

# Best Practices/Practice Guidelines

## Immunity & Chiropractic Clinical Practice

Matthew McCoy DC, MPH<sup>1</sup>, Christopher Kent DC, JD<sup>2</sup>, Anquonette Stiles DC, MPH<sup>3</sup>, Christie Kwon DC, MS, MPH<sup>3</sup>, Amy Haas DC, Ph.D<sup>3</sup>, Jon Chung DC<sup>4</sup>, Ian Shtulman DC, DAACP<sup>5</sup>, Suzzanne M. Candelaria-Perez BSc<sup>3</sup>, Christopher Long BS<sup>3</sup>, Brooke Mills AA<sup>3</sup>, Veronica Gutierrez DC<sup>6</sup>

### RECOMMENDATION

**Rating: Established**

**Evidence: E, L**

**A growing body of evidence supports our understanding of the role of the nervous system in immune system function. Basic science studies and clinical reports in the scientific literature provide supportive evidence of the beneficial effects of chiropractic care in improving function, including immune system function and quality of life. These guidelines support chiropractic practice in an evidence-informed, patient centered model. Evidence-informed practice involves the integration of the knowledge and experience of the chiropractor, the best available research evidence, and the needs and preferences of individual patients. Furthermore, chiropractors must be free to discuss, publish, and otherwise disseminate the best available evidence, and in practice, apply it to the needs of individual patients.**

*Foundation for Vertebral Subluxation Best Practices Initiative*

### Introduction

It is well established that the nervous system controls and coordinates all functions and systems of the human body including immunity and the immune system.<sup>1</sup> Consistent with this simple maxim of human physiology, many chiropractic practitioners hold that the impacts of chiropractic adjustment on the nervous system can confer overall salutogenic benefits in people undergoing chiropractic care.<sup>2-4</sup> Indeed, for well over a century, chiropractors around the world have accrued a significant body of collective clinical experience establishing that patients under chiropractic care often experience health improvements not limited to simple musculoskeletal complaints or resolution.

Recent events related to the Coronavirus Pandemic have brought this relationship between chiropractic care and overall promotion of health and wellness to the forefront, both within and outside of the chiropractic profession. Within the chiropractic profession, broad stroke assertions by researchers to the effect that no “credible” published scientific evidence supports claims of clinically relevant effectiveness of spinal adjustment and/or manipulation in boosting or strengthening the immune system.<sup>5</sup>

As a consequence of the assertions of the small cadre of researchers, certain chiropractic regulatory boards, chiropractic trade organizations and chiropractic educational institutions from around the world are claiming that there exists no credible, scientific evidence that would permit claims of effectiveness for conferring or enhancing immunity through spinal adjustment and/or manipulation to be made in communications by chiropractors.<sup>6</sup> Essentially, chiropractors have been effectively muzzled and throttled from discussing any connection between the nervous and immune systems. The conclusions of the flawed document have been refuted along with exposing the biases of the authors and the flaws of

1. *Vice President Foundation for Vertebral Subluxation*
2. *President Foundation for Vertebral Subluxation & Director of Center for Scholarly Activity Sherman College of Chiropractic*
3. *Research Fellow Foundation for Vertebral Subluxation*
4. *Private Practice – Palm Beach, Florida*
5. *Private Practice – Lake Worth, Florida*
6. *Guidelines Committee Foundation for Vertebral Subluxation*

the process itself.<sup>7</sup> This refutation of the highly flawed document has led to the development of a plan for a more robust examination of the actual existing literature and a related multi-prong plan for addressing this issue moving forward. This Best Practices document from the Foundation for Vertebral Subluxation is part of that effort.

## Methods

The purpose of this project was to perform a scoping review the existing literature on chiropractic, vertebral subluxation and immune function in order to inform the development of a Best Practices/Practice Guidelines statement. The Foundation for Vertebral Subluxation's (FVS) Best Practices/Guidelines Committee participated in a scoping review of existing literature available to a team of researchers and conducted further searches and gathering of documents based on that available literature. 125 papers were gathered and included in a review. Based on this review a document was produced that was evaluated by a panel of experts. The panel of experts then drafted a Best Practices statement.

This statement and the accompanying scoping review was then put through peer review with 200 chiropractors completing its review prior to publication. This scoping review is a living document and will be supplemented with an integrative review of the literature on chiropractic and immunity. The literature forming the basis of the Recommendations will then be updated according to the regular cycle established by the Foundation for Vertebral Subluxation's Best Practices Initiative.

## Results

### *Review of Chiropractic, Vertebral Subluxation and Immune Function*

#### *Vertebral Subluxation Theory, Neurology and Immune Function*

According to Rome:

". . . evidential support for the hypothesis of an association of a physiological and pathophysiological neurovertebral influence upon visceral function does exist in the health professions. This evidence consists of empirical observations, anecdotal reports, through to blinded randomised controlled trials and pure neurophysiological research"<sup>8</sup>

Rome argues further that there is more published evidence in favor of chiropractic involvement in the management of a number of visceral conditions than there is for many of the musculoskeletal conditions managed by manipulative therapy.

Despite this, Rome contends that ". . . the management of somato-autonomic related visceral conditions remains somewhat contentious, even though there would appear to be a similar degree of anecdotal efficacy, patient acceptance and satisfaction – as well as the more formal research."

The original chiropractic theory is centered on the principle that obstruction or interference in the nervous system caused by vertebral subluxation can affect internal physiological

function and the propagation of mental impulses and therefore plays a role in pathophysiology and dis-ease.<sup>9</sup>

The theory is based on the premise that the nervous system can be adversely affected by vertebral subluxation which can adversely affect the autonomic nervous system and therefore influence the internal milieu. Correction or reduction of the biomechanical component of the vertebral subluxation through specific chiropractic adjustment may positively influence associated pathophysiological conditions - doing so through afferent and efferent somatosensory and autonomic reflexes.<sup>9-11</sup>

According to Haldeman:

"Stimulation of a visceral receptor can cause reactions in the viscera themselves, can send afferent impulses to the medulla and higher centres, and can affect the somatic musculature. Stimulation of the somatic afferents similarly can have a widespread effect on sympathetic outflow to the viscera."<sup>12</sup>

Rome contends that the hypothesis has four integrally linked steps:<sup>8</sup>

1. That there can be sufficient somatic disturbance to alter the normal sensory input at that segmental level.
2. That this aberration would primarily consist of a bombardment of noxious somatic sensory input, and resulting in modulation of normal autonomic (ANS) activity
3. That resultant altered efferent somatovisceral activity may then interfere with the physiology of the innervated structures(s) involving that reflex level. This may be via central processing, neurologically directly onto that structure – or other mechanisms.
4. That in the case of that structure being an organ, such interference may be in the form of physiologic dysfunction, with associated symptoms, simulated disease of that organ, or possibly degrees of, or predisposition to pathology.

#### *Chiropractic and the Neuro-Immune Connection*

Interest in the autonomic-immune and somato-autonomic-immune association has been growing for some time. Cevikbas et al assert that autonomic nerves are involved in innate and adaptive immune pathways during allergic and atopic skin diseases.<sup>13</sup>

Sato reports on Kimira in 1994 who stated that somatic afferent stimulation produces a reflex effect on immune function, with autonomic nerves acting as the efferent pathway.<sup>14</sup>

According to Johnson, reviewing the sensory and sympathetic nerve supply within the cervical spine, ". . . the neuropeptide levels in the cell bodies located within the dorsal root ganglion of sensory nerves fluctuate according to the physiological state of the zygapophysial joint."<sup>15</sup>

Rome opines that:

"This observation would tend to support the concept of a connection between the state of the somatic component –

importantly a vertebral articulation, and at least the sympathetic nervous system – a somatosympathetic neurological circuit.”<sup>8</sup>

Sato in his paper on modulation of visceral functions by somatic afferent activity urges the reader:

“In this study of body homeostasis and environmental adaptation it would seem very important to further analyse the contribution of somatic afferent input to the autonomic nervous and hormonal regulation of visceral organ activity... (and)... that visceral functions can be moderated by somatic afferent input via various degrees of integration of autonomic nerves, hormones, and immunological processes.”<sup>16</sup>

In a paper on modulation of the immune system by the autonomic nervous system and its implication in immunological changes, Nagatomi et al state that the autonomic nervous system plays a major role in the regulation of the immune system.<sup>17</sup> Taken together, they assert:

“... the sympathetic nervous system does not simply suppress the immune system but might help organize the immune response sequentially and spatially by modulating the distribution of immunocompetent cells.”

As Rome points out:

“There is a valid basis for the concept of a somatosensory-autonomic-visceral role in chiropractic and published formal research by chiropractic and other professions, as well as clinical observations, have contributed towards substantiating this foundation. In fact, there is far more evidence in support of this chiropractic hypothesis, with virtually none refuting it.”<sup>8</sup>

Khalsa in a 2005 conference on the biology of manual therapies discussed the evidence that manual care triggers “. . . a cascade of cellular, biomechanical, neural, and/or extracellular events as the body adapts to the external stress.” They stress that this leads to responses by the central and autonomic nervous systems that lead to observed changes in circulating levels of various neuropeptides and regulatory proteins.<sup>18</sup>

In a 2008 paper, Cohn reviewed the literature on the connections between the nervous and the immune systems, and explored the contention that chiropractic adjustments may affect neuroimmune function. He concluded that there appear to be numerous modes of communication between the nervous system and the immune system. It also appears, not only in theory but in practice, that chiropractic adjustments may have a beneficial effect on the functioning of both the nervous and the immune system.<sup>19</sup>

Brown, in a review of the field of psychoneuroimmunology and chiropractic noted chiropractic’s non-surgical, drugless form of health care that seeks to optimize health and wellness via the relationship between structure, primarily the spine, and function, primarily the nervous system of the human body. Brown concluded his review asserting that chiropractic is well positioned to make a unique contribution to the field of psychoneuroimmunology.<sup>20</sup>

In a study looking at long term assessment of blood indices and immune panel profiling of subjects receiving chiropractic care, Boone and his colleagues found significant changes in blood indices and the immune profile in the study group suggesting that the positive correlation was a reflection of the hosts’ resistance to viral infection and destruction of virus infected cells. The relationship among lymphocyte subpopulations may have reflected a natural balancing or redistribution of the overall lymphocyte subpopulation as individual cell types respond to a variety of immune challenges.<sup>21</sup>

In another study by Boone and colleagues over a 9 month period, subjects received chiropractic adjustments, completed a self-reported quality of life questionnaire and had complete blood counts and immune panels. Subjects demonstrated significant reductions in all chiropractic indicators compared to baseline. A positive change in Life Enjoyment occurred and they concluded that the subjects appear to have maintained a healthy physiology based on the complete blood count and immune profile throughout the duration of the study.<sup>22</sup>

In a study of 650 children undergoing chiropractic the data revealed a pattern of subluxation correlated with numerous somatic, visceral and immune complaints that were helped following chiropractic care prompting the authors to recommend that these subluxations be discovered as early as possible in a child’s development in order to effect a correction.<sup>23</sup>

In a review of objective physiologic changes and associated health benefits of chiropractic adjustments in asymptomatic subjects Hannon reported statistically significant improvements in respiration, range of motion, heart rate variability and autonomic function, endocrine function, cardiovascular function, immune function, muscle strength and overall athletic ability of “healthy” or “normal” individuals.<sup>24</sup>

According to Hannon, other studies have documented statistically significant increases or improvements in neurocognitive functions such as reaction-time and information processing, visual acuity, stress and reproductive hormones, healing / recovery time, general health of senior citizens, and reduced labor times of pregnant women following or during chiropractic care.

Hannon asserted that “considering that these initial findings document objectively measured physiologic changes and their associated health benefits in nearly every major system of the human body, it is plausible that chiropractic care may benefit every function of the body. Furthermore, these data are congruent with numerous subjective studies that suggest chiropractic care is associated with accruing, long-term, overall health benefits.”<sup>24</sup>

In a study of 57 people looking at long term remission and alleviation of symptoms in allergy and Crohn’s disease patients following spinal adjustment for reduction of vertebral subluxations Takeda and his colleagues addressed the association between visceral disease and immune dysfunction from sympathetic segmental disturbances secondary to vertebral subluxation.<sup>25</sup>

Of the 17 patients who received spinal adjustments, 12 showed long-term and stable remission of their symptoms and of these, 9 experienced an alleviation effect. They found that vertebral subluxation is a common and characteristic finding in patients with allergies and Crohn's disease.

The authors concluded that according to the results of their study ". . . the possibility may be considered that chronic nerve compression secondary to vertebral subluxation in the thoracic and lumbar regions had a significant effect on the immune function of these allergy and Crohn's disease patients. It is further postulated that this nerve compression leads to a chronic functional disorder having a significant effect on digestion, absorption of nutrients and liquids, conveyance of food as well as various other functions of the digestive tract extending to excretion."<sup>25</sup>

In a comparative study of the health status of children raised under the health care models of chiropractic and allopathic medicine, Van Breda reported that those children raised under chiropractic care had less infections and took less antibiotics than their medical counterparts.<sup>26</sup>

The improved quality of life and improved health outcomes in relation to immune related health challenges by people undergoing chiropractic care mentioned above is further supported by similar outcomes reported by parents and their children in numerous studies conducted by Alcantara and his team at the International Chiropractic Pediatric Association (ICPA) through a Practice Based Research Network (PBRN) involving thousands of children.<sup>27,28</sup>

These studies are further buttressed by numerous case reports published in the peer reviewed literature showing improved health outcomes following chiropractic for allergies, asthma, sinusitis, sinus congestion, chronic colds, dermatitis and IgE levels.<sup>29-45</sup>

Positive health outcomes related to immune function is further reinforced by numerous case studies on otitis media and immune function in general.<sup>46-65</sup>

Based on this review there appears to be ample support for a biologically plausible and beneficial relationship between vertebral subluxation reduction, the nervous system and immune function. In the following section we will review the impact of chiropractic on immune biomarkers.

### **Impact of Chiropractic on Immune Biomarkers**

In the most recent review of the effects induced by spinal manipulation on the immune and endocrine systems, Columbi and Testa included studies if they evaluated the effects of manipulation on participants' biomarkers.<sup>66</sup>

The authors state that ". . . recent models propose that the observed pain modulatory effects of this form of manual therapy may be the result of more complex mechanisms. It has been suggested that other phenomena like neurophysiological responses and the activation of the immune-endocrine system may explain variability in pain inhibition after the administration of spinal manipulative therapy (SMT)."<sup>66</sup>

The aim of their paper was "to provide an overview of the available evidence supporting the biological plausibility of high-velocity, low-amplitude thrust (HVLAT) on the immune-endocrine system". Their search retrieved 13 relevant articles and two themes of discussion were developed. Nine studies investigated the effects of manipulation on cortisol levels and four studies examined the effects of manipulation on the immune system.

They concluded that spinal manipulation seems to trigger the activation of the neuroimmunoendocrine system and encouraged further research to obtain more insights about the biological effects of spinal manipulative therapy.<sup>66</sup>

Cytokines are cell signaling protein molecules secreted by cells of the immune system and are a category of signaling molecules used in intercellular communication. Spinal manipulation has been shown to reduce the production of pro-inflammatory cytokines and increase the blood levels of cytokines that are immuno-regulatory in nature.

Brennan, et al., demonstrated that upper thoracic spinal manipulation resulted in a significant increase in phagocytic activity of neutrophils and monocytes when compared to a sham manipulation or soft-tissue treatment.<sup>67</sup> In another study by Brennan, et al., they found that spinal manipulation results in viscerosomatic responses that affect the phagocytic activity of both neutrophils and mononuclear cells.<sup>68</sup>

In a small study by Selano and Grostic, it was found that upper cervical adjustments increased CD4 helper T-cell counts by 48 percent over the six-month duration of the study.<sup>69</sup>

Teodorczyk-Injeyan showed that chiropractic treated subjects have also shown attenuation of lipopolysaccharide induced production of the inflammatory cytokines unrelated to systemic levels of the neurotransmitter substance P.<sup>70</sup>

Research has explored the relationship of spinal manipulation, spino-autonomic reflexes and their influence on activity of immune and inflammatory cells. This research has shown a reduction in pro-inflammatory cytokines after spinal manipulation. This includes reduction of inflammatory cytokines, tumor necrosis factor and interleukin-1 $\beta$ .<sup>71</sup>

Spinal manipulation down-regulates inflammatory-type responses via a central mechanism and manipulation ameliorates the physiological responses of blood cells to an inflammatory stimulus suggesting that spino-visceral reflexes alter the functional activity of cells in the immune and inflammatory systems.

In 2010, Roy, et al., did pre- and post-intervention measures from blood samples and detected a reduction in pro-inflammatory cytokines interleukin 6 (IL-6) and C-reactive protein (CRP) after a series of nine chiropractic manipulations from T12-L5 using an adjusting instrument and related protocol in 10 chronic low back pain patients and 10 healthy subjects. Both IL-6 and CRP levels were lowered toward the values in healthy subjects showing that chiropractic is capable of attenuating the inflammatory response. The authors of the study suggest that it is plausible the inflammatory process can be reversed in those receiving adjustments.<sup>72</sup>

Increased secretion of interleukin-2 (IL-2) has also been found following chiropractic care. IL-2 is an important cytokine in T-cell-dependent immune responses. It also plays a role in the development, maintenance and survival of regulatory T cells making it critically important in immune tolerance. IL-2 is an immune-regulatory cytokine and signaling molecule necessary for the response to microbial infection as well as the body's ability to discriminate between self and non-self.

In one study, 76 asymptomatic subjects were randomized to receive an upper thoracic manipulation with cavitation or without cavitation, or were included in a control group. All subjects had their blood drawn before, 20 minutes and two hours after the intervention. Induced secretion of IL-2 increased significantly with the T-lymphocyte response becoming enhanced after spinal manipulation suggesting that manipulation may influence IL-2 immune regulated biological responses.<sup>73</sup>

In another study of 74 subjects the increased production of interleukin-2 as a result of thoracic manipulation was associated with increased antibody synthesis from monocytes. The study showed that there was increased synthesis of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies in peripheral blood mononuclear cells in those subjects who received thoracic manipulation. This means that antibody synthesis (IgG and IgM) induced by interleukin-2 is increased after manipulation.<sup>74</sup>

Studies demonstrate evidence indicating that chiropractic and spinal manipulation may influence immune system response. Studies suggest that manipulation consistently reduces the production of pro-inflammatory mediators associated with tissue damage and pain from articular structures. Other studies provide evidence that manipulation may induce and enhance production of the immune-regulatory cytokine IL-2 and the production of immunoglobulins.

In a study examining the effect of chiropractic spinal manipulative therapy on salivary cortisol levels by Tuchin, nine subjects received chiropractic over six weeks revealing reduction of salivary cortisol over the complete time frame of the study.<sup>75</sup>

According to Tuchin a number of studies have analyzed the relationship of salivary cortisol with stressful events. These studies, he suggests, have shown that salivary cortisol levels often increase in relation to increases in the level of stress. From this it has been demonstrated that the level of stress of a patient can be correlated with secreted cortisol levels.

In another study involving chiropractic and cortisol levels, plasma levels of beta-endorphin, adrenocorticotropic hormone (ACTH), and cortisol before and after intervention chiropractic was performed in 40 male subjects. Levels of immune-reactive ACTH, immune-reactive beta-endorphin, and cortisol were measured. No differences in ACTH or beta-endorphin were found between sham and treated groups, or between pre-and post-intervention in any group; cortisol levels fell over the course of the study in all groups. According to the authors of the study the findings suggest that manipulation is not a stressor that activates the hypothalamo-pituitary-adrenal axis.<sup>76</sup>

Whelan studied whether basal salivary cortisol levels can be properly detected and whether chiropractic manipulation has any direct effect on basal salivary cortisol levels in humans. Subjects were adult male students attending a chiropractic college. Salivary samples were collected for 5 weeks. During Week 1, samples were collected by the students at home upon waking. During Weeks 2 through 5, home samples were collected upon waking and were followed by an additional time course of samples collected in a laboratory setting before and after manipulation.<sup>77</sup>

According to the study's authors chiropractic manipulative therapy did not significantly change basal salivary cortisol levels. A decrease in salivary cortisol was detected over time on each trial testing day. Overall, cortisol levels significantly decreased from the time of the home samples until the pretreatment laboratory measurement). Cortisol levels subsequently decreased from pretreatment to 15 minutes after treatment. After treatment, there were progressive decreases in cortisol levels. The authors concluded that neither the anticipation of manipulation nor the spinal manipulative procedure itself induces a state of stress or anxiety.<sup>77</sup>

In a study to assess the effects of short-term and long-term chiropractic care on serum thiol levels in asymptomatic subjects, researchers found statistically significant differences in the serum thiol levels in three groups. Mean serum thiol levels were lowest in patients with active disease as well as patients with initial musculoskeletal complaints. Asymptomatic subjects under chiropractic care demonstrated higher mean serum thiol levels than patients with active disease. The researchers concluded that asymptomatic or primary wellness subjects under chiropractic care demonstrated higher mean serum thiol levels than patients with active disease and produced some values that were higher than normal wellness values.<sup>78</sup> Serum thiols are a measure of human health status and are a surrogate estimate of DNA repair enzyme activity, most notably poly ADP – ribose polymerase or PARP.

To be sure, the literature base supporting the clinical role of chiropractic in supporting immune function is widespread and it is buttressed by the expanded depth and breadth of the literature on those manual methods, in general, that are directed at improving the structure and function of the spine and nervous system. Osteopathy serves as an example of another profession that has devoted time and effort at researching this topic.

#### *Osteopathy and Immunity*

Osteopaths have long managed their patients with an eye toward immune support as have physical therapists, massage therapists and a host of other manual practitioners.

In osteopathic studies of Immunoglobulin A (IgA) it has been shown that Osteopathic Manipulative Therapy (OMT) has a positive effect on IgA levels in persons experiencing high stress. Results suggest that OMT may then have therapeutic preventive and protective effects on both healthy and hospitalized patients, especially those experiencing high levels of emotional or physiological stress and those at higher risk of acquiring upper respiratory tract infections.<sup>79</sup>

OMT has also been shown to aid in the recovery from pneumonia by enhancing the functioning of the immune system, and maximizing the effects of antibiotics. In addition, OMT has been associated with decreased hospital-stay duration, decreased use of intravenous antibiotics, and decreased incidence of respiratory failure or death in elderly patients hospitalized with pneumonia.<sup>80-98</sup>

Not surprisingly based on the above studies, osteopathy has also been credited with providing improved health outcomes during the 1918 Flu Pandemic.<sup>99-101</sup>

Smith reported that mortality among a total of 110,120 patients with influenza treated by the 2445 members who reported “authenticated detailed case reports” to the American Osteopathic Association was 0.25%. Mortality due to influenza in patients receiving traditional medical care, however, was ultraconservatively estimated at 5% to 6%. Among patients with pneumonia treated medicinally, mortality was estimated at 33%, and even as high as between 68% and 78% in some large centers. The death rate due to pneumonia among 6258 patients cared for by osteopathic physicians was 10%.<sup>101</sup>

#### *Chiropractic & the Spanish Flu Pandemic of 1918*

In turn, no review of the role of chiropractic and immune function would be complete without addressing its role during the 1918 Flu Pandemic.<sup>102-103</sup> While some in the chiropractic profession have dismissed these pandemic flu related data out of hand because they have not reviewed the actual data, the osteopathic profession does not seem to have any trouble promoting its success in a similar fashion and those same chiropractors refrain from criticizing the osteopaths or attempting to silence their discussions of it.

According to Rhodes:<sup>102</sup>

In Davenport, Iowa, 50 medical doctors treated 4,953 cases, with 274 deaths. In the same city, 150 chiropractors including students and faculty of the Palmer School of Chiropractic, treated 1,635 cases with only one death.

In the state of Iowa, medical doctors treated 93,590 patients, with 6,116 deaths - a loss of one patient out of every 15. In the same state, excluding Davenport, 4,735 patients were treated by chiropractors with a loss of only 6 cases - a loss of one patient out of every 789.

National figures show that 1,142 chiropractors treated 46,394 patients for influenza during 1918, with a loss of 54 patients - one out of every 886.

Reports show that in New York City, during the influenza epidemic of 1918, out of every 10,000 cases medically treated, 950 died; and in every 10,000 pneumonia cases medically treated 6,400 died. These figures are exact, for in that city these are reportable diseases.

In the same epidemic, under drugless methods, only 25 patients died of influenza out of every 10,000 cases; and only 100 patients died of pneumonia out of every 10,000 cases.

In the same epidemic reports show that chiropractors in Oklahoma treated 3,490 cases of influenza with only 7 deaths. In Oklahoma there is a clear record showing that chiropractors were called in 233 cases where medical doctors had cared for the patients, and finally gave them up as lost. The chiropractors saved all these lost cases but 25.

So powerful were the results seen by chiropractors that those results and the outpouring of support by the public were seen as a survival factor for a fledgling chiropractic profession seeking public acceptance.

Rhodes stated:

The first survival factor for chiropractic: they were the legal and legislative salvation. But the fabulous success of chiropractic in combating the 1917-1918 influenza outbreak was the public relations breakthrough that can certainly be called the second great survival factor. Better acceptance by the public followed and more patients meant financial safety for practicing chiropractors. Dedicated chiropractors came into the profession in increasing numbers and they had a sure sense of certainty, heady conviction, and a great willingness to fight for the cause.<sup>102</sup>

#### *Ron Pero's Research*

One final area of contention among those who criticize the state of the evidence related to chiropractic and immune function is the work of Ronald Pero. The highly flawed and biased review by the World Federation of Chiropractic's Research Committee<sup>5</sup> included an out of hand rejection of Pero's work stating:

*Numerous attempts have failed to retrieve this study. Without the original study to review, no scientific assessment of its claims can be made. Therefore, the "Pero and Flesia" study does not constitute credible, scientific evidence that spinal adjustment/manipulation enhances or confers immunity nor should it be used as a basis to provide care.*

And though they failed in their “numerous attempts” to secure data and though they admit they have no citation, they nevertheless formed an opinion about documents they never reviewed. The WFC Research Committee's failure at their claimed “numerous attempts” to locate data on Pero's work and their failure to accomplish that despite the involvement of 9 researchers with apparently extensive experience in literature searching and retrieval along with the combined resources of their collective libraries - leaves one to wonder how hard they actually looked. Given their failure to locate actual data they chose instead to review internet memes in order to arrive at their rejection.

While Pero's research was not published in a peer reviewed indexed journal, the hypothesis and findings of his study were published along with writings and transcripts of presentations he gave on the topic.<sup>104-106</sup> These are the apparent sources of data used in memes highly circulated among the chiropractic profession. Pero and Flesia put together a testable hypothesis for chiropractic stating:

“It is clear from the literature review and the data presented

above that spinal pathomechanics can cause hormonal changes that, in turn can lead to genotoxic responses, altered physiological states of health and disease. Hence it becomes imperative to research the possible scientific molecular basis for chiropractic.”<sup>104</sup>

Pero and Fleisa laid out the reasoning:

1. Spinal pathomechanical stress to the nervous system induces neurohormonal imbalance that can lead to other hormonal changes.
2. Either or both of the above may cause pathometabolic events resulting in a measurable increase in genotoxicity.
3. Genotoxicity leads to significantly altered physiological states of health via mutagenic or cytotoxic events.
4. Therefore, spinal pathomechanical stress leads to significantly altered physiologic states of health.
5. Spinal pathomechanics can be improved, corrected, and/or prevented by appropriate chiropractic intervention.
6. Therefore, appropriate chiropractic intervention can lead to significant lessening of mutagenic or cytotoxic events.

Pero and Fleisa concluded:

“We feel there is sufficient evidence available for interested scientists to proceed with the validation of the hypothesis that chiropractic intervention can prevent accumulation of DNA damage in cells and thereby reduce the incidence of altered physiologic states of health by such damage.”<sup>104</sup>

Some of Pero's work was contemporaneously reported in the November 1989 issue of the *East West Journal*. Referring to Pero's study, which he collaborated on with Fleisa and with a grant from the Chiropractic Basic Science Research Foundation (CBSRF), they reported on the conduct of a study to gauge resistance to hazardous environmental chemicals hypothesizing that people with cancer would have a suppressed immune response to toxic burdens. While they hypothesized that healthy people and people receiving chiropractic care should have a relatively enhanced response.<sup>106</sup>

Measuring 107 individuals who had received long term chiropractic care, Pero's team found that all chiropractic patients were "genetically normal" meaning they had no genetic reasons for increased resistance or susceptibility to disease. Any difference therefore had to be accounted for by environmental or therapeutic factors.

It was reported that the chiropractic patients had a 200% greater immune-competence than people who had not received chiropractic care and a 400% greater immune competence than people with cancer or other serious diseases. It was reported that the immune competence did not show a decline with age.

Pero concluded that "chiropractic may optimize whatever genetic abilities you have" so that you can fully resist serious disease. He stated: "I'm very excited to see that without

chemical intervention this particular group of patients under chiropractic care did show a very improved response. These changes come from chiropractic treatment.”<sup>106</sup>

## Conclusion

### *Evidence Informed Practice*

The issue of chiropractic and its role in managing patients relative to immune function is a serious and urgent matter. In the end it is really not a scientific or research deficit that brings us to this confrontation. It is instead due to a purposeful cleaving of the well-entrenched model of evidence informed practice by factions within the chiropractic profession that seek to limit the practice of chiropractic to the management of a narrow range of musculoskeletal conditions. The segment of the profession that holds to an “RCT” and musculoskeletal only standard and at the same time does not consider the desires of the patient, their values and the expertise of clinicians happens to be in general control of the regulatory, educational and research aspects of the profession. This faction of the profession has sought for several decades to restrict the practice of chiropractic to a musculoskeletal, pain based model and they have done so by limiting the “acceptable” evidence for chiropractic to randomized controlled clinical trials and through an embrace of extreme scientism.<sup>107-110</sup>

This faction within the profession is intentionally attempting to suppress the evidence that does exist and they provide false and misleading interpretation and commentary on that evidence. That false narrative has been adopted/endorsed by certain state regulatory boards, trade organizations and chiropractic schools to be used against chiropractors who say the words “nervous system” and “immune system” in the same sentence when communicating with patients and the public.

Senzon has written extensively on this issue in a 10 part series demonstrating that a small group of academics in the profession are staging a coup d'état by trying to “cleanse” the chiropractic lexicon.<sup>111-121</sup> These claims are supported by the critique and analysis of Villanueva-Russell.<sup>122</sup> In an evidence-based approach to historical writing, Senzon examines the flaws, breaks down historical errors that arguments rest upon, and lays out the rationale for establishing a shared base of knowledge for the entire profession. Senzon attempts to correct the errors in the literature regarding vertebral subluxation placed by numerous “subluxation deniers” who have peppered the scientific and historical literature with unreferenced and unsupported statements regarding the nature and historical issues surrounding vertebral subluxation.

Though the combined conclusions in regards to these musculoskeletal outcomes following manipulation is poor, it is promoted within the profession by that faction as if the science is settled.<sup>123-125</sup> In addition to the intellectual dishonesty of failing to acknowledge the weakness in their own arguments and the literature supporting it - they engage in misdirection by pointing instead to chiropractors who, for over 100 years, have witnessed improved health outcomes from providing manual care and how they are talking about immunity and then demand through flawed “research” that they should be silenced. No mention is made of similar health outcomes and

practices from the physical therapists, massage therapists, manual medicine practitioners or osteopathy.

### *Semantic Pathology*

Another issue that plagues the chiropractic literature is one of semantic pathology. Kent addressed this in his review of vertebral subluxation, semantic pathology, epistemic trespassing, and ethics.<sup>126</sup>

A function of language is differentiation. Language should be a tool for minimizing ambiguity, and establishing precision in communication. This necessitates the use of terminology that communicates the uniqueness of the thing being described. The use of terms that homogenize rather than differentiate foster ambiguity and imprecision. The practice of conflating terms, such as vertebral subluxation, joint dysfunction, adjustment, and spinal manipulation has ethical and political implications.

One example is the suggestion that the terms vertebral subluxation, joint fixation, joint dysfunction are interchangeable. They are not the same thing. There are significant operational and epistemological differences. Implicit in the term vertebral subluxation are both biomechanical and neurological elements. Vertebral subluxation is a relational neurological process that impacts the human experience, not merely a fixated joint. A fixated or tender joint might represent one manifestation of vertebral subluxation, not a synonym for vertebral subluxation. The notion that they are the same leads to confusion and ambiguity.

These issues will need to be addressed in any research protocol that involves assessing for the presence of vertebral subluxation and its relationship to changes in immune biomarkers.

An error is made in many studies of the effects of “manipulation” by lumping together all “hands on” techniques, while failing to address key issues, such as the examination criteria used to determine the presence of “manipulable lesions,” and how the investigators determine that the “manipulative treatment” was successful. Research designs based upon the haphazard application of ill-defined interventions selected by utilizing examination procedures whose reliability has not been established cannot be considered “scientific.”

An operational definition is a description of the procedures used to determine the means for measuring or observing something. To assess the effect of vertebral subluxation correction on a dependent variable (EEG activity, H-reflexes, health outcomes, etc) one must:

1. Define how the presence of vertebral subluxation will be determined. The methods used must be reliable (reproducible within and between examiners) and valid (measure what they claim to measure).
2. Define the intervention used to attempt correction of the vertebral subluxation.
3. Perform a pre-adjustment examination.
4. Apply the intervention (adjustment, placebo, control).

5. Perform a post-adjustment examination to determine that the subluxation has been reduced or corrected according to the criteria of the operational definition

Whether or not the chiropractic profession will address this political problem remains to be seen but a review of the available evidence as has been done here reveals the science supporting the clinical evidence so many chiropractors observe regularly in practice. The results of this research demands that we further explore the neuro-immuno-regulatory effects of chiropractic, adjustment and spinal manipulation and it provides a starting point for doing so. While adjustments reduce pain and inflammation, they also improve immune-regulatory function. How and to what extent should be the subject of future studies.

### **References**

1. Kenney MJ, Ganta CK. Autonomic nervous system and immune system interactions. *Compr Physiol.* 2014;4(3):1177–1200. doi:10.1002/cphy.c130051.
2. Kent C (2018) Chiropractic and Mental Health: History and Review of Putative Neurobiological Mechanisms. *Jou Neuro Psy An Brain Res: JNPB-103.*
3. Haas A, Russell D. Chiropractic contributes its unique salutogenic health care approach to the emergent COVID-19 crisis. *International Federation of Chiropractors and Organizations.* April 2020.
4. Alcantara J, Whettend A, Ohm J, Alcantara J. The relationship between quality of life and sense of coherence in patients presenting for care in a chiropractic practice-based research network. *Complementary Therapies in Medicine* 48 (2020).
5. Kawchuk G, Goertz C, Axén I, Descarreaux M, French S, Haas M, Hartvigsen J, Kolberg C, Maiers M. The Effect of Spinal Adjustment/Manipulation on Immunity and the Immune System: A Rapid Review of Relevant Literature. *World Federation of Chiropractic.* March 19, 2020.
6. WFC Review of Immunity & Chiropractic Fatally Flawed - Says Foundation for Vertebral Subluxation. *Chronicle of Chiropractic.* Saturday, March 28, 2020.
7. McCoy M, Kent C, Senzon S, Ebrall P. Critical Evaluation of the World Federation of Chiropractic's "Rapid Review" of the Effect of Spinal Adjustment/Manipulation on Immunity and the Immune System. *Foundation for Vertebral Subluxation.* March 2020.
8. Rome P. Neurovertebral Influence on Visceral and ANS Function: Some of the Evidence To Date - Part II: Somatovisceral. *Chiropr J Aust* 2010; 40: 9-33.
9. Boone R, Dobson G. A Proposed Vertebral Subluxation Model Reflecting Traditional Concepts and Recent Advances in Health and Science. *Annals of Vertebral Subluxation Research, Volume 1. Number 1. Pages 1-12.*
10. Boone R. Setting the Research Agenda. *Annals of Vertebral Subluxation Research, Volume 2. Number 2. Pages 1-2.*
11. McCoy M, Kent K. Vertebral Subluxation Research: An Agenda to Explore the Epidemiology of Vertebral Subluxation and the Clinical Outcomes Related to Management. *Annals of Vertebral Subluxation Research, Volume 2013. August 5, 2013. Pages 29-32.*



12. Haldeman S. Interactions between the somatic and visceral nervous systems. *ACA J Chiropr*;1971;5(Suppl):57-64.
13. Cevikbas F, Steinhoff A, Homey B, Steinhoff M. Neuroimmune interactions in allergic skin diseases. *Curr Opin Allergy Clin Immunol* 2007;7(5):365-373.
14. Sato A, Sato Y, Schmidt RF.12 p.254. (Citing Kimura A, Nagai N, Sato A. Somatic afferent regulation of cytotoxic activity of splenic natural killer cells in anesthetized rats. *Jpn J Physiol*. 1994;44:651-664.
15. Johnson GM. The sensory and sympathetic nerve supply within the cervical spine: review of recent observations. *Man Ther* 2004;9(2):71-76.
16. Sato A, Schmidt RF. The modulation of visceral functions by somatic afferent activity. *Japanese J Physiol* 1987;37:1-17.
17. Nagatomi R1, Kaifu T, Okutsu M, Zhang X, Kanemi O, Ohmori H. Modulation of the immune system by the autonomic nervous system and its implication in immunological changes after training. *Exerc Immunol Rev*. 2000;6:54-74.
18. Khalsa PS, Eberhart A, Cotler A, Nahin R. The 2005 conference on the biology of manual therapies. *J Manipulative Physiol Ther*. 2006;29(5):341-346.
19. Cohn A. Chiropractic and the Neuroimmune Connection. *Journal of Vertebral Subluxation Research*. September 30, 2008. Pages 1-5.
20. Brown E. Psychoneuroimmunology and Chiropractic. *Annals of Vertebral Subluxation Research*, Volume 2005. September 20, 2005. Pages 1-7.
21. Boone W, Oswald P, Holt K, Beck R, Singh K, Ashton A Long Term Assessment of Blood Indices and Immune Panel Profiling of Subjects Receiving Chiropractic Care: A Pilot Study. *Journal of Vertebral Subluxation Research*. June 7, 2006. Pages 1-11.
22. Boone W, Oswald P, Holt K, Beck R, Singh K, Ashton A. Physical, physiological, and immune status changes, coupled with self-perceptions of health and quality of life, in subjects receiving chiropractic care: A pilot study. *Annals of Vertebral Subluxation Research*, Volume 2006. July 5, 2006. Pages 1-6.
23. Ressel O, Rudy R. Vertebral Subluxation Correlated with Somatic, Visceral and Immune Complaints: An Analysis of 650 Children Under Chiropractic Care. *Annals of Vertebral Subluxation Research*, Volume 2004. October 18, 2004. Pages 1-23.
24. Hannon S. Objective Physiologic Changes and Associated Health Benefits of Chiropractic Adjustments in Asymptomatic Subjects: A Review of the Literature. *Annals of Vertebral Subluxation Research*, Volume 2004. September 20, 2005 ~ Pages 1-7.
25. Takeda Y, Arai S, Touichi H, Long Term Remission and Alleviation of Symptoms in Allergy and Crohn's Disease Patients Following Spinal Adjustment for Reduction of Vertebral Subluxations. *Annals of Vertebral Subluxation Research*, Volume 4.
26. Van Breda JM, Van Breda WM. Comparative study of the health status of children raised under the health care models of chiropractic and allopathic medicine. *J Chiropr Res*. 1989 Sum;5(4):101-103.
27. Alcantara J, Lamont A, Ohm J, Alcantara J. The Quality of Life of Children Under Chiropractic Care Using PROMIS-25: Results from a PBR Network. *J Altern Complement Med*. 2018 Apr;24(4):378-384. doi: 10.1089/acm.2017.0141. Epub 2017 Dec 20.
28. Alcantara J, Ohm J, Alcantara J. Comparison of pediatric self reports and parent proxy reports utilizing PROMIS: Results from a chiropractic practice-based research network. *Complement Ther Clin Pract*. 2017 Nov;29:48-52. doi: 10.1016/j.ctcp.2017.08.003. Epub 2017 Aug 31.
29. Galgano J, Turo D. Correction of Cervical Kyphosis & Health Concerns (asthma, allergies, sinusitis) Following a Single Adjustment Utilizing the Pierce Chiropractic Technique. *Annals of Vertebral Subluxation Research*, Volume 2011. June 9, 2011. Pages 37-43.
30. Egan A, Alcantara J. Resolution of Gastroesophageal Reflux in an Infant Following Chiropractic Care to Reduce Vertebral Subluxation: A Case Report & Review of Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2019. May 27, 2019. Pages 46-54.
31. Stone-McCoy P, Taylor C. Resolution of Asthma and other Functional Disorders Following Chiropractic Care to Reduce Vertebral Subluxations in a Nine Year Old Male: A Case Report. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2018. April 9, 2018. Pages 26-33.
32. Fedorchuk C, Opitz K. Improvement in Quality of Life and Improved Cervical Curve in an 11-year-old Child with Asthma Following Chiropractic Intervention: A Case Study. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2014. Issue 2. Pages 37-46.
33. Fujimoto T. Resolution of Allergic Dermatitis in an Infant Undergoing Chiropractic. *Annals of Vertebral Subluxation Research*, Volume 2007. August 27, 2007. Pages 1-6.
34. Korthuis M. Improved Allergen-Specific IgE Levels in an 8-year-old Female Following Chiropractic Care to Reduce Vertebral Subluxation: A Case Study & Selective Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2017. Issue 2. Pages 82-92.
35. Alcantara J, Van Roo L, Oman R. Chiropractic Care of a Pediatric Patient with Asthma, Allergies, Chronic Colds & Vertebral Subluxation. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2009. Pages 1-7. August 17, 2009.
36. Swift C, Wetterlin K, Alcantara J. Improved Health Outcomes in an Asthmatic Child Following Chiropractic Care with Bio-Geometric Integration: A Case Study. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2017. Pages 151-156.
37. Kachinsky B, Kachinsky J. Improvement in a Pediatric Patient with Neurofibromatosis Type 1 and Asthma: A Case Report. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2011.
38. Zonarich A, Aubin L. Chiropractic and Omega-3 Supplementation as Alternative Management for Asthma in a 6 year old. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2011.
39. Whittle-Davis H, Czegus K. Chiropractic Care of a Pediatric Patient With Asthma: A Case Report. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2011. Pages 77-81.
40. Davis H, Byrley A. Correction of Subluxation and Alleviation of Asthma Symptoms in a Pediatric Patient: A Case Study. *Journal of Pediatric, Maternal & Family*

- Health Chiropractic, Volume 2012. Pages 69-73.
41. Rectenwald R. Resolution of Severe Chronic Asthma in an Infant Following Upper Cervical Chiropractic Care to Reduce Subluxation. *Journal of Pediatric, Maternal & Family Health – Chiropractic*. Volume 2014. Issue 2.
  42. Jaszewski E, Willard A. Resolution of Asthma in a Teenager Following Subluxation-Based Chiropractic Management Utilizing the Pierce Results System: A Case Study & Selective Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2016.
  43. Graham R, Pistolese R. An Impairment Rating Analysis Of Asthmatic Children Under Chiropractic Care. *Annals of Vertebral Subluxation Research*, Volume 1. Pages 1-8.
  44. Elster E. Upper Cervical Chiropractic Care For A Nine-Year-Old Male With Tourette Syndrome, Attention Deficit Hyperactivity Disorder, Depression, Asthma, Insomnia, and Headaches: A Case Report. *Annals of Vertebral Subluxation Research*, Volume 2003.
  45. Fedorchuk C. Correction of Subluxation and Reduction of Dyspnea in a 7 Year-Old Child Suffering From Chronic Cough and Asthma: A Case Report. *Annals of Vertebral Subluxation Research*, Volume 2007.
  46. Cuthbert S, Rosner A. Applied Kinesiology Management of Candidiasis and Chronic Ear Infections. *Journal of Pediatric, Maternal & Family Health – Chiropractic*. December 29, 2010. Pages 208-210.
  47. Cooper J, Howell L. Resolution of Otitis Media in 10-Year-Old Child Following Improved Cervical Curve using Pierce Results System: Case Study & Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2017. Issue 2. Pages 93-108.
  48. Lachowich T, Alcantara J. Resolution of Chronic, Recurrent Otitis Media & Avoidance of Tympanostomy Surgery Following Chiropractic in a Three Year Old: A Case Report & Review of Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2019. September 23, 2019 ~ Pages 109-112.
  49. McWilliams S, Rose C. Resolution of Chronic Otitis Media, Improvements in Hearing and Avoidance of Tympanostomy Tubes in a 9½ Year Old Boy Undergoing Chiropractic Care. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2018. September 24, 2018. Pages 112-122.
  50. Marko S, Marko J. Resolution of Otitis Media and Nocturnal Enuresis in a 12-Year-Old Patient Following Chiropractic Care to Reduce Vertebral Subluxations: A Case Study and Selected Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2018. April 2, 2018. Pages 13-25.
  51. Stone-McCoy P, Boutilier A, Black P. Resolution of Otitis Media in a Nine Month Old Undergoing Chiropractic Care: A Case Study and Selective Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2010.
  52. Marino F, Butt A. Chiropractic Care of a Pediatric Patient Suffering from Recurrent Otitis Media and Respiratory Syncytial Virus: a Retrospective Case Report. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2010.
  53. Lanjopoulos C, Lanjopoulos D. Resolution of Chronic Otitis Media, Difficulty Sleeping, and Tactile Hypersensitivity in a Child Undergoing Subluxation-Based Chiropractic Care. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2012.
  54. Stone-McCoy P, Korn C. Resolution of Otitis Media & Avoidance of Tympanostomy Tubes in a 16-Month Old with Birth Trauma Following Subluxation Based Care: A Case Study and Selective Review of Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2013.
  55. O'Connor K, Schneider G, Alcantara J. Resolution of Otitis Media, Improvement in Hearing & Avoidance of Myringotomy Tubes Following Chiropractic Care in a Child: A Case Report & Selective Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2014.
  56. Steinberg B, Doerr A. Resolution of Chronic Otitis Media, Constipation & Sleep Disturbance Following Adjustment of Subluxations in a 2-year-old Child: A Case Study & Review of Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2016.
  57. Stone-McCoy P, Natori C. Chiropractic Care of a Toddler with Otitis Media Born Premature & Exposed Prenatally to Opiates and Amphetamines: A Case Study & Selective Review of Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2017. Issue 1. Pages 1-7.
  58. Feranti M, Alcantara J. Chronic Otitis Media, Failed Tympanostomy Tube Surgery & Resolution Following Adjustment of Vertebral Subluxation. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2016. Issue 1. Pages 5-8.
  59. Sonners M. Can chiropractic adjustments help decrease the incidence of acute otitis media? *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2010.
  60. Apfelblat A. Resolution of otitis media with chiropractic management. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2010. December 29, 2010.
  61. Fedorchuk C, Cohen A. Resolution of Chronic Otitis Media, Neck Pain, Headaches & Sinus Infection in a Child Following an Increase in Cervical Curvature & Reduction of Vertebral Subluxation. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2009.
  62. Brown C. Improved Hearing and Resolution of Otitis Media with Effusion Following Chiropractic Care to Reduce Vertebral Subluxation. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2009. Issue 1. Pages 1-7.
  63. Sigmon P, Alcantara J. Resolution of Chronic, Recurrent Bilateral Ear Infections Following Chiropractic Care in a One-year-old Infant: A Case Report & Review of the Literature. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2019. January 14, 2019. Pages 1-5.
  64. Basso E, Potrzebowski S. Resolution of Juvenile Idiopathic Arthritis & Improved Immune Function in a 16 year old Undergoing Chiropractic Care: A Case Study. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2014. Issue 4. Pages 65-69.
  65. Warhurst R, Gabai A. Improvement in Cystic Fibrosis in a Child Undergoing Subluxation-Based Chiropractic Care: A Case Study. *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2010.

66. Colombi A, Testa M. The Effects Induced by Spinal Manipulative Therapy on the Immune and Endocrine Systems. *Medicina (Kaunas)*. 2019 Aug 7;55(8).
67. Brennan PC, et al. Enhanced phagocytic cell respiratory burst induced by spinal manipulation: potential role of substance P. *JMPT*, 1991;14:399-408.
68. Brennan PC, et al. Enhanced neutrophil respiratory burst as a biological marker for manipulation forces: duration of the effect and association with substance P and tumor necrosis factor. *JMPT*, 1992;15:83-9.
69. Selano JL. The effects of specific upper cervical adjustments on the CD4 counts of HIV positive patients. *Chiro Res J*, 1994;3:32-9.
70. Teodorczyk-Injeyan J, Injeyan H, Ruegg R. Spinal manipulative therapy reduces inflammatory cytokines but not substance P production in normal subjects. *J Manipulative Physiol Ther*. 2006 Jan;29(1):14-21.
71. Omos G, MD, et al. Reduction in high blood TNF-a levels after manipulative therapy in 2 cervicogenic headache patients. *JMPT*, 2009;32(7):586-91.
72. Roy RA, Boucher JP, Comtois AS. Inflammatory response following a short-term course of chiropractic treatment in subjects with and without chronic low back pain. *Journal of Chiropractic Medicine*, 2010;9:107-114.
73. Teodorczyk-Injeyan JA, Injeyan HS, McGregor M, et al. Enhancement of in vitro interleukin-2 production in normal subjects following a single spinal manipulative treatment. *Chiropr Osteopat*, 2008;16:5.
74. Teodorczyk-Injeyan JA, et al. Interleukin-2 regulated in vitro antibody production following a single spinal manipulative treatment in normal subjects. *Chiropr Osteopat*, 2010;18:26.
75. Tuchin P. The effect of chiropractic spinal manipulative therapy on salivary cortisol levels. June 1998. *Australasian chiropractic & osteopathy: journal of the Chiropractic & Osteopathic College of Australasia* 7(2):86-92.
76. Christian GF, Stanton GJ, Sissons D, et al. Immunoactive ACTH, B-endorphin and cortisol levels in plasma following spinal manipulative therapy. *Spine* 1988; 13: 1411-7.
77. Whelan T, Dishman J, Burke J, Levine S, Sciotti V. The effect of chiropractic manipulation on salivary cortisol levels. *J Manipulative Physiol Ther*. 2002 Mar-Apr;25(3):149-53.
78. Campbell C, Kent C, Banne A, Amiri A, Pero R. Surrogate Indication of DNA Repair in Serum After Long Term Chiropractic Intervention – A Retrospective Study. *Annals of Vertebral Subluxation Research*, Volume 2005. February 18, 2005. Pages 1-5.
79. Saggio G, Docimo S, Pilc J, Norton J, Gilliar W. Impact of Osteopathic Manipulative Treatment on Secretory Immunoglobulin A Levels in a Stressed Population. *J Am Osteopath Assoc*. 2011;111(3):143-147.
80. Noll D, Degenhardt B, Morley T et al. Efficacy of osteopathic manipulation as an adjunctive treatment for hospitalized patients with pneumonia: a randomized controlled trial. *Osteopathic Medicine and Primary Care*. 2010;4(1):2. doi:10.1186/1750-4732-4-2.
81. Harakal JH. Manipulative treatment for acute upper-respiratory diseases. *Osteopathic Annals*. 1981;9(7):30-37.
82. Noll DR, Shores J, Bryman PN, Masterson EV: Adjunctive osteopathic manipulative treatment in the elderly hospitalized with pneumonia: a pilot study. *J Am Osteopath Assoc* 1999, 99:143-146.
83. Noll DR, Shores JH, Gamber RG, Herron KM, Swift J Jr: Benefits of osteopathic manipulative treatment for hospitalized elderly patients with pneumonia. *J Am Osteopath Assoc* 2000, 100:776-782.
84. Noll DR, Degenhardt BF, Fossum C, Hensel K: Clinical and research protocol for osteopathic manipulative treatment of elderly patients with pneumonia. *J Am Osteopath Assoc* 2008, 108:508-516.
85. Facto LL: The osteopathic treatment for lobar pneumonia. *J Am Osteopath Assoc* 1947, 46:385-392
86. Measel JW. The effect of the lymphatic pump on the immune response: I. Preliminary studies on the antibody response to pneumococcal polysaccharide assayed by bacterial agglutination and passive hemagglutination. *J Am Osteopath Assoc*. 1982;82(1):28-31.
87. Jackson KM, Steele TF, Dugan EP, Kukulka G, Blue W, Roberts A. Effect of lymphatic and splenic techniques on the antibody response to hepatitis B vaccine: a pilot study. *J Am Osteopath Assoc*. 1998;98(3):155-160.
88. Mesina J, Hampton D, Evans R, et al. Transient basophilia following the application of lymphatic pump techniques: a pilot study. *J Am Osteopath Assoc*. 1998;98(2):91-94.
89. Paul RT, Stomel RJ, Broniak FF, Williams BB Jr. Interferon levels in human subjects throughout a 24-hour period following thoracic lymphatic pump. *J Am Osteopath Assoc*. 1986;86(2):92-95.
90. Henderson AT, Fisher JF, Blair J, Shea C, Li TS, Bridges KG. Effects of rib raising on the autonomic nervous system: a pilot study using noninvasive biomarkers. *J Am Osteopath Assoc*. 2010;110(6):324-330.
91. Knott EM, Tune JD, Stoll ST, Downey HF. Increased lymphatic flow in the thoracic duct during manipulative intervention. *J Am Osteopath Assoc*. 2005;105(10):447-456.
92. Henley CE, Ivins D, Mills M, Wen FK, Benjamin BA. Osteopathic manipulative treatment and its relationship to autonomic nervous system activity as demonstrated by heart rate variability: a repeated measures study. *Osteopath Med Prim Care*. 2008;2(1):7-15.
93. Hodge L. Osteopathic lymphatic pump techniques to enhance immunity and treat pneumonia. *International Journal of Osteopathic Medicine*. 2012;15(1):13-21.
94. Knott EM, Tune JD, Stoll ST, Downey HF: Increased lymphatic flow in the thoracic duct during manipulative intervention. *J Am Osteopath Assoc* 2005, 105:447-456.
95. Hodge LM, King HH, Williams AG, Reder SJ, Belavadi T, Simecka JW, Stoll ST, Downey HF: Abdominal lymphatic pump treatment increases leukocyte count and flux in thoracic duct lymph. *Lymphat Res Biol* 2007, 5:127-134.
96. Breithaupt T, Harris K, Ellis J, Purcell E, Weir J, Clothier M, Boesler D: Thoracic lymphatic pumping and the efficacy of influenza vaccination in healthy young and elderly populations. *J Am Osteopath Assoc* 2001, 101:21-25.
97. Noll DR, Degenhardt BF, Stuart MK, Werden S, McGovern RJ, Johnson JC: The effect of osteopathic manipulative treatment on immune response to the

- influenza vaccine in nursing homes residents: a pilot study. *Altern Ther Health Med* 2004, 10:74-76.
98. Snider K, Snider E, Johnson J, Hagan C, Schoenwald C. Preventative Osteopathic Manipulative Treatment and the Elderly Nursing Home Resident: A Pilot Study. *The Journal of the American Osteopathic Association*, August 2012, Vol. 112, 489-501.
  99. D'Alonzo G, Influenza Epidemic or Pandemic? Time to Roll Up Sleeves, Vaccinate Patients, and Hone Osteopathic Manipulative Skills. *JAOA*. Vol 104. No 9. September 2004.
  100. McConnell CP. The treatment of influenza. Editorial. *J Am Osteopath Assoc*. 1918; :83-85. Reprinted in: *J Am Osteopath Assoc*. 2000;100:311-313.
  101. Smith RK. One hundred thousand cases of influenza with a death rate of one-fortieth of that officially reported under conventional medical treatment. *J Am Osteopath Assoc*. 1920;20:172-175. Reprinted in: *J Am Osteopath Assoc*. 2000;100:320-323.
  102. Rhodes W. The Official History of Chiropractic in Texas. Texas Chiropractic Association 1978.
  103. Palmer BJ. Fountain Head News. Volume 8. Saturday, January 18, 1918 No. 17-19.
  104. Johnson D, Pero R, Flesia J. Biochemical and endocrinological changes due to neuropathologic states that can lead to genotoxic consequences. A testable hypothesis for health effects induced by spinal pathomechanics. Chiropractic Basic Science Research Foundation.
  105. Lecture Transcript. The Flesia/Pero Hypothesis for the Validation of Chiropractic. Pages 1-16. Chiropractic Basic Science Research Foundation.
  106. Mead M. Boosting Your Immunity Through Chiropractic. *East West Journal*. November 1989. Pg 67.
  107. McCoy M. Canadian Chiropractors Under Attack by their Own Regulatory Board. Subluxation Management Marginalized Under Guise of Marketing Abuses. *Chronicle of Chiropractic*. Tuesday, October 16, 2018.
  108. Alcantara J. Evidence-Informed Pediatric Chiropractic: Investigational or Experimental? *Journal of Pediatric, Maternal & Family Health Chiropractic*, Volume 2015. Issue 1 ~ Pages 26-33.
  109. Bronfort, G., et al., Effectiveness of manual therapies: the UK evidence report. *Chiropractic & osteopathy*, 2010. 18(1): p. 1.
  110. Nelson, C., et al., Chiropractic as spine care: a model for the profession. *Chiropractic & Manual Therapies*, 2005. 13(1): p. 9.
  111. Senzon, S., The chiropractic vertebral subluxation part 1: The Need for a Complete Historical Record. *J Chiropr Hum*, 2018. 25: p. 10-21.
  112. Senzon, S., The chiropractic vertebral subluxation part 2: The Earliest Subluxation Theories from 1897-1907. *J Chiropr Hum*, 2018. 25: p. 22-35.
  113. Senzon, S., The chiropractic vertebral subluxation part 3: Complexity and Identity from 1908 to 1915. *J Chiropr Hum*, 2018. 25: p. 36-51.
  114. Senzon, S., The chiropractic vertebral subluxation part 4: New Perspectives and Theorists from 1916-1927. *J Chiropr Hum*, 2018. 25: p. 52-66.
  115. Senzon, S., Causation related to self-organization and health related quality of life expression based on the vertebral subluxation model, the philosophy of chiropractic, and the new biology. *J Vertebral Subluxation Res*, 1999. 3(3): p. 104-112.
  116. Senzon, S., The chiropractic vertebral subluxation part 5: The First Research Era from 1928-1949. *J Chiropr Hum*, 2018. 25: p. 67-85.
  117. Senzon, S., The chiropractic vertebral subluxation part 6: Renaissance of D.D. Palmer's Paradigm from 1949-1961. *J Chiropr Hum*, 2018. 25.
  118. Senzon, S., The chiropractic vertebral subluxation part 7: Technics and Models from 1962-1980. *J Chiropr Hum*, 2018. 25: p. 99-113.
  119. Senzon, S., The chiropractic vertebral subluxation part 8: Terminology, Definitions, and Historicity from 1966-1980. *J Chiropr Hum*, 2018. 25: p. 114-129.
  120. Senzon, S., The chiropractic vertebral subluxation part 9: Complexes, models, and consensus from 1981-1995. *J Chiropr Hum*, 2018. 25: p. 130-145.
  121. Senzon, S., The chiropractic vertebral subluxation part 10: Integrative and Critical Literature from 1983 to 1997. *J Chiropr Hum*, 2018. 25: p. 146-168.
  122. Villanueva-Russell, Y. Caught in the crosshairs: Identity and cultural authority within chiropractic. *Social Science & Medicine*, 2011. 72(11): p. 1826-1837.
  123. Rubinstein Sidney M, de Zoete Annemarie, van Middelkoop Marienke, Assendelft Willem J J, de Boer Michiel R, van Tulder Maurits W et al. Benefits and harms of spinal manipulative therapy for the treatment of chronic low back pain: systematic review and meta-analysis of randomised controlled trials *BMJ* 2019; 364 :l689.
  124. Paige N, Miake-Lye I, Suttrop Booth M, Beroes J, Mardian A, Dougherty P, Branson R, Tang B, Morton S, Shekelle P. Association of Spinal Manipulative Therapy With Clinical Benefit and Harm for Acute Low Back Pain Systematic Review and Meta-analysis. *JAMA*. 2017;317(14):1451-1460
  125. Assendelft WJ et al: Spinal manipulative therapy for low back pain. *Cochrane Database Sys Rev* 2004(1):CD000447.
  126. Kent C. Vertebral Subluxation: Semantic Pathology, Epistemic Trespassing, and Ethics. *Journal of Philosophy, Principles & Practice of Chiropractic*. Volume 2018. July 23, 2018. Pages 1-7.