

Safety of Chiropractic Spinal Manipulations: With a Review

A Timucin Atayoglu^{1,2*}, Ayten Guner-Atayoglu², Gulcin Kuran-Cetinkale² and M Ali Cetinkale²

¹Medipol University, Department of Family Medicine, Istanbul, Turkey

²Holistic and Integrative Medicine Association, Istanbul, Turkey

*Corresponding author: A Timucin Atayoglu, Medipol University, Department of Family Medicine, Istanbul, Turkey. President of Holistic & Integrative Medicine Association, Turkey, Tel: +905324649576; E-mail: atayoglu@gmail.com

Received date: February 23, 2017; Accepted date: March 16, 2017; Published date: March 20, 2017

Copyright: © 2017 Atayoglu TA. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Healthcare providers do consider the potential risk of harm that any treatment can cause. Chiropractic healthcare is a system of complementary medicine based on the manipulative treatment of misalignments of the joints, especially those of the spinal column. Recently, the use of chiropractic spinal manipulation has increased considerably while its safety has been debated and estimates vary widely for the incidence of serious complications. Some vascular and neurological incidents account for the criticism surrounding chiropractic. The aim of this review is to investigate the risk of serious complications of chiropractic spinal manipulations to enlighten further understanding on their prevention.

Keywords: Chiropractic; Complementary medicine; Complication; Safety; Spinal manipulation

Introduction

The healthcare professionals must consider the possible complications that any intervention might have. *Primum non nocere* or "first, do no harm" is a guiding dictum for all healthcare providers that whatever the intervention or procedure is performed, the patient's safety and well-being is the primary consideration [1].

Chiropractic is a form of complementary medicine concerned with the treatment of the neuromusculoskeletal system disorders [2]. The chiropractic practitioners often refer to their main technique as an adjustment of the spine and it involves manipulation that is the introduction of a high velocity and low amplitude thrust into a joint [3].

Chiropractic spinal manipulation (CSM) gained mainstream recognition in the 1960s, and today it is a very popular treatment option especially for neck and back pain [4]. If appropriately practiced, it is considered as relatively safe but as with all interventions, adverse incidents can happen [4].

Chiropractors commonly treat neck and back pain problems with CSM and there are a number of case studies show that to be effective [5]. However, its safety has been debated and there is controversy regarding the degree of risk of serious complications after CSM [6]. Unexpected strokes, myelopathies, radiculopathies or osteoarticular accidents have been considered as responsible for the criticism of CSM in the literature [5,7].

In this review we aim to search the literature on safety issues of CSM and the predictability of the adverse events. On the bases of relevant literature, we attempted to enlighten further understanding on the major risks associated with CSM and their prevention.

Method

Computerized literature searches were performed in the issue. The search terms used were 'adverse events', 'chiropractic', 'complications', 'risk', 'safety', 'spinal manipulation'. All reports, irrespective of language of publication, which contained data about risks associated with chiropractic spinal manipulation, were included, regardless of the profession of the therapist or the research methodology used for the report.

Result

In the literature, spinal manipulation has been associated with some serious vascular and neurological accidents after CSM, mostly of the upper spine [8]. On the other hand, to evaluate the safety of chiropractic procedures, a search on the articles that reported adverse reactions associated with chiropractic for the years 1966 to 2007 concluded that there was no strong data concerning the incidence or prevalence of adverse reactions after chiropractic intervention [9].

Eder and Tilscher [10] performed a survey of 168,000 CSM without a significant serious incident. Henderson and Cassidy [11] offered a report of more than a 500,000 CSM without a serious complication. Jaskoviak [12] reported approximately 5 million CSM of neck from 1965 to 1980 without any serious complications. Thiel et al. [13] obtained data from more than 50,000 cervical spine manipulations and there were no reports of serious adverse events, and estimates for serious cervical vascular accidents varied from 5 incidents per 100,000 CSM to 1 death per 4 million CSM. It was determined that there was inadequate data to be conclusive [13].

Among approximately 1.5 million cervical manipulations, Dvorak [14] found a rate of 1 serious complication per 400,000 neck manipulations, without any reported deaths. Patjin [15] found an overall rate of 1 serious complication in nearly 518,000 manipulations. According to Haldeman et al. [16], the risk of serious complications from cervical manipulation was about 1-2 per 1 million neck manipulations. In another study they estimated rate of Vertebral Basilar Accidents (VBAs) after manipulation of 1 in about 5 million

cervical manipulations [17]. Lee et al. [18] found 55 reported serious adverse events in about 50 million CSM. According to Carey [19], estimate risk of serious complications is 1 per 3 million neck manipulations.

Klougart et al. [20] concluded an estimated risk of 1 event of vascular accidents per 1.320,000 cervical spine treatments sessions. Ernst [21] concluded that CSM can result in adverse events such as VBAs followed by stroke or death, but the incidence of such events is not known, however, he concluded that the risk-benefit spinal manipulation is not evidently favorable [22]. Estimate of the risk of death according to Terrett [23], is about 1 fatality per 4 million cervical manipulations. A review analyzed cases that were reported between 1925 and 1997 concluded that no deaths have been attributed to CSM provided by licensed physical therapists [24].

In the literature, there are some case reports of very rare adverse events. Struwer et al. [25] described a case with hemothorax due to an intercostal venous lesion following thoracic spinal manipulation. Phrenic nerve injury causing diaphragmatic palsy was reported as a very rare complication of cervical chiropractic manipulation [26].

There are also case reports of neuropraxic injury of radial nerves and a cervical epidural haematoma after CSM for neck pain. In all the cases there were criteria to consider a causality relation between the neurological adverse events and the CSM [27]. According to Biller et al. [28], there is low evidence supporting an association between CSM and internal carotid artery accident as well.

According to data that was reviewed by Patijn [15], there was a risk of one lumbar disc hernia (LDH) in more than 8 million CSM and one cauda equina syndrome (CES) in more than 4 million CSM. According to data found by Haldeman and Rubinstein [29], estimates of the risk of causing LDH or CES with CSM ranged from one in 1 million to one in over 100 million. Shekelle et al. [30] estimated the rate of occurrence of CES as an adverse event of CSM to be about one per 100 million manipulations.

Michaeli [31] surveyed 153 practitioners in South Africa who reported one minor or transient complication per 38,137 CSM. According to Stern et al. [32], the risk of complication of CSM for patients with low back pain and sciatica was less than 5%. Assendelft et al. [33] estimated the incidence of CES to be less than one per 1 million CSM. Oliphant [34] evaluated the safety of CSM and showed that an estimate of the risk of CSM causing a deteriorated LDH or CES in a patient presenting with LDH was calculated from published data to be less than 1 in 3.7 million.

Discussion

Although they are very rare, CSM can result in serious complications [7]. However, dissimilar results have been published in

the literature on the incidence of serious risks associated with CSM [26] and there is insufficient data to be decisive [9].

The risk factors demonstrated in the literature associated with complications of CSM include misdiagnosis, failure to recognize the onset or progression of neurological signs or symptoms, improper technique, CSM performed in the presence of a coagulation disorder or herniated nucleus pulposus [35].

Complications associated with CSM remain rare and most of the adverse effects reported in literature are benign and remain transitory [36]. On the other hand, some life-threatening complications have been reported after CSM [26,37]. VBAs and CES are the leading causes of claims as serious complications of CSM [7,38]. However, estimates vary widely regarding the serious complications.

Some authors have encountered cases of vascular events such as VBAs after CSM of neck and it has been believed to account for 6-9% of cervical artery accidents [39] whereas according to some other researchers the causality is not strongly documented [40]. Practitioners should also be careful not to perform CSM on an already-dissected artery, since the patient with vertebral artery dissection can present with neck pain as the only symptom [41].

A variety of pre-manipulation tests are used for determining the effect of spinal motion on vertebral artery patency. In George's test, the bilateral blood pressure and pulse rates are measured first, and the subclavian and carotid arteries are auscultated. Then the patient is asked to rotate the head right and left, and then rotate, laterally bend and extend, each side for 15 seconds in the seated position (Maigne's test) and in the supine position (DeKleijn's test). A test is positive if it provokes signs or symptoms of vertebrobasilar insufficiency e.g. nystagmus or symptoms of vertigo, dizziness, tinnitus, visual blurring, slurring of speech, nausea, or faintness and may indicate vascular compromise or stenosis of the carotid or vertebral arteries. Arteriosclerosis, osteophytes or congenital atresia of the artery might be possible causes of vertebrobasilar insufficiency [42].

CES consists of neurogenic bowel and bladder disturbances, saddle anesthesia, bilateral leg weakness and sensory changes [43,44]. There have been case reports of CES observed in which an association between CSM [43]. CES represents a surgical emergency and CSM is contraindicated in the presence of CES [45]. CES has been seen as an adverse event of physical procedures performed on patients affected by LDH [43-45]. However, according to some authors some cases of CES reported in the literature might have been incorrectly attributed to CSM [11,46-48]. According to WHO guidelines the presence of an acute CES represents an absolute contraindication to CSM (Table 1) [4].

1	Anomalies such as dens hypoplasia, unstable os odontoideum, etc.
2	Acute fracture
3	Spinal cord tumor
4	Acute infection such as osteomyelitis, septic discitis, and tuberculosis of
5	Meningeal tumor
6	Haematomas, whether spinal cord or intracanalicular

7	Malignancy of the spine
8	Frank disc herniation with accompanying signs of progressive neurological deficit
9	Basilar invagination of the upper cervical spine
10	Arnold-Chiari malformation of the upper cervical spine
11	Dislocation of a vertebra
12	Aggressive types of benign tumours, such as an aneurismal bone cyst, giant cell tumour, osteoblastoma or osteoid osteoma
13	Internal fixation/stabilization devices
14	Neoplastic disease of muscle or other soft tissue
15	Positive Kernig's or Lhermitte's signs
16	Congenital, generalized hypermobility
17	Signs or patterns of instability
18	Syringomyelia
19	Hydrocephalus of unknown aetiology
20	Diastematomyelia
21	Cauda equina syndrome

NOTE: In cases of internal fixation/stabilization devices, no osseous manipulation may be performed, although soft-tissue manipulation can be safely used. Spinal manipulative therapy may also only be absolutely contraindicated in the spinal region in which the pathology, abnormality or device is located, or the immediate vicinity. [4]

Table 1: Absolute contraindications to spinal manipulative therapy according to WHO guidelines [4].

The guidelines are useful, because CSM should be avoided in the presence of any absolute complications accordingly and most of the complications can be prevented by excluding patients with contraindications for CSM. According to some guidelines [4] anomalies such as dens hypoplasia, unstable os odontoideum, etc., acute fracture, spinal cord tumor, acute infection such as osteomyelitis, septic discitis, and tuberculosis of the spine, meningeal tumor, haematomas, whether spinal cord or intracanalicular, malignancy of the spine, frank disc herniation with accompanying signs of progressive neurological deficit, basilar invagination of the upper cervical spine, Arnold-Chiari malformation of the upper cervical spine, dislocation of a vertebra, aggressive types of benign tumors, such as an aneurismal bone cyst, giant cell tumor, osteoblastoma or osteoid osteoma, internal fixation/stabilization devices, neoplastic disease of muscle or other soft tissue, positive Kernig's or Lhermitte's signs, congenital, generalized hypermobility, signs or patterns of instability, syringomyelia, hydrocephalus of unknown aetiology, diastematomyelia, cauda equina syndrome are considered as absolute contraindications for CSM [4]. However, in the relevant literature whether a condition is an absolute or a relative contraindication is a controversial issue. Multiple sclerosis, which has Lhermitte's sign, is commonly treated with spinal manipulation. The cause must be elicited but it is not always a contraindication for spinal manipulation. Instability may negate spinal manipulation at one segment but not the adjacent segments. In fact, as in degenerative spondylolisthesis, spinal manipulation may be given for alignment while specific stabilization exercises are given to stabilize the segment. Syringomyelia again must be diagnosed for etiology but is not always a contraindication for spinal manipulation. For example, scoliosis may be accompanied with

a synrinx, not Arnold-Chiari, or other etiology found and spinal manipulation given. The great majority of neck pain patients will show degenerative disc disease. Therefore proper clinical diagnosis is required prior to performing cervical spine manipulation to identify specific levels of degenerative processes. There are also some studies on spinal cord stimulators and post-surgical spines treated with low velocity low amplitude spinal manipulation with no serious adverse reactions [49,50].

The safety of CSM in the treatment of neck or lumbar problems might be compared with other commonly accepted treatments for the similar conditions. It was reported that, significant complications may occur in 1-4% of NSAID using patients [51]. It has been shown that the risk of CES in surgically treated LDH patients is about 0.5% [52] and the complication rate with cervical spine surgery in the US is about 2% [53].

Conclusion

Safety concern of CSM is an important topic. Treatments must be safe in order to practice in a manner reflecting the principles of "primum non nocere." There should be an emphasis on evidence-based care.

CSM should be practiced only by qualified and well-experienced practitioners. They must be aware of the adverse events and should be cautious when recommending CSM for the treatment of neck pain, especially in the presence of preexisting degenerative disease of the cervical spine [26]. The described serious adverse events promptly recommend the implementation of a risk alert system [27]. All patients should be clearly informed about the potential complications, although

they are rare. Information about the risks should be included in an informed consent procedure for CSM.

The evidence-based advantage of CSM should be presented. Therefore, a full medical history and correct diagnosis are important to be able to rule out contraindications to CSM. Most of the complications can be prevented by excluding patients with contraindications for CSM. Therefore, it is recommended that the procedures described in the updated guidelines be applied prior to CSM, and that CSM be avoided in the presence of any absolute complications. Chiropractic practitioners should be aware of the absolute contraindications, where any use of CSM is inappropriate because it places the patient at undue risk (Table 1). In the presence of the relative contraindication, treatment can be modified so that the patient is not at undue risk. In such a case, mobilization or low-force and soft-tissue techniques can be preferred.

Proper clinical diagnosis is required prior to performing cervical spine manipulation to identify specific levels of degenerative processes. It is important to include a neurologic examination on all CSM patients. Neurological tests such as George, DeKelyn, etc are standard tests for vertebral artery insufficiency sensitivity. A positive test is considered a contraindication to cervical manipulation even though their absence does not rule out the possibility of vertebral artery insufficiency. Such tests may help screen for patients who may be at greater risk for vertebral artery dissection following cervical spine manipulation. However, it is important to be alert that their use has potential to cause harm too [43,54].

The ability to recognize a lesion to a specific spinal region by clinical examination may help prioritize diagnostic imaging decisions. Magnetic resonance imaging (MRI) is not accepted as a must for neck and back pain patients before conservative treatments [36]. However, it is useful to be able to compare the outcomes of patients undergoing CSM interventions. If there are significantly deteriorated signs in patients further investigation should be performed and MRI is a reliable method for diagnosing most of the spinal cord pathologies. Therefore, it should be assessed especially for patients with sudden aggravated or new onset of symptoms. Today MRI is not anymore as expensive as it used to be in the past; hence the practitioners may consider requiring it easily.

Whether the adverse events related to CSM are unpredictable events with no predictive indicators or that prediction can be possible, CSM should remain under very strict control. In the literature, estimates vary widely regarding the complications of CSM.

This review has several limitations. Some relevant published articles might have been missed. We need objective data on the relationship between CSM and complications. Therefore, population-based nested case-control studies are required to determine accurately the incidence of complications following CSM.

References

1. Smith CM (2005) Origin and uses of primum non nocere--above all, do no harm! *J Clin Pharmacol* 45: 371-377.
2. Chapman-Smith DA, Cleveland CS (2005) International status, standards and education of the chiropractic profession. In: Haldeman S, Dagenais S, Budgell B, et al. *Principles and Practice of Chiropractic* McGraw-Hill. 3rd edn, 111-134.
3. Maitland GD (2005) *Vertebral Manipulation*. 5th edn. Butterworths, London: 1986.
4. World Health Organization (2005) WHO guidelines on basic training and safety in chiropractic.
5. Jagbandhansingh MP (1997) Most common causes of chiropractic malpractice lawsuits. *J Manipulative Physiol Ther* 20: 60-64.
6. Ernst E, Posadzki P (2012) Reporting of adverse effects in randomised clinical trials of chiropractic manipulations: a systematic review. *N Z Med J* 125: 87-140.
7. Evans DP, Burke MS, Lloyd KN, Roberts EE, Roberts GM (1978) Lumbar spinal manipulation on trial. Part I--clinical assessment. *Rheumatol Rehabil* 17: 46-53.
8. Ernst E (2001) Life-threatening complications of spinal manipulation. *Stroke* 32: 809-810.
9. Gouveia LO, Castanho P, Ferreira JJ (2009) Safety of chiropractic interventions: a systematic review. *Spine (Phila Pa 1976)* 32: 2375-2378.
10. Eder M, Tilscher H (1990) *Chiropractic therapy: diagnosis and treatment*. Rockville, Md: Aspen Publishers, p: 61.
11. Henderson DJ, Cassidy JD (1988) Vertebral Artery syndrome. In: Vernon H. *Upper cervical syndrome: chiropractic diagnosis and treatment*. Baltimore: Williams and Wilkins, pp: 195-222.
12. Jaskoviak P (1980) Complications arising from manipulation of the cervical spine. *J Manip Physiol Ther* 3: 213-219.
13. Thiel HW, Bolton JE, Docherty S, Portlock JC (2007) Safety of chiropractic manipulation of the cervical spine: a prospective national survey. *Spine (Phila Pa 1976)* 32: 2375-2378.
14. Dvorak J, Orelli F (1985) How dangerous is manipulation to the cervical spine? *Manual Medicine* 2: 1-4.
15. Patijn J (1991) Complications in Manual Medicine: A Review of the Literature. *J Manual Medicine* 6: 89-92.
16. Haldeman S, Chapman-Smith D, Petersen DM (1993) Guidelines for chiropractic quality assurance and practice parameters. Gaithersburg, Md: Aspen Publishers 170-172.
17. Haldeman S, Carey P, Townsend M, Papadopoulos C (2002) Clinical perceptions of the risk of vertebral artery dissection after cervical manipulation: the effect of referral bias. *Spine J* 2: 334-342.
18. Lee KP, Carlini WG, McCormick GF, Albers GW (1995) Neurologic complications following chiropractic manipulation: a survey of California neurologists. *Neurology* 45: 1213-1215.
19. Carey PF (1993) A report on the occurrence of cervical cerebral vascular accidents in chiropractic practice. *J Can Chiropr Assoc* 37: 104-106.
20. Klougart N, Leboeuf-Yde C, Rasmussen LR (1996) Safety in chiropractic in practice, part 1: the occurrence of cerebrovascular accidents after manipulation to the neck in Denmark from 1978-1988. *J Manipulative Physiol Ther* 19: 371-377.
21. Ernst E (2007) Adverse effects of spinal manipulation: a systematic review. *J R Soc Med* 100: 330-338.
22. Ernst E (2011) Response to critiques of deaths after chiropractic. *Int J Clin Pract* 65: 106.
23. Terrett AG, Kleynhans AM (1992) Cerebrovascular complications of manipulation. In: Haldeman S edn. *Principals and Practice of Chiropractic*. Norwalk, Ct: Appleton & Lang, pp.579-98.
24. Di Fabio RP (1999) Manipulation of the cervical spine: risks and benefits. *Phys Ther* 79: 50-65.
25. Struener J, Frangen TM, Ziring E, Hinterseher U, Kiriazidis I (2013) Massive hemothorax after thoracic spinal manipulation for acute thoracolumbar pain. *Orthop Rev (Pavia)* 5: e27.
26. John S, Tavee J (2015) Bilateral diaphragmatic paralysis due to cervical chiropractic manipulation. *Neurologist* 19: 65-67.
27. Gouveia LO, Castanho P, Ferreira JJ, Guedes MM, Falcão F, et al. (2007) Chiropractic manipulation: reasons for concern? *Clin Neurol Neurosurg* 109: 922-925.
28. Biller J, Sacco RL, Albuquerque FC, Demaerschalk BM, Fayad P, et al. (2014) Cervical arterial dissections and association with cervical manipulative therapy: a statement for healthcare professionals from the american heart association/american stroke association. *Stroke* 45: 3155-3174.

29. Haldeman S, Rubinstein SM (1992) Cauda equina syndrome in patients undergoing manipulation of the lumbar spine. *Spine (Phila Pa 1976)* 17: 1469-1473.
30. Shekelle PG, Adams AH, Chassin MR, Hurwitz EL, Brook RH (1992) Spinal manipulation for low-back pain. *Ann Intern Med* 117: 590-598.
31. Michaeli A (1993) Reported occurrence and nature of complications following manipulative physiotherapy in South Africa. *Aust J Physiother* 39: 309-315.
32. Stern PJ, Côté P, Cassidy JD (1995) A series of consecutive cases of low back pain with radiating leg pain treated by chiropractors. *J Manipulative Physiol Ther* 18: 335-342.
33. Assendelft WJ, Bouter LM, Knipschild PG (1996) Complications of spinal manipulation: a comprehensive review of the literature. *J Fam Pract* 42: 475-480.
34. Oliphant D (2004) Safety of spinal manipulation in the treatment of lumbar disk herniations: a systematic review and risk assessment. *J Manipulative Physiol Ther* 27: 197-210.
35. Powell FC, Hanigan WC, Olivero WC (1993) A risk/benefit analysis of spinal manipulation therapy for relief of lumbar or cervical pain. *Neurosurgery* 33: 73-78.
36. Senstad O, Leboeuf-Yde C, Borchgrevink C (1997) Frequency and characteristics of side effects of spinal manipulative therapy. *Spine (Phila Pa 1976)* 22: 435-440.
37. Hurwitz EL, Morgenstern H, Vassilaki M, Chiang LM (2005) Frequency and clinical predictors of adverse reactions to chiropractic care in the UCLA neck pain study. *Spine (Phila Pa 1976)* 30: 1477-1484.
38. Kirkaldy-Willis WH, Cassidy JD (1985) Spinal manipulation in the treatment of low-back pain. *Can Fam Physician* 31: 535-540.
39. Haneline MT, Lewkovich GN (2005) An analysis of the etiology of cervical artery dissections: 1994 to 2003. *J Manipulative Physiol Ther* 28: 617-622.
40. Ernst E (2010) Vascular accidents after neck manipulation: cause or coincidence? *Int J Clin Pract* 64: 673-677.
41. Mas JL, Henin D, Bousser MG, Chain F, Hauw JJ (1989) Dissecting aneurysm of the vertebral artery and cervical manipulation: a case report with autopsy. *Neurology* 39: 512-515.
42. Greenstein GM (1997) *Clinical Assessment of Neuromusculoskeletal Disorders*. Saint Louis: Mosby.
43. Tamburrelli FC, Genitiempo M, Logroscino CA (2011) Cauda equina syndrome and spine manipulation: case report and review of the literature. *Eur Spine J* 20 Suppl 1: S128-131.
44. Kostuik JP, Harrington I, Alexander D, Rand W, Evans D (1986) Cauda equina syndrome and lumbar disc herniation. *J Bone Joint Surg Am* 68: 386-391.
45. Quon JA, Cassidy JD, O'Connor SM, Kirkaldy-Willis WH (1989) Lumbar intervertebral disc herniation: treatment by rotational manipulation. *J Manipulative Physiol Ther* 12: 220-226.
46. Terrett AG, Kleynhans AM (1992) Complications from manipulation of the low back. *Chiropr J Aust* 27: 129-140.
47. Ernst E (2001) Prospective investigations into the safety of spinal manipulation. *J Pain Symptom Manage* 21: 238-242.
48. Lisi AJ, Holmes EJ, Ammendolia C (2005) High-velocity low-amplitude spinal manipulation for symptomatic lumbar disk disease: a systematic review of the literature. *J Manipulative Physiol Ther* 28: 429-442.
49. Perrucci RM, Coulis CM (2017) Chiropractic management of post spinal cord stimulator spine pain: a case report. *Chiropr Man Therap* 25: 5.
50. Gudavalli MR, Olding K, Joachim G, Cox JM (2016) Chiropractic Distraction Spinal Manipulation on Postsurgical Continued Low Back and Radicular Pain Patients: A Retrospective Case Series. *J Chiropr Med* 15: 121-128.
51. Bjorkman DJ (1999) Current status of nonsteroidal anti-inflammatory drug (NSAID) use in the United States: risk factors and frequency of complications. *Am J Med* 107: 3S-8S.
52. Kardaun JW, White LR, Shaffer WO (1990) Acute complications in patients with surgical treatment of lumbar herniated disc. *J Spinal Disord* 3: 30-38.
53. Fineberg SJ, Oglesby M, Patel AA, Pelton MA, Singh K (2013) Outcomes of cervical spine surgery in teaching and non-teaching hospitals. *Spine (Phila Pa 1976)* 38: 1089-1096.
54. http://www.chirocolleges.org/georges_test.html