



## Integrative Pain Medicine: A Holistic Model of Care

**T**he field of integrative pain medicine spans a vast number of approaches and disciplines. This issue of *Pain: Clinical Updates* focuses on three areas of biological research of particular interest to integrative pain medicine: nutrition and the microbiome, neuroplasticity, and myofascial research. An exhaustive discussion of the field would require several volumes of text. As the scientific basis for these therapies expands, the overlap with conventional care is growing.

### Evaluating Alternative and Integrative Medicine

- **Allopathic medicine** refers to conventional medicine as taught in medical schools. The allopathic system generally engages the patient around a problem or a disease and spends more effort on disease management than on health promotion.
- **Complementary and alternative medicine (CAM)** refers to everything outside of the conventional teachings. It includes chiropractic, massage, yoga, midwifery, naturopathy, and other health-care disciplines and practices.

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- **Integrative medicine (IM)** is the integration of all available and appropriate health-care strategies and disciplines for the patient's benefit.

A 2009 report from the Institute of Medicine (IOM) Summit on Integrative Medicine and the Health of the Public echoed the earlier position of the World Health Organization (WHO): Health is more than the absence of disease. The IOM report outlined key features of Integrative Medicine: "integration across the lifespan to include personal, predictive, preventive, and participatory care." Other key components include person-centered care; integration of teams from all disciplines, including CAM; a focus on prevention and disease minimization; and "seamless engagement of the full range of established health factors—physical, psychological, social, preventive, and therapeutic."<sup>1</sup> The ideal practice would involve multiple disciplines and professions coordinated to work with mutual cooperation to achieve the best outcomes.

In the United States, the National Health Interview Surveys have demonstrated increased use of CAM, with out-of-pocket expenditures by patients estimated at \$33.9 billion in 2007. More than 38% of American adults and almost 12% of children had used some form of CAM within the previous 12 months, with pain being the most common reason for consulting CAM practitioners.<sup>2</sup>

The WHO estimates that 80% of people in the Southern Hemisphere use traditional (that is, non-allopathic) medicine as part of their primary care. In the Northern Hemisphere, the frequency of alternative medicine use is increasing and already exceeds 75% in some first-world countries.<sup>3</sup> Yet in the United States and Canada, conventional medicine generally receives the highest level of reimbursement from public and private insurers alike. Therefore, patients who seek treatment in CAM and IM settings usually are willing to pay for it. In accordance with this increasing demand for IM services, the National Institutes of Health (NIH) have established the National Center for Complementary and Alternative Medicine to expand research and knowledge in this area.

Numerous publications have explored why people are turning to IM despite the cost. Among the cited reasons is the fundamental difference between IM and conventional care: IM has health as its main focus rather than disease. There is a balance between the specifics of a given diagnosis, such as a degenerative L4–5 disk, and the whole patient—body, mind, and spirit. Therefore, IM pays more attention to factors such as obesity, nutritional status, unmanaged stress, social supports, coping skills, ergonomics, and exercise. Recognition of the innate capacity of people to heal through self-care strategies is a

cornerstone of IM, and this approach empowers patients to assume control over their health. The practitioner is present as a guide to partner with the patient in a healing journey. The existing time-based fee-for-service model, the overreliance on technology, and the inability of the establishment medical system to treat chronic disease adequately are also reasons patients turn to CAM and IM practitioners.<sup>4</sup>

### **Integrative Pain Medicine and Mitigation of Risk**

Perhaps the most compelling reason to embrace integrative pain strategies is to mitigate the risk to patients. Awareness is growing of serious adverse effects of medications, including the escalating rates of inadvertent overdoses from prescription opioids and the development of opioid tolerance and opioid-induced hyperalgesia.<sup>5</sup> The statistics on nonsteroidal anti-inflammatory drugs (NSAIDs) show that deaths in the United States from these drugs now exceed deaths from HIV/AIDS.<sup>6</sup> The tallies of medical mistakes—from the 1999 IOM report, *To Err is Human*,<sup>7</sup> to a paper by B. Starfield<sup>8</sup> in 2000, to a report by J.T. James in 2013<sup>9</sup>—highlight the heavy toll wrought by health care provided in hospitals, which now ranks as the third-leading cause of death in the United States.

Prevailing pain-management practices, which include liberal use of surgery, interventions, and drugs, are not adequately addressing the growing cohort of chronic pain patients. The reports on pain prepared by the IOM<sup>10</sup> and the U.S. Army Surgeon General's Pain Management Task Force both concluded that tinkering with the prevailing system of care will not address the problem. These reports speak of the culture change needed to address an inadequate

system. Military medicine has been very specific in its prescriptive recommendations: Flip the therapeutic order, and rather than beginning with drugs or costly and risky interventions and surgeries, begin with yoga, massage, chiropractic care, or acupuncture.

### **Nutrition and the Microbiome**

Integrative pain medicine begins with an assessment of nutritional status because you “change your body chemistry every time you eat.”<sup>11</sup> That is, you can increase or decrease inflammation with dietary choices. Excessive inflammation increases free-radical damage of tissues, impedes healing mechanisms, and reduces pH to levels where normal enzymatic reactions essential for cellular function no longer are optimized. An anti-inflammatory diet, such as the Mediterranean diet—which is high in vegetables, legumes, fruits, whole grains, fish, and healthy oils but low in meat—can improve overall health characteristics<sup>12</sup> and reduce inflammation.<sup>13</sup> High-glycemic foods cause high HbA1c, precipitate insulin resistance and diabetes, and promote obesity and pro-inflammatory states—all conditions associated with increased likelihood of chronic pain.

Industrialization has dramatically changed how we grow our food and how we prepare it for consumption. The WHO has taken the position that factory farms are not a sustainable agricultural process, advocating instead small organic farms that foster biodiversity. In the developed world there is a calorie surplus but a micronutrient deficiency. The populace relies far too heavily on processed foods packed with salt, sugar, unhealthy oils, and grain byproducts that are problematic for many consumers. In addition, there is a growing literature about the nutritional benefits of eliminating heavily

processed foods such as naturally or artificially sweetened carbonated beverages (with the exception of plain carbonated water); high-glycemic processed cereals, breads, and pastries; and aspartame and sucralose.

Why the focus on nutrition? Specific nutritional deficiencies can be associated with pain states. For example, a Mayo Clinic study discovered that pain patients with insufficient levels of vitamin D were taking twice the amount of opioids for twice as long as patients without a deficiency.<sup>14</sup> Plotnikoff and Quigley studied nonelderly and non-housebound primary care patients with persistent, nonspecific musculoskeletal pain that was refractory to pharmacological treatment and found these individuals had an unexpectedly high rate of vitamin D deficiency.<sup>15</sup> What's more, vitamin B<sub>12</sub> and folate deficiencies are well known to be associated with pain and neuropathic changes. It is less well recognized that proton pump inhibitors cause vitamin B<sub>12</sub> deficiencies as well as magnesium deficiencies and dysbiosis in the gut. Each of these conditions may be associated with increased pain.

There is a growing body of knowledge regarding the microbiome,<sup>16</sup> the mass of microorganisms that inhabit our body and outnumber our body's own cells by a factor of 10 to 1. The balance of microorganisms can determine health or disease by affecting the absorption of nutrients, causing or preventing excessive gut permeability, affecting the function of the immune system, or stimulating unhealthy fermentation within the gut, and dysbiosis may be responsible for some forms of abdominal pain. Processed foods and drugs such as proton pump inhibitors, NSAIDs, antibiotics, steroids, and hormones can adversely affect the microbiome.

The NIH has created the Human Microbiome Project, a consortium devoted to the study of the microbiome. A PubMed search on “human microbiome” displayed 11,459 articles dating to the 1950s, with 10,520 published within the last 10 years.<sup>17</sup>

## **Mind-Body Medicine and Neuroplasticity**

Scientific medical exploration has greatly expanded our knowledge of the individual organ systems of the body by looking at them more or less in isolation. The emerging field of mind-body medicine (MBM) is exploring the connections between the systems—what were treated as gaps between the systems, as it were. We now know there are no gaps and that all body systems interact through the same communication molecules, creating an instantaneous communication network.

Candace Pert, the first scientist to isolate opioid receptors in the brain, also studied communication molecules and was able to elucidate these interconnections. The science of stress (detailed in Pert’s research, that of neuroimmunology expert Esther Sternberg, Nobel Prize winner Elizabeth Blackburn’s, and elsewhere) focuses on how the communication systems in the brain between the cortex, limbic system, and hypothalamic-pituitary-adrenal axis influence the output to the periphery—all organs, endocrine glands, and the nervous system, including sympathetic and parasympathetic branches. This synthesis leads to modulations from mind to brain to body.<sup>18</sup> The field is often called “psycho-neuroendocrinimmunology.”

Closely related to MBM is the growing science of neuroplasticity: the ability of the brain and nervous system to change themselves. Pain scientists have transformed their understanding

of chronic pain states through discoveries concerning microglial activation and the development of sensitization. The basic science in the field goes far beyond microglia to show that some of the complex phenomena of pain may be caused by alterations in nervous system function. Somatosensory cortical changes develop in chronic pain states,<sup>19, 20</sup> causing alterations in sensory perception, changes in motor patterns, and co-contractions in what should be isolated muscle groups. This understanding opens new therapeutic opportunities through neuroplastic mechanisms.

The National Center for Complementary and Alternative Medicine has made MBM research a significant focus in its new five-year strategic plan. This plan states that the “growing body of basic research evidence suggests that mindfulness and other meditation practices engage neurobiological mechanisms known to be involved in cognition, emotion regulation, and behavior.”<sup>21</sup> Mind-body strategies include mindfulness and other meditation practices, biofeedback, yoga, other mindfully done exercises, and any practice affecting the autonomic nervous system, such as acupuncture.

MBM techniques, through their demonstrated ability to affect the mind-brain-body physiology, are cost-effective interventions that many participants find “transformational” in mitigating the effects of chronic stress. In a controlled study on mindfulness-based meditation practice by Kabat-Zinn et al., the treatment group decreased pain-related drug use, and “activity levels and feelings of self-esteem increased.” Most improvements were maintained at the 15-month follow-up, and this study showed a high level of compliance with ongoing meditation practice.<sup>22</sup>

Other studies have found mind-body interventions useful as adjunctive therapy to ameliorate pain, enhance treatment response, and reduce the use of more costly and risky interventions. A trial at a Ford Motor plant found a 58% reduction in prescription pain medication use when acupuncture and mind-body practices were used to treat low back pain.<sup>23</sup> Compliance is a factor in achieving sustained benefits.<sup>24</sup>

Research has elucidated the connection between the proinflammatory state that characterizes chronic stress and the aggravation of pain states through the mediation of the hypothalamic-pituitary-adrenal axis. Being in pain is a further stress. Directing patients toward MBM practices can help cut through the cycle of stress and thereby foster a sense of well-being.<sup>25</sup> The Nobel Prize in Medicine in 2009 was awarded for research on telomeres and the enzyme telomerase that maintains these nucleotide sequences. Shortened telomeres are associated with reduced longevity, but research has shown that intensive changes in lifestyle and nutrition can preserve the length of telomeres.<sup>26</sup> Chronic stress causes accelerated telomere shortening and therefore premature aging.<sup>27</sup> Telomerase activity and telomere length both improve with MBM skills training.<sup>28</sup>

## **Myofascial System**

Myofascial pain (MFP) is a very common type of pain and a source of dysfunction; figures of its prevalence vary widely, in part because a proper myofascial examination is not usually part of a standard medical examination, and so most cases are missed. However, the literature describing myofascial trigger points (mTrP), the hallmark of MF pain, is extensive. J.H. Kellgren<sup>29</sup> in Great Britain; Cornell University

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Because of the rapid advances in the medical sciences, the publisher recommends independent verification of diagnoses and drug dosages.

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professor and White House physician Janet Travell and David Simons, an Air Force flight surgeon and Veterans Affairs physician in the United States; and Chan Gunn in Canada have all written detailed works describing the pathophysiology of mTrPs, with a strong focus on physical findings.

Travell and Simons wrote the *Myofascial Trigger Point Manual*,<sup>30</sup> which outlines in great detail the muscles commonly affected, the location of the most common mTrPs, the pain patterns and dysfunctions that result, and methods of treatment. Gunn's work presents a coherent theory of the etiology of MFP. He postulates that mTrPs are caused by subtle pressures on spinal nerve roots, which are documented by cadaver studies as being common.<sup>31</sup> The result is subtle nerve dysfunction resulting in supersensitivity in the structures innervated by the affected nerve roots.<sup>32,33</sup>

### Dysfunctions resulting from supersensitivities, according to Walter Cannon's law of denervation supersensitivity.<sup>34</sup>

- **Motor**—Tight bands in affected muscles as a result of contraction without an action potential
- **Sensory**—Pain that may be spontaneous or may occur in response to nonpainful stimuli
- **Autonomic**—Pilomotor, sudomotor, and vasomotor phenomena in myotomal patterns

Sikdar and Shah have been able to image mTrPs through elastography,<sup>35</sup> and by using a technique called microcentesis<sup>36</sup> they have begun to analyze the unique proinflammatory milieu surrounding these painful points. They have demonstrated these physical findings only in individuals with myofascial injuries.

Fascia has long been regarded by medicine as an inert structure that defines tissue planes and delineates margins for dissections during surgery. Recent research is now leading to an expanded recognition of the dynamic and energetic functions of fascia. As

described by Ida Rolf in the 1930s, the pull of fascia in one area sends forces in all directions and acts more as a connector than a boundary between body structures. Fascia is a web of connective tissue that surrounds each muscle fiber; it surrounds, separates, and connects all our organs and allows them to slide past one another when necessary.<sup>37</sup> This expanded definition helps explain some of the mysteries of both the function and dysfunction in the myofascial system.

Helene Langevin of Harvard University has studied acupuncture and connective tissue and has demonstrated that stimulation by acupuncture needles inserted into muscle fascia causes fibroblasts to realign themselves.<sup>38,39</sup> Her group has also demonstrated through elastography that thoracolumbar fascia transfers forces in unexpected directions and has self-regulatory features that may

expand our understanding of low back pain.<sup>40</sup> Elastography can discern differences in the characteristics of thoracolumbar fascia between back pain patients and those with no back pain.

Chaudhry et al. are publishing quantitative biomechanics modeling for assessing rotational stiffness and viscoelasticity of lower back tissues with potential functional implications.<sup>41</sup> The impact of the acupuncture needle on the myofascial system is also demonstrated in Gunn's IMS therapy, which uses acupuncture needles and western medical pathoanatomical models to guide therapy. NIH has an extensive bibliography on myofascial therapies.

Traditional Chinese medicine (TCM), including acupuncture, has a long history of use for chronic and

acute medical conditions, including pain. It cuts across all three major themes discussed here—nutrition and the microbiome, neuroplasticity, and the myofascial system. TCM is a system of medicine that is ancient, complex, and detailed. It is holistic and views health as a result of balance and harmony between dynamic qualities in the relationship between different functions, rather than considering only structural, physical characteristics. Yin and yang represent opposite but complementary aspects of Qi (pronounced chi), which is roughly translated as vital energy. These concepts have been difficult to marry with the concepts used in western scientific enquiry, but functional neuroimaging is helping to bridge the gap because it is able to demonstrate altered function in response to treatments.<sup>42</sup>

In 1997, the NIH convened a Consensus Development Conference on acupuncture that concluded: “There is sufficient evidence of acupuncture’s value to expand its use into conventional medicine and to encourage further studies of its physiology and clinical value.”<sup>43</sup>

## The Evidence Base

The field of integrative medicine is vast and varied; hence, the options for integrative pain medicine are too numerous to cover here in detail. This overview of some key areas of active research and promising interest is meant to start the conversation and is by no means a comprehensive list of meritorious topics. We need more-rigorous investigation of low-risk, and

relatively low-cost, interventions that characterize integrative medicine.

The NIH has stated that the “needs of the public and health-care providers (both conventional and CAM) for reliable, objective, evidence-based information regarding CAM remains compelling.”<sup>44</sup> Conventional medical research is recognizing the limitations of the randomized clinical trial to provide data relevant to patients in real-life clinical practice. The development and validation of “whole systems” research methodologies<sup>45-47</sup> have opened the door to research on the effectiveness of IM practices, resulting in a growing evidence base. Whole-systems research is based on real-world practice parameters; it examines outcomes and can be used in instances where interventions are difficult to blind or control with an appropriate placebo intervention.

Currently, one of the best uses of research is in the assessment of the risk/benefit equation. Many of the Cochrane Reviews conclude that the data on IM interventions are insufficient to make definitive recommendations but that some small-to-moderate effects have been demonstrated, and CAM practices may be useful adjuncts. The evidence for many high-risk conventional practices is also insufficient. Current standard medical treatments

for pain carry considerable cost, morbidity, and mortality. The inclusion of integrative strategies has the opportunity to lower the risk using theoretically plausible treatments that are continuing to come under scientific scrutiny.

Most experts acknowledge that the cost of conventional care is unsustainable. The focus on health as a positive attribute has led to extensive attention to lifestyle choices as primary interventions. We have extensive cost-effectiveness data on chronic conditions such as heart disease, diabetes, obesity, cancer, smoking-related diseases, and arthritis; each of these conditions has implications for the development of pain syndromes. Lifestyle interventions in large-scale, high-quality research, published in impactful journals, have shown outcomes, which, if claimed for a drug or procedure, would never be believed.<sup>21,48-50</sup> Improvements in blood pressure, heart disease risk, obesity, diabetes, cancer rates, and prescription pain medication use have been impressive.

We cannot afford to ignore these realities; it is imperative that as health-care providers we have an open mind to low-cost, low-risk integrative strategies that our patients are already embracing.

### Resources for Complementary and Alternative Medicine

For more information on the CAM-licensed professions, see the website for the Academic Consortium for Complementary Alternative Health Care ([www.accahc.org](http://www.accahc.org)) and *ACCAHC Clinicians' and Educators' Desk Reference*, 2013. For information on Integrative Medicine, see the website for the Consortium of Academic Health Centers for Integrative Medicine, [www.imconsort.org](http://www.imconsort.org). For a more extensive discussion on the topic, see *Holistic Pain Relief*, New World Library, 2013.

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