Treating Pain with Functional Medicine: A Case Study

Tal Cohen, DAOM, MS-HNFM





What is the leading cause of joint pain?

Injury
 Excess weight
 Overuse



• Standard of care includes:

- NSAIDs
- Cortisol Injection
- Opioids
- Physiotherapy
- Chiropractic
- Back surgery



Back pain is increasing...



🕈 > News > 2009 > February > Chronic low back pain on the rise: UNC study finds 'alarming increase' in prevalence

NEWS	
2007	

2006

Chronic low back pain on the rise: UNC study finds 'alarming increase' in

Pic:

University of North Carolina at Chapel Hill School of Medicine

Study:

Hartvigsen J et al. Low Back Pain Series: What Low Back Pain Is and Why We Need to Pay Attention. *Lancet*, June 2018; Volume 391, Issue 10137; p2356-2367.

The number of years people lived with disability caused by low back pain <u>increased</u> by 54% between 1990 and 2015.

September

"Considering the social and economic costs of chronic low back pain, these findings are alarming " said the study's principal investigator Timothy S. Carey, M.D., director of the







"Arthritis is the leading cause of disability among adults in the U.S."

Affecting 23% of all adults, or more than 54 million people

"arthritis will increase almost 49% to more than 78 million in 2040. About half of those with arthritis are working age adults—age 18 to 64 years."



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

What is causing joint pain?

While joint degeneration is believed to be caused by of aging, trauma, excess weight, or overuse, in the majority of the population:

"Inflammation has now been strongly implicated in the pathogenesis (development) of OA"

Sokolove, J., & Lepus, C. M. (2013). Role of inflammation in the pathogenesis of osteoarthritis: latest findings and interpretations. Therapeutic advances in musculoskeletal disease, 5(2), 77–94. https://doi.org/10.1177/1759720X12467868

Therapeutic Advances in

Musculoskeletal Disease





Pain is driven by chronic inflammation



Anti-Inflammatory Therapy in Standard of Care

- NSAIDs
- Cortisol Injection
- Steroids





Pain is driven by chronic inflammation





Ongoing (chronic) inflammation is associated with many chronic diseases!





Female Patient in her 50s

- Teacher for many years (describes it as enjoyable but stressful profession)
- She was suffering from back pain for over 10 years (6 to 9/10 pain scale, to the point that she couldn't stand)
- She described the pain as soreness and pressure that increased with prolonged standing or when she was tired.
- General fatigue in afternoon
- After two pain clinics, she tried cortisone injections, physical therapy and chiropractic, and several pain medications (including opioids).
- Goal: Live without back pain and without the drugs.

We did a physical examination (full ROM, but tender to touch) and reviewed her symptoms





Step #1 (Identify the imbalance): Her symptoms indicated possible subclinical adrenal fatigue.

Step #2 (Confirm): Used Functional lab tests.

Step #3 (Repair): We focused on supporting her adrenal function.

Results: Within a few weeks, her pain reduced almost completely and her energy increased.

*Not using pain medication after two months.

Most doctors don't talk about it, however...



Adrenal glands, also referred to as anti-inflammatory or stress glands, are important for healthy function.

Adrenal glands are essential for a healthy inflammatory response



Adrenals secrete Cortisol, a powerful anti-inflammatory substance.

The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone; compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis. Hench PS, Kendall EC, Proc Staff Meet Mayo Clin. 1949 Apr 13; 24(8):181-97.

- React to stressors like <u>illness</u>, injury, and even <u>emotional or psychological stress</u>.
- ✓ Control blood sugar
- ✓ Regulate blood pressure
- ✓ Regulating weight

Adrenal glands

The Relationship Between Pain and Cortisol: A Survival Mechanism

• "Cortisol also may facilitate the consolidation of fear-based memories for future survival and avoidance of danger."

Hannibal, K. E., & Bishop, M. D. (2014). Chronic stress, cortisol dysfunction, and pain: a psychoneuroendocrine rationale for stress management in pain rehabilitation. Physical therapy, 94(12), 1816–1825. https://doi.org/10.2522/ptj.20130597





Cortisol Increases (glucose) Levels

- "In the liver, high cortisol levels increase gluconeogenesis"
- "Gluconeogenesis is a metabolic pathway that results in the production of glucose from glucogenic amino acids, lactate, or glycerol 3- phosphate found in triglycerides"
 - Kuo T, McQueen A, Chen TC, Wang JC. Regulation of Glucose Homeostasis by Glucocorticoids. Adv. Exp. Med. Biol. 2015;872:99-126.
 - Thau L, Gandhi J, Sharma S. Physiology, Cortisol. [Updated 2020 May 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538239/





Healthy adrenals are essential for healthy function and pain-free life!

Adrenal Daily Cycle



Cortisol levels

Cortisol & Inflammation

Inflammatory cytokines IL-6 (3 hours)

Plasma levels of cortisol

C-Reactive Protein Increased

Steensberg A, Fischer CP, Keller C, Møller K, Pedersen BK. IL-6 enhances plasma IL-1ra, IL-10, and cortisol in humans. *Am J Physiol Endocrinol Metab*. 2003;285(2):E433-E437. doi:10.1152/ajpendo.00074.2003









What if you suffer from high emotional/physical stress?

"A prolonged or exaggerated stress response may perpetuate cortisol dysfunction, widespread inflammation, and pain."

Hannibal, K. E., & Bishop, M. D. (2014). Chronic stress, cortisol dysfunction, and pain: a psychoneuroendocrine rationale for stress management in pain rehabilitation. Physical therapy, 94(12), 1816–1825. https://doi.org/10.2522/ptj.20130597



"Clinically anxious participants exhibited significantly lower levels of morning cortisol and significantly higher levels of IL-6, independent of age, sex, and depressive symptoms."

O'Donovan, A., Hughes, B. M., Slavich, G. M., Lynch, L., Cronin, M. T., O'Farrelly, C., & Malone, K. M. (2010). Clinical anxiety, cortisol and interleukin-6: evidence for specificity in emotionbiology relationships. Brain, behavior, and immunity, 24(7), 1074–1077. https://doi.org/10.1016/j.bbi.2010.03.003





What type of stress activates the adrenals?











What happens when your stress glands are fatigued?





A study published in 2012 measured the function of adrenals and level of inflammation in 869 adults (age 45 to 84) in the U.S.



People who had **lower cortisol levels** in the morning had higher levels of inflammation (Tumor Necrosis Factor and IL-6)

DeSantis, A. S., DiezRoux, A. V., Hajat, A., Aiello, A. E., Golden, S. H., Jenny, N. S., Seeman, T. E., & Shea, S. (2012). Associations of salivary cortisol levels with inflammatory markers: the Multi-Ethnic Study of Atherosclerosis. Psychoneuroendocrinology, 37(7), 1009–1018. https://doi.org/10.1016/j.psyneuen.2011.11.009



We reviewed the patient's adrenal lab results and this is what we found.

Analyte	Result	Unit	L	WR	H (Optimal Range	Reference Interval
Cortisol Morning	16	nmol/L		>		18 - 35	5.1-40
Cortisol Noon	3.6	nmol/L	4	•	6	6.0 - 12	2.1 - 16
Cortisol Evening	1.4	nmol/L	+			2.0-5.0	1.5-8.0
Cortisol Night	0.83	nmol/L	4	>		1.0-4.0	0.33 - 7.0



Analyte	Result	Unit	L	WR	I	H Optimal R	ange	Reference Inte	rval
Cortisol Morning	16	nmol/L	\diamond			18 - 35		5.1-40	
Cortisol Noon	3.6	nmol/L				6.0 - 12		2.1 - 16	
Cortisol Evening	1.4	nmol/L	+			2.0-5.0		1.5 - 8.0	
Cortisol Night	0.83	nmol/L				1.0-4.0		0.33-7.0	

Adrenal dysfunction -> low cortisol Might lead to higher inflammation



Analyte	Result	Unit	L	WR H	Optimal Range	Reference Interval
Cortisol Morning	16	nmol/L	\diamond		18 - 35	5.1-40
Cortisol Noon	3.6	nmol/L	\diamond		6.0 - 12	2.1 - 16
Cortisol Evening	1.4	nmol/L	+		2.0 - 5.0	1.5 - 8.0
Cortisol Night	0.83	nmol/L			1.0-4.0	0.33 - 7.0
DHEA*	34	pg/mL	Ŧ			106 - 300

DHEA, also called the master hormone) is one of the most abundant hormones in humans.

It is produced mostly in the adrenal glands (and some in the brain).

It is also called the "anti-aging" hormone because our body uses it to create other hormones, such as estrogen or testosterone.

DHEA is important for healthy adrenal function

 (DHEA-S) levels are valuable in patients suspected of having adrenal insufficiency:

 "In establishing the diagnosis of central adrenal insufficiency, we recommend measurements of baseline serum cortisol and DHEA-S levels."

 "Low DHEA might indicate lower Adrenocorticotropic hormone (hypothalamicpituitary-adrenal axis function)"

Al-Aridi R, Abdelmannan D, Arafah BM. Biochemical diagnosis of adrenal insufficiency: the added value of dehydroepiandrosterone sulfate measurements. Endocr Pract. 2011;17(2):261-270. doi:10.4158/EP10262.RA





Al-Aridi R, Abdelmannan D, Arafah BM. Biochemical diagnosis of adrenal insufficiency: the added value of dehydroepiandrosterone sulfate measurements. Endocr Pract. 2011;17(2):261-270. doi:10.4158/EP10262.RA

- "Although serum DHEA-S levels are low in patients with primary or central adrenal insufficiency, a low level of this steroid is not sufficient by itself for establishing the diagnosis."
- You have to look at the whole picture: symptoms and measuring cortisol 4 times per day + DHEA
- Secreted Immunoglobulin A (sIgA) levels might indicate the state of immune reaction

50mg daily DHEA in Patients with Addison's Disease:

- "DHEA reversed ongoing loss of bone mineral density at the femoral neck, but not other sites.
- Circulating DHEAS rose significantly in both sexes, with testosterone increasing to low normal levels only in females.
- DHEA enhanced total body lean mass
- "There was no significant benefit of DHEA treatment on fatigue or cognitive or sexual function."

Gurnell, E. M., Hunt, P. J., Curran, S. E., Conway, C. L., Pullenayegum, E. M., Huppert, F. A., Compston, J. E., Herbert, J., & Chatterjee, V. K. (2008). Long-term DHEA replacement in primary adrenal insufficiency: a randomized, controlled trial. The Journal of clinical endocrinology and metabolism, 93(2), 400–409. https://doi.org/10.1210/jc.2007-1134



We focused on improving her adrenal function (so her body can produce cortisol).

Plus, guide her to get the nutrients needed for her adrenal to function.



Treatment Protocol:

- Stress reduction techniques (breathing, meditation, reading a good book before sleep instead of TV or watching the news)
- Adaptogenic herbs to support healthy adrenal function:
 - Ashwagandha (>250mg/day) & Ginseng (>100mg/day) in am
 - Vitamin C (>250mg twice daily)
 - Antioxidants & phytonutrients (Amazing Grass powder)
 - DHEA 50mg per day
 - Anti-inflammatory support (Boswellia, Curcumin, and Ginger)
 - A few sessions of acupuncture stimulation of BL-23 points (adrenal support)



After two months, the client reported:

- ✓ Back pain was gone
- ✓ Energy increased
- ✓ She was not taking and dependent on pain medication anymore

Vitamin C & Adrenal Function

- "The adrenal gland is among the organs with the highest concentration of vitamin C in the body."
- "Interestingly, both the adrenal cortex and the medulla accumulate such high levels of ascorbate. Ascorbic acid is a cofactor required both in catecholamine biosynthesis and in adrenal steroidogenesis."

Patak P, Willenberg HS, Bornstein SR. Vitamin C is an important cofactor for both adrenal cortex and adrenal medulla. Endocr Res. 2004;30(4):871-875. doi:10.1081/erc-200044126





B vitamins are also important for:

- Steroid biosynthesis, derivatives B3 (niacin), B5 (pantothenic acid), B7, and B9
- Reducing emotional stress: vitamins B1, B6 and B12
- Mitochondrial function



Ashwagandha and Cortisol

- In comparison to placebo, serum cortisol levels reduced with both Ashwagandha 250 mg/day (P < 0.05) and Ashwagandha 600 mg/day (P < 0.0001).
- Use of Ashwagandha led to significant reduction in perceived stress scale (PSS) and improvement in sleep.

Salve, J., Pate, S., Debnath, K., & Langade, D. (2019). Adaptogenic and Anxiolytic Effects of Ashwagandha Root Extract in Healthy Adults: A Double-blind, Randomized, Placebocontrolled Clinical Study. *Cureus*, *11*(12), e6466. https://doi.org/10.7759/cureus.6466

Resources:

- Kelly GS. Nutritional and botanical interventions to assist with the adaptation to stress. Altern Med Rev. 1999 Aug;4(4):249-65. PMID: 10468649
- Tarasov IuA, Sheĭbak VM, Moĭseenok AG. Funktsional'naia aktivnost' kory nadpochechnikov pri nedostatochnosti pantotenata i vvedenii vitamina ili ego proizvodnykh [Adrenal cortex functional activity in pantothenate deficiency and the administration of the vitamin or its derivatives]. Vopr Pitan. 1985 Jul-Aug;(4):51-4. Russian. PMID: 4060684.
- Jaroenporn S, Yamamoto T, Itabashi A, Nakamura K, Azumano I, Watanabe G, Taya K. Effects of pantothenic acid supplementation on adrenal steroid secretion from male rats. Biol Pharm Bull. 2008 Jun;31(6):1205-8. doi: 10.1248/bpb.31.1205. PMID: 18520055.
- Anand SS. Protective effect of vitamin B6 in chromium-induced oxidative stress in liver. J Appl Toxicol. 2005 Sep-Oct;25(5):440-3. doi: 10.1002/jat.1077. PMID: 15986493.
- Kelly GS. Nutritional and botanical interventions to assist with the adaptation to stress. Altern Med Rev. 1999 Aug;4(4):249-65. PMID: 10468649.
- Wesselink E, Koekkoek WAC, Grefte S, Witkamp RF, van Zanten ARH. Feeding mitochondria: Potential role of nutritional components to improve critical illness convalescence. Clin Nutr. 2019 Jun;38(3):982-995. doi: 10.1016/j.clnu.2018.08.032. Epub 2018 Aug 31. PMID: 30201141.

Why is it important to recognize and properly treat adrenal insufficiency and unhealthy levels of cortisol?



Adrenal **Insufficiency &** Nutritional Deficiencies Can Affect Patients With Different Chronic **Diseases**!



- Association between
 elevated levels of cortisol
 and obesity, hypertension,
 and increased risk of
 cardiovascular diseases
- Patients with depression
- Patients with diabetes:
 Elevated cortisol levels was associated with elevated fasting plasma glucose (FPG) and hemoglobin A1c (HbA1c)





- Patients with Arthritis: 66% of patients with rheumatoid arthritis and consumption of steroids had lower levels of cortisol
- Patients with osteoarthritis: Association between cortisol levels and pain level in women with osteoarthritis
- Patients with autoimmune conditions (such as Hashimoto or low thyroid)
- Patients who were taking steroids: Administration of steroids led to significant reduction in adrenal function, as measured as lower cortisol in 20% of the children and undetectable levels of cortisol in 10% of the children with inflammatory bowel disease (IBD).
- PMS and hormonal imbalance: Association between hormonal imbalance and cortisol levels

Resources:

- Joseph, R. M., Ray, D. W., Keevil, B., van Staa, T. P., & Dixon, W. G. (2018). Low salivary cortisol levels in
 patients with rheumatoid arthritis exposed to oral glucocorticoids: a cross-sectional study set within UK
 electronic health records. RMD open, 4(2), e000700. <u>https://doi.org/10.1136/rmdopen-2018-000700</u>
- Carlesso, L. C., Sturgeon, J. A., & Zautra, A. J. (2016). Exploring the relationship between disease-related pain and cortisol levels in women with osteoarthritis. Osteoarthritis and cartilage, 24(12), 2048–2054. <u>https://doi.org/10.1016/j.joca.2016.06.018</u>
- Erichsen MM, Løvås K, Skinningsrud B, Wolff AB, Undlien DE, Svartberg J, Fougner KJ, Berg TJ, Bollerslev J, Mella B, Carlson JA, Erlich H, Husebye ES. Clinical, immunological, and genetic features of autoimmune primary adrenal insufficiency: observations from a Norwegian registry. J Clin Endocrinol Metab. 2009 Dec;94(12):4882-90. doi: 10.1210/jc.2009-1368. Epub 2009 Oct 26. PMID: 19858318.
- Sidoroff, M., & Kolho, K. L. (2014). Screening for adrenal suppression in children with inflammatory bowel disease discontinuing glucocorticoid therapy. BMC gastroenterology, 14, 51. <u>https://doi.org/10.1186/1471-230X-14-51</u>
- Wirix, A. J., Finken, M. J., von Rosenstiel-Jadoul, I. A., Heijboer, A. C., Nauta, J., Groothoff, J. W., Chinapaw, M. J., & Kist-van Holthe, J. E. (2017). Is There an Association Between Cortisol and Hypertension in Overweight or Obese Children?. Journal of clinical research in pediatric endocrinology, 9(4), 344–349. https://doi.org/10.4274/jcrpe.4802
- Whitworth, J. A., Williamson, P. M., Mangos, G., & Kelly, J. J. (2005). Cardiovascular consequences of cortisol excess. Vascular health and risk management, 1(4), 291–299. <u>https://doi.org/10.2147/vhrm.2005.1.4.291</u>
- Huang Y, Zhou R, Wu M, Wang Q, Zhao Y. Premenstrual syndrome is associated with blunted cortisol reactivity to the TSST. Stress. 2015;18(2):160-8. doi: 10.3109/10253890.2014.999234. Epub 2015 Jan 23. PMID: 25518868.
- Fraser R, Ingram MC, Anderson NH, Morrison C, Davies E, Connell JM. Cortisol effects on body mass, blood pressure, and cholesterol in the general population. Hypertension. 1999 Jun;33(6):1364-8. doi: 10.1161/01.hyp.33.6.1364. PMID: 10373217.
- Whitworth JA, Saines D, Scoggins BA. Blood pressure and metabolic effects of cortisol and deoxycorticosterone in man. Clin Exp Hypertens A. 1984;6(4):795-809. doi: 10.3109/10641968409044039. PMID: 6723088.
- Dienes, K. A., Hazel, N. A., & Hammen, C. L. (2013). Cortisol secretion in depressed, and at-risk adults. Psychoneuroendocrinology, 38(6), 927–940. <u>https://doi.org/10.1016/j.psyneuen.2012.09.019</u>
- Ortiz R, Kluwe B, Odei JB, Echouffo Tcheugui JB, Sims M, Kalyani RR, Bertoni AG, Golden SH, Joseph JJ. The association of morning serum cortisol with glucose metabolism and diabetes: The Jackson Heart Study. Psychoneuroendocrinology. 2019 May;103:25-32. doi: 10.1016/j.psyneuen.2018.12.237. Epub 2018 Dec 27. PMID: 30623794; PMCID: PMC6450778.

Treating Pain with Functional Medicine: A Case Study

Tal Cohen, DAOM, MS-HNFM



