofascial pain syndrome

Viscero-somatic

- Cross sensitization typically occurs between organs within the thoraco-upper abdominal or pelvic-lower abdominal areas.
- "Cross-talk" between the two areas has been reported.
  - Peripheral and central mechanisms.
  - Growing support to simultaneously address pathology in other neurally related organs.
  - Behavioral, morphological and physiological.

Viscero-visceral

Functional Somatic Syndromes

- Conditions in which physical symptoms are not fully explained by an established, alternative medical disorder.
- Common, disabling, and incur a significant use of health care resources.
- Must be interpreted from a neurophysiological perspective.
  - Central sensitization.
  - ...and so much more.


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Basics of referred pain in the thoracic spine

**Viscero-visceral**

- Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS), historically considered as regional gastrointestinal disorders with heightened colonic sensitivity.
- Increasingly recognized to have concurrent dysfunction of other visceral and somatic organs, such as urinary bladder hyperactivity, leg pain, and skin hypersensitivity.
- Interorgan sensory cross talk, termed “cross-organ sensitization.”
  - Organs, anatomically distant from one another, afferently interact through projecting their sensory information into dorsal root ganglia (DRG) and then the spinal cord for integrative processing.
- Dichotomizing afferents, sensory convergence in the spinal cord, spinal nerve conduction, and extensive sprouting of central axons of primary afferents each has significant roles in the process of cross-organ sensitization.
- Retrograde sensitization (I) of primary afferent neurons by spinal mediators creates a feed-forward loop in visceral and viscerosomatic cross-organ sensitization.

Basics of referred pain in the thoracic spine

**Viscero-somatic**

- Irritable bowel syndrome (IBS) is one of the most debilitating and common gastrointestinal disorders; nevertheless, its pathophysiology is still unclear.
- It affects 11% of the world’s population.
  - Characterized by alternating periods of pain and/or motility disorders with periods of remission and without any evidence of any structural and functional organic variation.
- Altered contractile ability of the diaphragm muscle might adversely influence intestinal motility.
  - The diaphragm has neurological links in correlation with the presence of chronic symptoms associated to IBS, like chronic low back pain, chronic pelvic pain, chronic headache, and temporomandibular joint dysfunction, vagus nerve inflammation, and depression and anxiety.
  - Interplay between an individual’s breath dynamic and intestinal behavior is still an unaddressed point in the physiopathology of IBS.
- It is worth considering (and researching) the importance of breathing in this syndrome.

Basics of referred pain in the thoracic spine

**Viscero-somatic or Somato-visceral**

Back pain and spinal pathology in patients with functional upper abdominal pain

- Viscerosomatic or somatovisceral reflexes with trigger zones either in the viscera or in the skin, muscles, tendons, or ligaments could be part of the pathophysiology in this syndrome.
- Fifty-one percent of the patients had symptoms of irritable bowel syndrome, and 41% had heartburn, which was significantly related to the experience of back pain.
- And the back pain was further related to local pathology....!!
Many pain conditions tend to co-occur, influencing the clinical expressions of each other in various ways. The pathophysiology of these pain associations is complex and multifactorial...

Major interactions observed in particular, in visceral pain (especially ischemic heart disease, irritable bowel syndrome, dysmenorrhea/endometriosis and urinary pain), fibromyalgia, musculoskeletal pain and headache.

Visceral pain, headache and musculoskeletal pains (myofascial pain from trigger points, joint pain) can enhance and perpetuate pain symptoms from visceral pain conditions and trigger migraine attacks when located in the referred pain area from an internal organ or in cervico-facial areas, respectively – [somato-viscero-somatic]

Effective treatment of one of the conditions can improve symptoms from the other, thus suggesting a systematic and thorough evaluation of the pain patient for a global effective management of their suffering.

Peripheral and central sensitization are key in the transition from acute to chronic pain. Development of chronic pain is particularly common following various surgical procedures, with many postsurgical patients experiencing persistent pain for significant periods.

The incidence of chronic post surgical pain, CPSP, can be reduced through early identification of perioperative, genetic, physiologic, and psychologic factors.

Models predicting the development of CPSP continue to improve and may help focus preventative efforts in patients at highest risk.

There is a growing body of evidence supporting the use of multimodal analgesia and anesthetic techniques in the reducing rates of CPSP development.

Considerations of chronic pain in the trunk

Pain after thoracic surgery - acute

Consequence of Acute Pain in Thoracotomy:
Pain is associated with acute physiological changes and adverse clinical consequences as listed by organ system below.

<table>
<thead>
<tr>
<th>System</th>
<th>Physiological Change</th>
<th>Consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>Decreased lung compliance, hypoventilation, reduced capacity</td>
<td>Hypoxia and hypercarbia</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Increased heart rate</td>
<td>Increased risk of heart attack or congestive heart failure</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Increased catecholamine, adrenocorticotropic hormone, cortisol, angiotensin</td>
<td>Hyperglycemia, catabolic state</td>
</tr>
<tr>
<td>Hematological</td>
<td>Increased blood viscosity, altered coagulation pathways, fibrinolysis</td>
<td>Increased risk of thromboembolism</td>
</tr>
<tr>
<td>Immunological</td>
<td>Impaired function</td>
<td>Increase risk of infection</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Reduced emphyse and bowel motility</td>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td>Urological</td>
<td>Increased sympathetic outflow</td>
<td>Urinary retention</td>
</tr>
</tbody>
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Acute pain can lead to central sensitization, which reduces the mechanical threshold and exaggerates the response to noxious stimuli.

Risk factors for chronic post surgical pain, CPSP
• Type and approach of surgery, female gender, being a young adult, genetic predisposition, and psychosocial factors
• Preexisting patient conditions
  • pain present preoperatively, and any pre-existing painful conditions in other parts of the body
  • perioperative factors, such as duration and type of surgery, extent of nerve damage intraoperatively, and severity and duration of acute postoperative pain.
• A recent study has also demonstrated that the severity of pain in CPSP is correlated with the mRNA expression of the signal transduction genes...

Chronic postsurgical pain
preventive strategy may help patients avoid the distress of chronic pain.

- The preventive strategies include modification of the surgical technique, good pain control throughout the perioperative period, and preoperative psychological intervention focusing on the psychosocial and cognitive risk factors.
- Because chronic post surgical pain usually has a neuropathic pain component;
  - High voltage-dependent calcium channel antagonists, antidepressants, topical lidocaine and topical capsaicin are the main pharmacological treatments.
  - Paracetamol, NSAIDs and weak opioids can be used according to symptom severity.
  - Other drugs that may be helpful are ketamine, clonidine, and intravenous lidocaine infusion.
- Pain interventions; examples include transcutaneous electrical nerve stimulation; botulinum toxin injections; pulsed radiofrequency, nerve blocks, nerve ablation, neuromodulation via spinal cord stimulator.
- Physical therapy, cognitive behavioral therapy and lifestyle modifications are also useful for relieving the pain and distress.

Considerations of chronic pain in the trunk
Perception
• It is well-recognized that, despite similar pain characteristics, some people with chronic pain recover, whereas others do not.
• There are many possible contributions and interactions of biological, social, and psychological perturbations that underlie the evolution of treatment-resistant chronic pain.
  - Behavior and brain are intimately implicated in the production and maintenance of perception.
  - Differences in relative contribution of dimensions such as stress, age, genetics, environment, and immune responsivity may produce different risk profiles for disease development, pain severity, and chronicity.

Other that may be helpful are ketamine, clonidine, and intravenous lidocaine infusion.

Considerations of chronic pain in the trunk
Perception
• It is theoretically possible for all people to develop chronic pain. What differentiates responses to the same perturbation? Perturbations may take place at genetic, cellular, neuronal, whole brain systems, and at psychological levels.
  • We propose the concept of "stickiness" as capturing the multiple influences on the persistence of pain and pain behavior, and their stubborn resistance to therapeutic intervention.
  • The neurobiology of reward and aversion address how alterations in synaptic complexity, neural networks, and systems may contribute to pain stickiness.
New discoveries in chronic thoracic pain

Genetics and EpiGenetics

- Persistent or chronic pain is a complicated clinic condition that impacts the lives of approximately a quarter of the population
- This clinic condition can be developed from acute pain resulting from tissue damage or be associated with numerous human diseases
- Similar to varied individual pain sensitivity, there is a large difference in vulnerability of individuals to develop persistent pain
- Although the mechanisms underlying this variation remain largely unknown, efforts have been spent to look for genetic mechanisms and gene expression


Micronutrient Deficiencies

- Virtually all gastric surgical procedures may over time lead to micronutrient deficiencies as a result of the above-exposed link between a healthy stomach and the homeostasis of several micronutrients such as iron, cobalamin, ascorbic acid, and magnesium amongst the most important.


- Genetic testing can be a critical tool for health and medical diagnosis, treatment, and prevention. Genetics along with environment and behavior are the key to providing the best assessment, intervention, and tailored changes for an individual.
- Nutrigenomics is the study of the effect of specific nutrients on gene expression
- Nutrigenetics refers to the study of genetic variations of an individual
- Both nutrigenomics and nutrigenetics may be a strategy to improve understanding of the gene-diet interaction and to prevent chronic nutrition-related diseases
- Since many micronutrients control energy metabolism, deficiencies can result in an array of symptoms, ranging from anemia to neurological dysfunction
- Subclinical micronutrient deficiency can lead to increased risks for coronary artery disease, infections, age-related macular degeneration, and oxidative damage

Genetic Variants and Their Effect on Vitamin and Mineral Pathways and Response to Supplementation

- Genetic variations in specific genes among vitamin and mineral metabolic pathways are associated with altered nutrient homeostasis and adverse health outcomes.
- Single nucleotide polymorphisms (SNPs), are the most common type of genetic variations among people.
- In the human genome, SNPs may occur at every 1000 nucleotides, which means that a person may have 4–5 million SNPs.
- SNPs are known to impact micronutrient status or chronic diseases related to micronutrient metabolism.
- The ability to identify a person having genetic variants involved in vitamin and mineral metabolism may reduce the chance of developing micronutrient deficiencies that can lead to various diseases.
- Studies that associate genetic variants and micronutrient metabolism have researched vitamin D, vitamin B12, folic acid, thiamine, and iron.

Epigenetics

- Although intensive research on neurobiological mechanisms of chronic pain has been carried out, this disorder is still poorly managed by current drugs such as opioids and nonsteroidal anti-inflammatory drugs.
- Inflammation, tissue injury and/or nerve injury-induced changes in gene expression in sensory neurons of the dorsal root ganglion, spinal cord dorsal horn and pain-associated brain regions are thought to participate in chronic pain genesis; however, how these changes occur is still elusive.
- Epigenetic modifications including DNA methylation and covalent histone modifications control gene expression.
- Recent studies show that peripheral noxious stimulation changes DNA methylation and histone modifications and that these changes may be related to the induction of pain hypersensitivity under chronic pain conditions.

New discoveries in chronic thoracic pain

Genetics - Micronutrition

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Epigenomics

- Neurological and inflammatory pain promote a large number of persisting adaptations at the cellular and molecular level, allowing even transient tissue or nerve damage to elicit changes in cells that contribute to the development of chronic pain and associated symptoms.
- There is evidence that injury-induced changes in chromatin structure drive stable changes in gene expression and neural function, which may cause several symptoms, including allodynia, hyperalgesia, anxiety, and depression.

- Chronic visceral pain is persistent pain emanating from thoracic, pelvic, or abdominal origin that is poorly localized with regard to the specific organ affected.
- Prevalence can range up to 25% in adult population as chronic pain is a common feature of many severe diseases, which may be mediated by distinct structural or neurological abnormalities.
- Mounting evidence suggests that changes in epigenetic mechanisms are involved in the top-down or bottom-up regulation of pain pathways and the development of chronic pain.
- Epigenetic changes can lead to long-term alterations in gene expression profiles of neurons and consequently alter functionality of peripheral nerves, dorsal root ganglia, spinal cord, and brain neurons.
- However, epigenetic modifications are dynamic, and thus, detrimental changes may be reversible. Hence, external factors/therapeutic interventions may be capable of modulating the epigenome and restore normal gene expression for extended periods of time.
- Targeting these epigenetic mechanisms, such as persistent stress, may represent a novel approach to treat chronic visceral pain.


Epigenetics is the study of heritable modifications in gene expression and phenotype that do not require a change in genetic sequence to manifest their effects. Environmental toxins, medications, diet, and psychological stresses can alter epigenetic processes such as DNA methylation, histone acetylation, and RNA interference. As epigenetic modifications potentially play an important role in inflammatory cytokine metabolism, steroid responsiveness, and opioid sensitivity, they are likely key factors in the development of chronic pain. Although our knowledge of the human genetic code and disease-associated polymorphisms has grown significantly in the past decade, we have not yet been able to elucidate the mechanisms that lead to the development of persistent pain after nerve injury or surgery. Significant laboratory and clinical data support the notion that epigenetic modifications are affected by the environment and lead to differential gene expression. Epigenetic analysis is needed to identify mechanisms critical to the development of chronic pain after injury, and may provide new pathways and target mechanisms for future drug development and individualized medicine.

- Chronic pain after surgery is a major public health problem and a major concern for perioperative physicians. Thoracic surgery presents a unique challenge, as thoracotomy is among the highest risk surgeries to develop persistent postsurgical pain. Recent advances have linked chronic pain states to genetic and epigenetic changes. It is possible that epigenetic changes driving chronic pain occur in the perioperative setting via histone modification and DNA methylation. The transition from acute to chronic pain after thoracic surgery may be mediated by epigenetics. Research is examining pharmaceuticals that inhibits histone modifications and controls DNA methylation. Structural and chemical changes in DNA are influenced by experience (such as pre- or post-surgical pain). Epigenetic modifications are remarkably reversible and heavily influenced by the environment, to include nutrition.
Myofascial Syndrome of is difficult to Differential making part because abdominal wall pain: complex urinary, may for 10% medical musculoskeletal, and endocrine are further influenced by psychological factors...

Abdominal Myofascial Pain Syndrome
- Primary cause of chronic pelvic pain, CPP, is difficult to determine, making treatment potentially inadequate, in part because of the complex interaction between gastrointestinal, urinary, gynecologic, musculoskeletal, neurologic and endocrine systems, that are further influenced by psychological factors...
- Prevalence of CPP is 3.8% among women aged 15–73 years, and from 14% to 24% among women of reproductive age, with a direct impact on marital, social and professional life.
- About 60% of women with CPP never receive a specific diagnosis and 20% are never undergo evaluation
- There is evidence that the musculoskeletal system is compromised in some way in most women with chronic pelvic pain and that in 15% of these cases chronic pelvic pain is associated with abdominal myofascial pain syndrome.

Anterior Cutaneous Nerve Entrapment Syndrome
- Clinical findings:
  - Superficial tenderness
  - Positive skin pinch test
  - Carmalt's test
    - Palpate the tender region, ask patient to tense abdominal wall by either elevating the head/shoulders or by straight leg raising
    - Positive: Pain is the same or worse indicating neuropathy
    - Negative: Pain is better, indicating a visceral source that is now being protected by the overlying muscle 'guard'

Differential diagnosis of abdominal pain
- Anterior Cutaneous Nerve Entrapment Syndrome
  - Intercostal nerve entrapment
    - Cutaneous branch at the level of the rectus abdominis, called anterior cutaneous nerve, T7-T11 generally
    - Site accounts for 15% to 30% of patients referred to pain clinic for nonspecific abdominal pain
  - Patient complaints:
    - Sharply localized pain, with dull persistent ache, occasionally refers posteriorly
    - Pain ranges from mild to excruciating, can be intermittent or constant, can be relapsing-remitting
    - Worse with conditions that increase abdominal pressure or cause nerve traction
    - Cleavage, post-operative scarring, tight clothing
    - Better with sitting or lying

Differential diagnosis of abdominal pain
- Anterior Cutaneous Nerve Entrapment Syndrome
  - Chronical abdominal wall pain
    - May account for 10% of general medical practice
  - Musculoskeletal Differential Diagnoses, includes
    - Abdominal myofascial pain syndrome
    - Nerve entrapment
      - Rectus abdominis nerve entrapment syndrome
        - Involving cutaneous branch of one or more thoracic intercostal nerves
      - Ilioinguinal and iliohypogastric nerve entrapments (T12-L1)
      - Nerve root irritation: thoracic
      - Slipped rib tip (8th to 10th)
Treatment

- Anterior cutaneous nerve block
- Intercostal nerve block
- Fasciotomy

**Note:**
- Also described in children
- Cases with 10 to 16 and year old's
- All had pain with nausea
- Somato-visceral referral


Clinical manifestation of lateral thoracic disc herniation at T10-11, T11-12, or T12-L1
- Severe abdominal pain
- May have abdominal weakness
- Lateral disc herniation or foraminal stenosis causing nerve root compression/irritation
- Can cause severe chest or abdominal pain and dysesthesia
- Pain can be visceral in nature
- Absent abdominal reflexes
- Abdominal weakness may be overlooked, but coughing, sneezing or straining may accentuate a ‘bulging’ at the weak zone of the abdominal wall.
Differential diagnosis of abdominal pain

Slipping Rib Tip Syndrome

- In a sports clinic:
  - 54 athletes of 162 were identified with slipping rib tip
  - 70.4% were female, 29.6% male
  - Mean age 19, but ranged from 4 to 40 years
  - Average number of specialist consultations was 2.3
  - 1/5 of patients given psychiatric diagnosis

Sports: most commonly running, lacrosse, field hockey, rowing

Treatment
- NSAIDs, topical anti-inflammatories
- Manual therapy
- Injections
- Surgical resection

Epigenetics and Chronic Pain

- Aberrations in the epigenetic landscape have previously been associated with human diseases such as cancer and schizophrenia, and drugs that target epigenetic processes are currently used as therapeutic agents.

- Epigenetic processes might regulate long-term pain states and targeting epigenetic mechanisms might be useful for the management of chronic pain.
  - Recent animal studies have reported injury-induced changes in epigenetic processes in the central nervous system.
  - The picture that has emerged is that of very complex epigenetic programs that depend on the injury.
  - However, some studies have reported the successful use of nonspecific epigenetic tools to improve the hypersensitivity that develops in animal models of long-term pain states.

- Summary:
  - The field of epigenetics and pain is rapidly emerging but further investigation is needed to fully comprehend the contribution of epigenetic processes to chronic pain states.
  - Although injury-induced epigenetic changes are well described, we do not assert that currently available global tools such as histone deacetylase inhibitors can be used successfully for the long-term treatment of chronic pain states.
Various treatment considerations

The study by McGillion et al. examined psychological factors associated with chronic pain following cardiac surgery. They found that chronic postcardiac surgery pain is associated with various psychological factors, including depression and anxiety disorders, sleep disturbances, fatigue, and somatic preoccupation.

Chronic Pain Following Cardiac Surgery: Prospective Study

- Chronic post surgical pain has been associated with the development of anxiety and depressive disorders, sleep disturbances and fatigue, as well as poor self-rated health.
- Chronic pain after cardiac surgery is associated with younger age.
- Majority of studies report no association with the type or length of surgery.
- The science of pain genetics is evolving; investigations of this nature are complex, requiring extensive research infrastructure for genotyping and related proteome methods.
- Three psychological factors that do show promise as modifiable, potential risk factors include pain-related beliefs, gender-based pain expectations and somatic preoccupation and coping.


Spinal Mobilization Effects on the Sympathetic Nervous System:

- Gate control mechanisms and biomechanical effects.
- Anatomical positioning of the sympathetic trunk and paravertebral ganglia.
- Sympathetic dampening with mechanical hypogastic effect in both healthy and symptomatic patients.
- Multi-system centrally coordinated response.

Various treatment considerations

Manual Therapy

Traction:
- Enhances modulation of mechanoreceptor activity.
- Direct relationship with sympathetic somatic convergence – Visceral response.


Various treatment considerations

Micronutrients - animal studies

L-acetylcarnitine, a drug marketed for the treatment of chronic pain, causes analgesia by epigenetically up-regulating type-2 metabotropic glutamate (mGlu2) receptors in the spinal cord.

- Because the epigenetic mechanisms are typically long-lasting, we hypothesized that analgesia could outlast the duration of L-acetylcarnitine treatment in models of inflammatory and neuropathic pain.
- A seven-day treatment with L-acetylcarnitine produced an antiallodynic effect.
- L-acetylcarnitine-induced analgesia persisted for at least 14 days after drug withdrawal.
- In contrast, the analgesic effect of pregabalin, amitriptyline, and N-acetylcysteine disappeared seven days after drug withdrawal.
- L-acetylcarnitine treatment enhanced mGlu2/3 receptor protein levels in the dorsal region of the spinal cord. This effect also persisted for two weeks after drug withdrawal and was associated with increased levels of acetylated histone H3 bound to the Grm2 gene promoter in the dorsal cord.
- When treated for 2 weeks with L-Acetylcarnitine, analgesia persisted 37 days after drug withdrawal, compared to 15 days for the pregabalin, amitriptyline, tramadol...
Effects of natural compounds on models of neuropathic pain induced by chronic constriction injury of the sciatic nerve.

- Systemic administration of koumine (an indole alkaloid present in Gelsemium elegans (type of grass)) mechanical allodynia in rats by reducing astrocyte-mediated neuroinflammation.

Combination of several herbal products, including N-Palmityloethanolamide (PEA) (found in soy lecithin, egg yolk), beta-carophyllene (in cannabis), carnosic acid (found in rosemary and sage) and myrrh extract administered orally, was as effective as gabapentin, a first line drug for treating neuropathic pain in a chronic constriction injury.

Antinociceptive effects of the methanol extract of Anisomeles indica (catmint plant)

Bulleyaconitine A, a diterpenoid alkaloid isolated from Aconitum Bulleyanum (Monk’s Hood), produced antinociceptive effect

- In addition, this compound showed anxiolytic effects and improved gastrointestinal function in rats with chronic visceral pain.

Nutraceuticals

- Traditional Chinese medicine herb from the rhizome of Ligusticum chuanxiong, for the treatment of migraine.
- The results of this systematic review article indicated that this herb can reduce frequency, duration and pain severity of migraine, with a low rate of side effects.

Various treatment considerations

Music

- Music can enhance analgesia and antiseizure effects of several drugs in animal models of pain.
- Playlist comprised several Mozart compositions.
- Although the analgesic effects of music “per se” or as adjunct to analgesic drugs have been previously described in patients, this particular study presented the first animal study on music-enhanced antinociceptive activity of analgesic drugs.

Various treatment considerations

Nutraceuticals - Animal studies

Spinal cord stimulator for abdominal/visceral pain

- Chronic abdominal pain is a debilitating condition known for its multifactorial nature. Despite varying etiologies of abdominal pain, this series suggests BurstDR spinal cord stimulation sustained for >2 years might be effective as a treatment for abdominal pain syndromes.
- Anterior Cutaneous Nerve Entrapment Syndrome (ACNES) is a debilitating neuropathic pain condition. DRG stimulation was found effective with an implanted DRG Axiom System.
- Chronic abdominal pain (CAP) can arise from multiple conditions, including inflammatory disorders, trauma because of injury or surgery, or structural or functional causes.

- Twenty-three of 24 subjects had successful trial stimulation and proceeded to permanent implant. After 12 months of treatment, 79.3% of subjects were responders (pain relief of ≥50%) and 14 of 22 subjects (63.6%) were remitters (sustained ≤3.0 cm visual analog scale scores). Secondary outcomes, including measures of disability, mental and physical wellbeing, sleep quality, perception of improvement, and satisfaction, showed greatly improved quality of life. Most subjects also reported concurrent reduction or resolution of nausea and/or vomiting.

References:

• Chronic pain affects roughly 50 million Americans, or 20.4% of the national population.
• Spinal cord stimulation (SCS) is a cost-effective interventional treatment modality for patients with chronic neuropathic and radicular pain.
  • traditionally used for patients with post-laminectomy syndrome, complex regional pain syndrome, or chronic back pain that is refractory to other less invasive techniques.
  • There have been a few cases describing the use of SCS at higher levels to successfully attain coverage of visceral abdominal pain.
• This case involved a patient who suffered from chronic back pain and radiculopathy with post-laminectomy syndrome as well as chronic abdominal pain.
  • High-frequency SCS alleviated the patient's post-laminectomy pain as well as his abdominal pain.
  • Adds to the growing evidence supporting the use of SCS for treating chronic visceral pain syndromes.


• Spinal cord stimulation (SCS) is a well-established treatment modality for chronic pain.
  • Thoracic radiculopathy has been reported as a complication of SCS paddle lead implantation by several authors and commonly presents as abdominal pain.
  • Of 86 cases, 7 patients who had immediate postoperative abdominal pain, 8%.
• Etiology of immediate postoperative abdominal pain after thoracic paddle lead implantation for SCS is most likely thoracic radiculopathy. We hypothesize that small, transient epidural hematomas could be the cause of this thoracic radiculopathy.
• All patients with immediate postoperative abdominal pain and no other neurologic deficits after thoracic paddle lead implantation for SCS should first be treated conservatively with observation and pain management.


• Better understanding of symptoms and interactions
• Think about various inventories: McGill Pain Questionnaire, Catastrophizing Questionnaire
  • Discoveries in research and deeper anatomical - molecular – studies now explain these experiences.
• Greatest success in outcomes, then, will be multifocal.
  • What we say: education, reassurance
  • What we do: all encompassing from structure to movement
  • Referral / specialty sources: pain control
  • What our patients do: Healing 101
    • Sleep
    • Nutrition
    • Stress management – sense of well being
    • Encourage movement