

# Focus on Research

## December 2001

### Upper Cervical Spine Adjustments And Alterations In Heart Rate Variability In Healthy Young Adults

*Budgell B, Hirano F. Auton Neurosci 2001;91:96-9.*

This study examined the effects of chiropractic adjustments to the upper cervical spine, on heart-rate variability (HRV), in a cohort of healthy young adults. The authors used a cross-over research design, to explore and contrast changes in HRV in one group, who received a sham procedure, and another group who received authentic chiropractic adjustment. The authors found that upper cervical adjustments were associated with significant alterations in both heart rate and measures of heart-rate variability compared to the control group. In particular, there was an increase in the ratio of low- frequency (LF)-to-high-frequency (HF) components of the power spectrum of heart-rate variability, **which likely reflect a shift in balance between sympathetic and parasympathetic output to the heart.**

**ASRF Editor's comment:** This is a very significant study which, although it raises more questions than it answers, has now established a baseline from which to begin work, with a relatively new tool (Power Spectral Analysis of Heart Rate Variability), in delineating the relationship between adjustment, subluxation and the autonomic nervous system.

### Rear-End Collisions And Future General Health

*Berglund A, Alfredsson L, Jensen I, Cassidy DJ, Nygren A. Journal of Clinical Epidemiology 2001;54:851-6.*

A diversity of persistent health related problems have been documented in persons after suffering a motor vehicle crash (MVC). A cohort study was conducted to determine whether exposure to a rear- end collision, with or without whiplash injury, is associated with future health complaints. The objective of the present report was to focus on outcomes other than neck pain. Included in the study were persons 18 to 65 years of age and covered by traffic insurance at one of the largest insurance companies in Sweden. Claim reports were collected from the period November 1987 to April 1988. Drivers exposed to a rear-end collision were divided into two subgroups: those with reported whiplash injury (n 232) and those without a reported whiplash injury (n 204). For comparison, 3688 subjects who were unexposed to MVCs were selected, with consideration taken to the age and gender distribution in the ex-posed subgroups.

The prevalence of different health complaints among the study subjects was estimated according to a mailed questionnaire at follow-up in 1994, 7 years after the rear-end collision. When exposed subjects with whiplash injury were compared to unexposed subjects, increased relative risks in the range of 1.6-3.7 were seen for headache, thoracic and low back pain, **as well as for fatigue, sleep disturbances and ill health.** No corresponding increased risks were found among the exposed subjects without reported whiplash injury.

The authors conclude that, **“rear-end collisions resulting in reported whiplash injuries seem to have a substantial impact on health complaints, even long after the collision.”**

## Belgium Cuts Antibiotic Use By 12%

Watson R. News, *BMJ* 2001;323:710.

Belgian public health authorities successfully reduced consumption of antibiotics in the country by 12% last winter. The program was launched by public health and social affairs ministers Magda Aelvoet and Frank Vandenbroucke last November.

As a result of the campaigns success, the government intends to organize a second campaign this year. This will contain even more explicit messages and advise people that antibiotics are not necessary for flu, sore throats, or bronchitis.

## Asthma In Spain Linked To Cereal Used In Baby Food

*Armentia, A., Bañuelos, C., Arranz, M. L., et al.* Early introduction of cereals into children's diets as a risk-factor for grass pollen asthma. *Clinical & Experimental Allergy* 2001;31:1250-5

The findings, from a team of 9 researchers from the Rio Hortega Hospital, Valladolid, Spain, revealed that **84.4% of asthma sufferers in Spain who had eaten cereal as babies were now sensitive to grass pollen and had Asthma, compared with only 15.1% of those who were breast-fed.**

The prevalence of asthma has increased dramatically from the 1950s to the 1990s. Despite extensive research into possible links to diet most findings until recently have been inconclusive. After identifying allergens from cereals that show cross-reactivity with proteins in grass pollen the authors of a study, which was just published in the *Journal of Clinical & Experimental Allergy*, hypothesized that an intake of cereals during early life might cause IgE sensitization to cereals. To test their hypothesis the authors carried out a cross-sectional study and an observational case-control analysis of reviewed data on 16381 patients with Asthma..

**It was found that babies who were fed cereal in the first few months of their lives were six times more likely to develop Asthma. (OR = 5.95; 95% CI 3.89-9.10).**

The authors of the study chose the date 1959 to be the cut off point for evaluating the risk factor because it was at the start of the 60's that cereal formulas were introduced into children's diets before the age of 3 months. That was also the time when Asthma cases began to increase rapidly. It is concluded that, "These findings document the progression of asthma in a large sample of people who were influenced by similar environmental conditions and studied with the same methods. This study represents the largest database of patients in which a common food is shown to be a risk factor for asthma."

**ASRF Editor's comment:** Case-control studies are notoriously unreliable. To take the results of a case-control study seriously the Odds Ratio (OR) should be more than four. Furthermore, the Confidence Interval (CI) should be narrow and should not include the number one. The paper reviewed above fulfills these criteria.

## Is The Garden Hose Theory Of Vertebral Subluxation Dead?

**References:** In 1973 the well known Yale Anatomist, Edmund Crelin PhD, carried out a study in which he examined the effects of gross rotational, compressive, and torsional forces on 6 cadaver spines. He entitled the study, "The First Scientific Test of the Chiropractic Theory."(1) Based on his study Crelin concluded that, "Any reduction in the size of the intervertebral foramina during the application of a bending force to produce flexion, extension, and lateral bending of the adult columns was insignificant in relation to the spinal nerves passing through the foramina." Crelin obviously thought that his experiment accurately duplicated the true conditions under which nerve root compression or irritation might occur. He concluded, "This experimental study demonstrates conclusively that the subluxation of a vertebra as defined by chiropractic, does not occur."

However, much of what Crelin did in his study failed to simulate what we now know happens at the level of the IVF.

A study(2) carried out by Lynton Giles DC, PhD, from the Spinal Research Laboratory, Griffith University, Australia, explored the validity of Crelin's work. Furthermore, Giles sort to determine the proximity of neural structures to the boundaries of the interpedicular zone of the intervertebral canal in cadaveric adult human spines at the L4-5 and L5-S1 spinal levels. Giles concluded that Crelin's study abounds with methodological flaws and that within the interpedicular zone of the IVF, the distance between neural structures and the boundary can be as little as 0.4 (SD 0.4) mm.

A recent review(3) examined the possible clinical relevance of nerve root compression as a component of the vertebral subluxation. The authors carried out a number of literature searches on the World Wide Web via the Pub Med website.

Some of their findings are worth quoting:

Mild nerve root compression can exist without pain... Mechanical changes lead to circulatory changes in the nerve root and DGR(4) ... The nerve alterations that occur as a result of pressure start with a reduced nutritional supply with as little as 10 mmHg.(5) ... The role of ephaptic transmission, or cross talk between nerve fibers, is generally spoken of in terms of pain(6)...It seems just as possible for cross talk to other nerve fibers. Nerve fibers that are not responsible for pain, but the functioning of other tissues.

The authors of the literature review(3) conclude with the following statements:

“...pressures of as little as 10 mm Hg can alter nerve root and dorsal root ganglion function.” “...within the normal range of motion pressures generated in the IVF may exceed 30 mm Hg.” “There is evidence of mild nerve root compression occurring at 15.4% to 78% of levels inspected.”

“The concept that a vertebral subluxation can induce clinically significant pressure increases at the level of the IVF is supported by the literature.”

“The chiropractic adjustment can effect a restoration of normal H-reflex in compressed nerve roots without altering the H-reflex at uninvolved levels.”

The authors conclude that more research is needed to decipher the susceptibility of nerve roots and DRG's to mild pressure increases that may be associated with subtle movement restrictions throughout the spine. **However, the authors feel that those who think the nerve root compression model is obsolete need to take a better look at the research.**

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4. Hause M. Pain and the Nerve Root. Spine 1993;18:20-53.
5. Olmarker K, et al. Compression-Induced Changes of the Nutritional Supply to the Porcine Cauda Equina. J Spinal Disorder 1990;3:25-9.

#### **Risk Of Cardiovascular Events Associated With New Anti-Inflammatory Drugs**

Mukherjee D, Nissen SE, Topol EJ. JAMA 2001;286:954-9.

In clinical trials, rofecoxib was found to be as effective as other NSAIDs for management of pain and inflammation. Rofecoxib is one of a new range of anti-inflammatory drugs called COX-2 inhibitors. In trials that compare rofecoxib with ibuprofen, diclofenac and indomethacin, less GI damage has been observed with the use of rofecoxib, in a meta-analysis.

**However, by decreasing vasodilatory and antiaggregatory prostacyclin production, it has become apparent that COX-2 antagonists may lead to increased prothrombotic activity.**

The objective of this review was to define the cardiovascular effects of COX-2 inhibitors when used for arthritis and musculoskeletal pain in patients without coronary artery disease, we performed a MEDLINE search to identify all English-language articles on use of COX-2 inhibitors published between 1998 and February 2001.

The authors also reviewed relevant submissions to the US Food and Drug Administration by pharmaceutical companies. Their search yielded 2 major randomized trials, the Vioxx Gastrointestinal Outcomes Research Study (VIGOR; 8076 patients) and the Celecoxib Long-term Arthritis Safety Study (CLASS; 8059 patients), as well as 2 smaller trials with approximately 1000 patients each.

The results from VIGOR showed that the relative risk of developing a confirmed adjudicated thrombotic cardiovascular event (myocardial infarction, unstable angina, cardiac thrombus, resuscitated cardiac arrest, sudden or unexplained

death, ischemic stroke, and transient ischemic attacks) with rofecoxib treatment compared with naproxen was 2.38 (95% confidence interval, 1.39-4.00; P = .002).

The annualized myocardial infarction rates for COX-2 inhibitors in both VIGOR and CLASS were significantly higher than that in the placebo group of a recent meta-analysis of 23 407 patients in primary prevention trials (0.52%): 0.74% with rofecoxib (P = .04 compared with the placebo group of the meta-analysis) and 0.80% with celecoxib (P = .02 compared with the placebo group of the meta-analysis).

In Conclusion the authors state, "The available data raise a cautionary flag about the risk of cardiovascular events with COX-2 inhibitors."

### **Body Mind Chiropractic Connection**

Mental illness occurs in more than 10% of people 65 and older, and in half of those older than 85. One reason for increased mental problems in the elderly may be a lack of exercise. A recent study published in the *Archives of Internal Medicine* focused on this relationship between exercise and mental health.

The cognitive performance of nearly 6,000 women, who were 65 years of age or older, was measured over an 8 year period using a test that quantified concentration, language, and memory. The level of physical activity of the participants was also quantified - Calories burned were estimated using reports on the duration and intensity levels of physical activities reported by the women.

It was found that women with greater activity levels, in terms of blocks walked or calories burned, were less likely to experience cognitive decline. Here's a breakdown of the important numbers:

- Women who burned the most calories were less likely to experience cognitive decline than women who burned the fewest calories.
- Women who walked the most were less likely to experience cognitive decline than women who walked the least.
- For every 10 blocks walked per day, women reduced their risk of cognitive decline by 13%. What does that have to do with chiropractic????

Everything

The findings from a recent randomized clinical trial(2) suggests that people over the age of 85 who receive ongoing chiropractic care (for 3 years or more):

- \* Are more likely to exercise vigorously
- \* Are less likely to be hospitalised
- \* Are less likely to need to use a nursing home
- \* Are more likely to report a better health status
- \* Are less likely to need to use prescription drugs
- \* Are more likely to be active in the community

References:

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### **Effect Of Local Autonomic Denervation On Responsiveness Of Lymphocytes**

Arce A, Castillon P, Cardinali DP, Esquifino AI. *J Auton Nerv Syst* 1997;62:155-62. Departamento de Fisiologia, Facultad de Medicina, Universidad de Buenos Aires, Argentina.

This study was performed to determine:

- (1) whether local sympathetic and/or parasympathetic denervation of rat submaxillary lymph nodes brought about changes in lymph node cellularity, natural killer activity and lipopolysaccharide (LPS) and concanavalin A (Con A) induced cell proliferation in Freund's adjuvant-injected rats;
- (2) whether the effect of the immunosuppressant cyclosporine was affected in rat submaxillary lymph nodes by a single or combined unilateral ganglionectomy plus decentralization.

The local autonomic denervation of rat submaxillary lymph nodes was achieved by a unilateral sympathetic superior cervical ganglionectomy and/or the unilateral section of chorda tympani (that resulted in ipsilateral parasympathetic decentralization of the submandibular territory).

A unilateral ganglionectomy, or the combination of ganglionectomy plus decentralization, performed 7 days earlier, decreased significantly cellularity in ipsilateral submaxillary lymph nodes, while a unilateral decentralization failed to affect it.

Natural killer activity increased ipsilaterally after ganglionectomy or decentralization, and decreased after the combined surgical procedure. LPS-induced cell proliferation augmented significantly after ganglionectomy or decentralization, while Con A-induced T lymphocyte proliferation remained unaffected. In the sham-operated side, cyclosporine decreased submaxillary lymph node cell number and natural killer activity, while it increased the proliferative response to LPS. The depressive effect of cyclosporine on lymph node cellularity was no longer observed in ganglionectomized or decentralized lymph nodes. The stimulatory effect of cyclosporine on lymphocyte proliferation induced by LPS was reversed both by ganglionectomy or by decentralization and was suppressed by the combined surgical procedure.

**The results further indicate that an appropriate sympathetic and parasympathetic local environment are needed for immunomodulation in lymphoid tissue.**

### **Asthma Increase Caused By Paracetamol**

The connection between asthma and paracetamol was first proposed in a previous ecological analysis of the respiratory health survey's data (Eur Respir J 2000;16:817-23), which found that the **prevalence of wheeze increased by 0.52% in 13-14 year olds and by 0.26% in adults (p<0.0005) per gram of drug taken per person per year**. The authors of that study proposed a mechanism whereby paracetamol strips reduced glutathione from the airway, shifting the balance of oxidant and antioxidant and causing inflammation.

The results of a new study, the world's largest asthma study, published in the European Respiratory Journal (2001;18:598-611), **further supports a link between paracetamol use and an increased susceptibility to asthma.**

The European community respiratory health survey was a cross sectional study of atopy, asthma, and other chronic respiratory disorders that was carried out in 22 countries and involved some 140 000 participants.

Its most startling finding was the uneven geographical distribution of these respiratory symptoms. There was a fourfold difference in the prevalence of nasal allergy between the most and least affected countries, a six fold difference in the prevalence of current asthma, and an eight fold difference in the prevalence of wheeze.

The researchers noted that asthma and allergy symptoms were most prevalent in countries with per capita sales averaging over 20mg of paracetamol per year.

### **The Autonomic Nervous System --An Integrative Interface Between Two Supersystems: The Brain And The Immune System**

*Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES. Pharmacol Rev 2000;52:595-638.*  
National Institutes of Health, Bethesda, Maryland, USA.

The brain and the immune system are the two major adaptive systems of the body.

During an immune response the brain and the immune system **"talk to each other"** and this process is essential for maintaining homeostasis. Two major pathway systems are involved in this cross-talk: the hypothalamic-pituitary-adrenal (HPA) axis and the **sympathetic nervous system (SNS)**.

This overview focuses on the role of SNS in neuroimmune interactions, an area that has received much less attention than the role of HPA axis. Evidence accumulated over the last 20 years suggests that norepinephrine (NE) fulfills the criteria for neurotransmitter/neuromodulator in lymphoid organs. **Thus, primary and secondary lymphoid organs receive extensive sympathetic/noradrenergic innervation.** Under stimulation, NE is released from the sympathetic nerve terminals in these organs, and the target immune cells express adrenoceptors.

**Through stimulation of these receptors, locally released NE, or circulating catecholamines such as epinephrine, affect lymphocyte traffic, circulation, and proliferation, and modulate cytokine production and the functional activity of different lymphoid cells.** Although there exists substantial sympathetic innervation in the bone marrow, and particularly in the thymus and mucosal tissues, our knowledge about the effect of the sympathetic neural input on hematopoiesis, thymocyte development, and mucosal immunity is extremely modest.

## Modulation Of The Immune System By The Autonomic Nervous System

Nagatomi R, Kaifu T, Okutsu M, et al. Exerc Immunol Rev 2000;6:54-74.

Dept. of Medicine & Science in Sports & Exercise, Tohoku University Grad School of Medicine, Sendai, Japan.

This review examines the role of the autonomic nervous system in the regulation of the immune system to understand the alteration of immunological parameters under the influence of stressors and exercise.

Sympathetic innervation in secondary lymphoid organs plays a major role in immune regulation.

Catecholamine released from the nerve terminal serves as the major mediator when bound to adrenergic receptors present on immunocompetent cells. Experiments using chemical and surgical denervation, catecholamine knock-out mice, and receptor antagonist and agonists revealed several important points. Sympathetic nerve activity is generally suppressive for the immunocompetent cells in the blood stream except neutrophils. Sympathetic activity facilitates detachment of T cells and NK cells from blood vessels without affecting functional adhesion molecule expression. Th1 cells express more beta 2 adrenergic receptors than Th2 cells, indicating a greater influence of sympathetic activity on Th1 response. Sympathetic action was also shown to regulate the production of chemokines. Taken together, 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.

## Complexity and clinical care (An Abridged Version)

BMJ 2001; 323: October

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A complex adaptive system is a collection of individual agents with freedom to act in ways that are not always totally predictable, and whose actions are interconnected so that the action of one part changes the context for other agents. (1) In relation to human health there are several levels of such systems.

- The human body is composed of multiple interacting and self regulating physiological systems including biochemical and neuroendocrine feedback loops
- The behavior of any individual is determined partly by an internal set of rules based on past experience and partly by unique and adaptive responses to new stimuli from the environment
- The web of relationships in which individuals exist contains many varied and powerful determinants of their beliefs, expectations, and behavior
- Individuals and their immediate social relationships are further embedded within wider social, political, and cultural systems which can influence outcomes in entirely novel and unpredictable ways
- All these interacting systems are dynamic and fluid
- A small change in one part of this web of interacting systems may lead to a much larger change in another part through amplification effects.

For all these reasons neither health nor human behavior is predictable and neither can safely be "modeled" in a simple cause and effect system. (2) The human body is not a machine and its malfunctioning cannot be adequately analysed by breaking the system down into its component parts and considering each in isolation. Despite this fact, cause and effect modeling underpins much of the problem solving we attempt in clinical encounters; this perhaps explains why we so often fail. (3)

## Principles For Decision Making In The Complex Zone

(adapted from Zimmerman et al(4)) Zimmerman B, Lindberg B, Plsek P. *Edgware: insights from complexity science for health care leaders*. Irving, TX: VHA Press, 1998.

**Use intuition and muddle through** - Doctors frequently make what would be the best but not definitively the "right" decision on the basis of experience, evidence, and knowledge of the patient's story (5)

**Experiment** Try different management options with patients, using an empirical trial of treatment or a plan-do-study-act cycle (6)

**Minimum specification** Offer patients general goals, suggestions, and examples but do not attempt to work everything out for them your tidy solution is unlikely to be compatible with all aspects of their lifestyle and values

**Chunking** Instead of trying to sort out every problem, try solving one or two (using problem solving techniques, for instance(7)); other solutions may follow naturally once a new pattern has emerged **Use metaphors** - Communication can be difficult when issues are complex. Using metaphors can often create a shared understanding for example, "you seem like a tree bowed over by the wind" or "what does that last hypo remind you of?"

**Provocative questions** - Ask questions that might throw light on basic assumptions, especially when the patient is "stuck" for example, "if you got better, might this cause some problems for you?"

## Promoting Health

Individuals operate within networks of relationships and information sources that have a profound effect on their health choices, some of which are easily identifiable and fairly stable (for example, family, friends, colleagues) while others are more ambiguous or ephemeral (a newspaper health column, a trip to an alternative practitioner, the internet). The activities and influences of these networks are often hidden from the clinician in other words, they serve as a "shadow system."<sup>(1)</sup>

The growing literature on changing patients' behavior in relation to lifestyle focuses on those who are "resistant to change." Complexity science suggests that "readiness to change" occurs when a system is in a state far from equilibrium; there is then sufficient tension to change.<sup>(8,9)</sup> In such circumstances a small influence can have a large effect on behavior<sup>(10)</sup>.

Aiming for concordance means working with system attractors that define the context for a patient. Change literature emphasizes the importance of providing alternatives that are compatible with the system to be changed.<sup>(11)</sup> If the patient is already in a state far from equilibrium offering a new attractor is likely to have a synergistic and powerful effect.

The effectiveness of interventions is highly dependent on the context in which health care is delivered.<sup>(3)</sup> The placebo effect might be thought of as the patient's own complex system self adjusting from the old attractor (disease state), through the effect of a new attractor ("remembered wellness"), to the context of the body being fit.<sup>(12)</sup>

## Conclusion

We all know from experience that the management of clinical problems is rarely simple. Yet most of us were taught to adopt a mental model of the human body as a machine and illness as due to malfunction of its parts. Such linear models drive us to break down clinical care into ever smaller divisions and to express with great accuracy and precision the intervention to be undertaken for each malfunction. Complexity science suggests that health result from complex, dynamic, and unique interactions between different components of the overall system. Effective clinical decision making requires a holistic approach that accepts unpredictability and builds on subtle emergent forces within the overall system. Complexity theory saves both clinician and patient from a futile quest for certainty and upholds the use of intuition and personal experience when general scientific rules are to be applied to the individual in context.

## ASRF Editor's Comments:

You know healthcare is changing when a series of articles about complexity theory are featured in the British Medical Journal.

The effectiveness of interventions is highly dependent on the context in which health care is delivered. If we relate the chiropractic adjustment to the above discussion, what matters is not only the technique used or the line of drive... . . . or the amount of torque . . . but the whole atmosphere in which the adjustment is given. What are your practice members experiencing (Visually, Auditory, Kinesthetic, Olfactory) as they receive their adjustments?"

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