Collagen, Hypermobility and Scoliosis

Are Nutritional Deficiencies and Gastrointestinal Malabsorption Possible Causes of the Increase in Hypermobility Spectrum Disorders?

Hypermobility is a connective tissue disorder and is often present in people with scoliosis. Experts estimate that up to 10% of the general population may have some degree of hypermobility, with women affected about three times more often than men.

Joint Hypermobility in Children with Idiopathic Scoliosis:
https://scoliosisjournal.biomedcentral.com/articles/10.1186/1748-7161-6-22

JHM was diagnosed in more than half of the subjects with idiopathic scoliosis **(51.4%),** whilst in the control group it was diagnosed in only 19% of cases (p = 0.00015). A significantly higher JHM prevalence was observed in both girls (p = 0.0054) and boys (p = 0.017) with IS in comparison with the corresponding controls.

Connective tissue is the material between the cells of the body that gives tissues form and strength. Connective tissue is made up of dozens of proteins, including collagen. It is the principle structural protein of the body; ligaments, tendons, cartilage, discs and connective tissue are all made from collagen. In muscle tissue it serves as a major component of endomysium (a thin, delicate layer of connective tissue that surrounds the individual muscle fibres)

Hypermobility is an abnormality of collagen which subsequently leads to biomechanical failure owing to ligamentous laxity, a factor in poor proprioception. Muscles have to work harder in people with hypermobility so muscles fatigue sooner and they feel tired. The lumbar spine is one of the most mobile sections of the spine and in the hypermobile person often moves excessively.

It is generally thought that the cause of congenital or benign hypermobility is that through genetics, the body doesn't make enough collagen or doesn't make a good quality collagen.

But maybe hypermobility could also be caused by nutritional deficiencies and/or environmental factors? It is well established that most of the symptoms of hereditary connective tissue disorders are identical to symptoms of nutritional deficits.
Gastrointestinal and Nutritional Issues in Joint Hypermobility Syndrome and EDS, Hypermobility Type – Marco Castori, 2015

Is this a random coincidence, or could nutrition and other environmental factors be a common underlying link in connective tissue disorders?

Could we reverse symptom severity by tackling nutrient status and thus improve quality of life for people with hypermobility/scoliosis via a nutritional medicine approach?

As connective tissue is present throughout the body, many different structures around the body including the digestive tract can be affected by hypermobility. Connective tissue is present in the digestive tract and is essential to the passive mechanical movements needed to complete digestion. Connective tissue is also

present around the nerves of the digestive tract and abnormalities of this can potentially make the gut more sensitive.

Therefore, it is essential to address any gastrointestinal issues first.

Nutritional Deficiencies

Vitamin D acts as a hormone in the human body. Produced by the skin or ingested, it is metabolized and the end product of this pathway acts in various systems and performs vital roles in maintaining the structure and function of the musculoskeletal tissues. Recent evidence suggests a material impact of vitamin D on bone mineral density and on the development of deformities, such as adolescent idiopathic scoliosis.

Dr. David Ayoub is a practicing radiologist in Springfield, Illinois and notes that vitamin D deficiency can actually mimic Ehlers-Danlos Syndrome, (a connective tissue disease characterized by hypermobile skin and hypermobile joints) because it's associated with joint hypermobility.

"We know that collagen requires vitamin D as well. We didn't know that traditionally, but research in the last 10 years has shown it's important for collagen pathways, just like vitamin C is." *American Journal of Roentgenology*

Recently in a study of 313 patients undergoing spinal fusion surgery, orthopaedic surgeons at Washington University School of Medicine in St. Louis found that more than half had inadequate levels of vitamin D, including one-fourth who were more severely deficient.

Magnesium is a needed co-factor for vitamin D utilization, meaning that a lack of magnesium can cause vitamin D to be unavailable to the body. Enzymes are protein molecules that stimulate every chemical reaction in the body. All the enzymes that metabolize vitamin D require magnesium.

Magnesium is a critical component of collagen formation and repair but calcium will fill up cells and 'calcify' cells in magnesium's place when there is a deficiency of magnesium. This can lead to defective collagen formation over time in the presence of a chronic magnesium deficiency. One study explained it by showing that magnesium deficiency 'hinders the mechanism by which fibroblasts (collagen creating cells) degrade defective collagen.'

In other words, when magnesium deficiency is present, the old collagen cells that need to be replaced get replaced with unhealthy calcified cells rather than flexible new healthy cells.

A magnesium deficiency causes the nervous system to be out of balance. This in turn, will keep muscles tight and prevent them from staying in a relaxed condition. Muscle contractions are common in scoliosis and hold the spine in a distorted position. If stretch receptors in muscles are affected by mercury toxicity and low magnesium and affect electrical transmission to the muscles, this may be a contributing factor in scoliosis.

Magnesium is a critical nutrient in the formation of a properly functioning phospholipids bilayer which surrounds cell membranes; it is this membrane which allows communication between cells.

Magnesium deficiency induced in beagles resulted in abnormal changes in their joint cartilage. The magnesium deficient beagles all had weakness in their legs, and one dog's legs hyper-extended to a 90 degree angle. Hyper-extended joints are a sign of several connective tissue disorders, including scoliosis.

Another study shows higher levels of calcium in idiopathic scoliosis muscles than in other forms of scoliosis or in normal control muscles.

Spine (Phila Pa 1976) 1978 Jun; 3(2):142-5. X-ray fluorescence analysis of muscles in scoliosis. Yarom R, Robin GC, Gorodetsky R. http://www.ncbi.nlm.nih.gov/pubmed/663764?dopt=Abstract

In the case of connective tissue such as joints, ligaments and tendons, this can lead to susceptibility to joint problems, tendonopathies, fibromyalgia, worn cartilage, osteoarthritis and even certain heart problems that are related to connective tissue dysfunction.

When there is a relative overabundance of intracellular calcium due to a magnesium deficiency, mercury is less effectively removed from cells. This toxic metal then bio-accumulates within the cells and makes certain tissues more vulnerable. The body's primary mercury detoxifying molecule is glutathione which requires magnesium for its synthesis.

Therefore, magnesium is essential in the bio-synthesis of collagen, as it helps produce proteins that are later transformed into collagen.

Zinc's connective tissue importance extends to bone formation by signalling specialised cells called osteoblasts to begin collagen synthesis. Zinc deficiencies in animals resemble connective tissue diseases in man. Zinc depletion in chicks cause abnormalities in collagen. Zinc deficiencies in monkeys can cause soft bones, which in turn can cause hypermobility and scoliosis. Zinc deficiencies in monkeys can be passed down from earlier generations.

Gymnasts often develop scoliosis, delayed puberty and hypermobility, perhaps because they tend to be low in zinc?

Marginal deficiencies in **manganese, zinc, copper and pyridoxine** have been shown to affect the expression as well as severity of idiopathic scoliosis. The highest incidence of idiopathic scoliosis occurs in the period of rapid growth that correlates with increased needs for manganese, zinc, copper and pyridoxine. Manganese is essential to normal proteoglycan metabolism. Zinc deficiencies result in defective collagen formation.

Nutrition as an environmental factor in the etiology of idiopathic scoliosis
J.Manipulative Physiol Ther Worthington V. and Shambaugh P. (1993) -

There is evidence that poor nutrition may play a part in the etiology of idiopathic scoliosis. This possibility should be examined further in humans.

Dr Paul Harrington, world-renowned orthopaedic surgeon, suggests that a nutritional deficit and its associated hormonal influences during a young girl's vulnerable growing years may initiate the scoliotic process. Harrington states that, "during growth a balanced intake of proteins and vitamin C is essential to the support of normal collagen."

Without adequate amounts of dietary **vitamin C**, the body can't actually form or store collagen. This makes vitamin C a mandatory co-factor in collagen synthesis. It's responsible for holding cells together during the creation of collagen.

Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts

Boyera N, et al. Int J Cosmet Sci. 1998.
https://www.ncbi.nlm.nih.gov/m/pubmed/18505499/

Collagen: The Fibrous Proteins of the Matrix

Molecular Cell Biology. 4th edition
https://www.ncbi.nlm.nih.gov/books/NBK21582/

Nutritional deficiencies as a result of exposure to mercury
The picture below demonstrates widespread distribution of mercury in the body of a mouse. (white areas) Connective tissue is very prone to mercury binding. One of the reasons for this is that mercury is particularly keen to bind to two amino acids; methionine and cysteine. Both amino acids contain sulphur hydrogen (SH)-groups. Sulfhydryl bonds (SH) are common in protein molecules that make up various hormones and enzymes. Mercury easily replaces the hydrogen in these bonds, thereby deactivating the protein. Collagen tissues are rich in SH-groups.

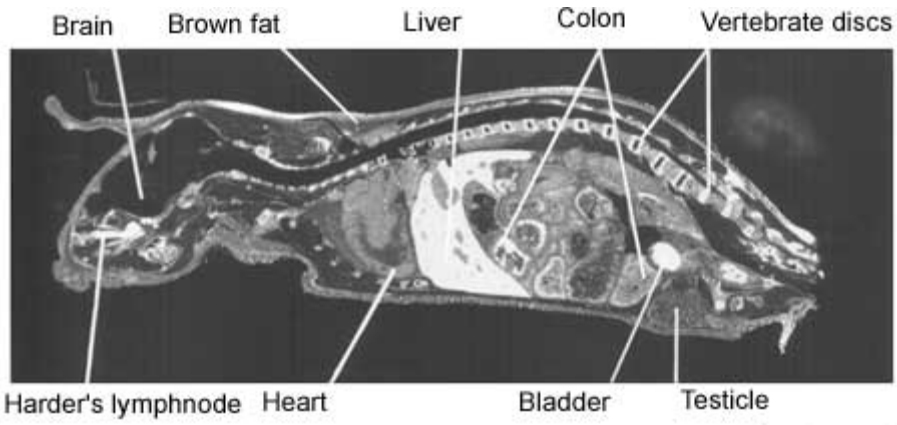

Figure 1 Distribution of radioactivity in male mouse 6 hours after intravenous injection of 203HgCl2 (mercury chloride) Magnification 2x
The autoradiography is courtesy of Anette Ceo.
(Melisa Diagnostics)

Dr Boyd Haley, Professor of Chemistry/Biochemistry, University of Kentucky, USA, discovered that Matrix Metallo Proteinase enzyme, (MMP) was activated by mercury and Thimerosal (mercury preservative used in vaccines) at very low concentrations and degraded collagen which is 40 to 60% of the body's protein. **MMP is the only enzyme to be activated and not inhibited by mercury.**

Mercury is a 'heavy metal' which displaces essential intracellular minerals, such as magnesium and zinc.

If a child is born with a magnesium and/or zinc deficiency, does it predispose him to retaining mercury and developing hypermobility and/or scoliosis?

Mercury attaches to DNA in the absence of zinc.

Metallothionein is a circulating protein that works in conjunction with zinc, to eliminate mercury and other heavy metals from the body. Severe zinc depletion and toxic metal overload may disable Metallothionein function. Furthermore, mercury exposure causes zinc depletion in its own right.

Vitamin D helps remove mercury and other metals from the body safely by radically increasing the amount of intracellular glutathione.

Increased frequency of delayed type hypersensitivity to metals in patients with connective tissue disease – Vera Stejskal

http://www.understandingscoliosis.org/Increased-frequency-of-delayed-type-hypersensitivity-to-metals-in-patients-with-connective-tissue-disease--nw540.aspx

Connective tissue disease (CTD) is a group of inflammatory disorders of unknown aetiology. We examined the frequency of delayed type hypersensitivity (DTH) (Type IV allergy) to metals in patients with CTD.

Mercury Is Taken Up Selectively by Cells Involved in Joint, Bone, and Connective Tissue Disorders - Roger Pamphlett and Stephen Kum Jew

https://www.frontiersin.org/articles/10.3389/fmed.2019.00168/full?fbclid=IwAR2nmBFvPfTDx6aO28tcX645nZRApsIG72RuGBfWtM-FPHz2dCQfsRv0USc

Fibroblasts in several organs often involved in multisystem connective tissue disorders, take up mercury.

Vertebral defects in fourhorn sculpin, exposed to heavy metal pollution in the Gulf of Bothnia. A Bengtsson et al, 1988. Journal of Fish Biology

Studies suggest that the etiology of lesions induced by inorganic chemicals, including mercury, may be a decrease in collagen as a result of the binding by inorganics of active sites on prolyhydroxylase (prolyhydroxylase is an enzyme involved in the production of collagen).

Bluegill Sunfish exposed to mercury showed higher levels of anatomical asymmetry than other populations. Ames et al -

Reference: **Fish Deformities and Pollution in Some Swedish Waters.** Bengt-Erik Bengtsson, *Ambio* Journal

Teratogenic effects of injected methylmercury on avian embryos

Heinz GH[1], Hoffman DJ, Klimstra JD, Stebbins KR, Kondrad SL, Erwin CAAuthor Environ Toxicol Chem. 2011 Jul;30

Some deformities, such as lordosis and scoliosis, misshapen heads, shortening or twisting of the neck, and deformities of the wings, were seldom observed in controls but occurred in much greater frequency in mercury-treated individuals.

Conclusion

1. What if the 'reference nutrient intake' is too low for people with joint hypermobility for some nutrients? Do they need a higher than average requirement for some key nutrients to stay healthy?

2. Could exposure to mercury from dental amalgams, vaccines and fish, cause nutritional deficiencies and destroy and degrade collagen? Would this accelerate the progression of connective tissue disorders, resulting in the development of hypermobility or/and scoliosis?

3. Does mercury adhere to the cell membrane wall, creating damage to the extracellular matrix of the cell, (ECM) especially collagen, which is the major structural protein of ECM?

3. Women lose collagen at a faster rate than men, partly due to sex hormones altering collagen proteins; could this be why more females than males have scoliosis?

Rebecca Dutton, 2018

References

1. **Joint Hypermobility in Children with Idiopathic Scoliosis:**

https://scoliosisjournal.biomedcentral.com/articles/10.1186/1748-7161-6-22

2. Gastrointestinal and Nutritional Issues in Joint Hypermobility Syndrome and EDS, Hypermobility Type – Marco Castori, 2015

3. A Critical Review of the Classic Metaphyseal Lesion: Traumatic or Metabolic? *American Journal of Roentgenology*
David M. Ayoub[1], Charles Hyman[2], Marta Cohen[3] and Marvin Miller

4. Vitamin D status of adults undergoing surgical spinal fusion. Stoker GE, Buchowski JM, Bridwell KH, Lenke LG, Riew KD, Zebala LP Presented Nov. 3 at the 26th Annual Meeting of the North American Spine Society in Chicago, Ill.

5. New clues about vitamin D functions in the nervous system, Emmanuel Garcion ,Nelly Wion-Barbot Claudia N Montero-Menei, François Berger, Didier Wion http://www.sciencedirect.com/science/article/pii/S1043276001005471

6. Association between Vitamin D Levels and Adolescent Idiopathic Scoliosis,

Rodrigo Martins Borges Ferreira Batista, Délio Eulálio Martins, Marcelo Wajchenberg, Marise Lazaretti, Eduardo Barros Puertas,
Maria Teresa de Sande e Lemos Ramos Ascensão Terreri, Lilian Fukusima Hayashi

http://www.scielo.br/pdf/coluna/v13n4/1808-1851-coluna-13-04-00275.pdf

7. Vitamin D Status of Adults Undergoing Surgical Spinal Fusion

Stoker GE, Buchowski JM, Bridwell KH, Lenke LG, Riew KD, Zebala LP.

http://www.drmagaziner.com/vitamin-d-for-joint-pain/

8. Magnesium deficiency in the pathogenesis of mitral valve prolapse, Galland LD, Baker SM, McLellan RK

Magnesium 1986; 5 (3-4):165-74.
http://www.ncbi.nlm.nih.gov/pubmed/3014234
J Nutr. 1980 Oct; 110(10):2095-102.

9. X-ray fluorescence analysis of muscles in scoliosis. Spine (Phila Pa 1976). 1978 Jun; 3(2):142-5 Yarom R, Robin GC, Gorodetsky R.
http://www.ncbi.nlm.nih.gov/pubmed/663764?dopt=Abstract – calcium higher in idiopathic scoliosis.

10. Effect of zinc deficiency on bone collagenase and collagen turnover, J Nutr. 1980 Oct; 110(10):2095-102.
Starcher BC, Hill CH, Madaras JG.
http://www.ncbi.nlm.nih.gov/pubmed/6252304?dopt=Abstract

11. Studies of marginal zinc deprivation in rhesus monkeys V. Fetal and infant skeletal effects Am J Clin Nutr. 1984 Dec; 40(6):1203-12.
Leek JC, Vogler JB, Gershwin ME, Golub MS, Hurley LS, Hendrickx AG.
http://www.ncbi.nlm.nih.gov/pubmed/6507342?dopt=Abstract

12. Skeletal and Skin Lesions of Zinc-Deficient Chickens and Swine. Possible Relationship to "Connective Tissue Diseases of Man" The American Journal of Clinical Nutrition, Vol 22, No 9, Sept 1969, pp1268 -1277, USA.
William G. Hoekstra.
http://ajcn.nutrition.org/content/22/9/1268.long

13. Zinc may increase bone formation through stimulating cell proliferation, alkaline phosphatase activity and collagen synthesis in osteoblastic MC3T3-E1 cells Nutr Res Pract. 2010 October; 4(5): 356–361
Hyun-Ju Seo,[1] Young-Eun Cho,[2] Taewan Kim,[3] Hong-In Shin,[4] and In-Sook Kwun[2]

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2981717/

14. Serum zinc in highly trained adolescent gymnasts Biol Trace Elem Res. 1995 Jan-Mar; 47 (1-3):273-8.
Brun JF, Dieu-Cambrezy C, Charpiat A, Fons C, Fedou C, Micallef JP, Fussellier M, Bardet L, Orsetti A.

http://www.ncbi.nlm.nih.gov/pubmed/7779557

15. Zinc Deficiency and Its Inherited Disorders Genes & Nutrition Vol. 1, No. 1, pp. 41-50, 2006 – A Review
M. Leigh Ackland and Agnes Michalczyk

http://www.newcenturyhealthpublishers.com/genes_and_nutrition/about/pdf/Leigh.pdf

16. Zinc status in patients with idiopathic scoliosis. Spine (Phila Pa 1976). 1990 Feb; 15(2):65-6.
Dastych M[1], Vlach O.

http://www.ncbi.nlm.nih.gov/pubmed/2326713

17. Nutrition as an environmental factor in the etiology of idiopathic scoliosis J.Manipulative Physiol Ther Worthington V. and Shambaugh P. (1993)

18. Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts

Boyera N, et al. Int J Cosmet Sci. 1998.

https://www.ncbi.nlm.nih.gov/m/pubmed/18505499/

19. Collagen: The Fibrous Proteins of the Matrix

Molecular Cell Biology. 4th edition

https://www.ncbi.nlm.nih.gov/books/NBK21582/

20. Increased frequency of delayed type hypersensitivity to metals in patients with connective tissue disease – Vera Stejskal

http://www.understandingscoliosis.org/Increased-frequency-of-delayed-type-hypersensitivity-to-metals-in-patients-with-connective-tissue-disease--nw540.aspx

21. Mercury Is Taken Up Selectively by Cells Involved in Joint, Bone, and Connective Tissue Disorders - Roger Pamphlett and Stephen Kum Jew

https://www.frontiersin.org/articles/10.3389/fmed.2019.00168/full?fbclid=IwAR2nmBFvPfTDx6aO28tcX645nZRApsIG72RuGBfWtM-FPHz2dCQfsRv0USc

22. .Vertebral defects in fourhorn sculpin, Myoxocephalus quadricornis L., exposed to heavy metal pollution in the Gulf of Bothnia. J. Fish Biol. 33(4):517-29. Bengtsson, A., B.E. Bengtsson, and G. Lithner 1988.