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Dear Women and Men of the Scottish Parliament,

IN SUPPORT OF PETITION NO. PE01463 I can attest that the petitioners' struggles to obtain an endocrine diagnosis and effective treatment are both real and common. There is no quality control, no accountability in endocrinology; if the physicians cannot find and correct the hormonal cause of a patient's suffering, they can attach a label: chronic fatigue, fibromyalgia, depression, anxiety, etc. These symptom-diagnoses have no known cause or diagnostic test; they are convenient excuses for the failure to diagnose and properly treat. For 8 years I have been helping patients like the petitioners with hormone restoration—but only by “breaking the rules” of conventional endocrinology. Endocrinology still operates on the early 20th century idea that the endocrine system functions perfectly unless there is **damage or disease** affecting the primary gland or hypothalamic-pituitary system. If no such disease is evident and if the hormone level falls **anywhere** within the laboratory's range, they “rule out” hormone deficiency as a cause of the patient's symptoms. Their unjustified belief in the **perfection** of hypothalamic-pituitary function also causes them to rely on the **wrong tests** to detect thyroid and cortisol deficiencies. Because they neither rely on clinical criteria, nor do the proper tests, nor understand the reference ranges, nor replace sex hormones, they are **blind** to the frequency of hormone deficiencies, the many interactions among hormones, and the benefits that are possible with hormone optimization. When they do treat, they follow arbitrary rules rather than attempt to restore well-being. This insensitive, ineffective endocrinology is causing much unnecessary suffering, and women suffer the most due to the complexity and fragility of their reproduction-oriented hormonal system. Endocrinology must become a **clinical discipline**—guided by the patient's signs and symptoms first, and by the most sensitive laboratory tests second.

Reference Range Endocrinology: Hormones are the most powerful molecules in the human body, affecting every system, every tissue, and every aspect of our well-being and health. We are unable to test the action of a hormone in the tissues, for which symptoms remain the most sensitive indicator. We can, however, look at an **indirect** indicator: the level of the hormone in the blood. Laboratories report the level with a population reference range, which physicians mistake for a **diagnostic range**. They assume that experts have reviewed all relevant evidence and decided that the reported ranges define “optimal” or “sufficient” levels. They are afraid to diagnose if the result is “normal”. Lab reports are confusing because they contain a mixture of physician-adjudicated diagnostic ranges (e.g. blood sugar—diabetes) and population ranges. **Hormone reference ranges are just population statistics**, including 2 standard deviations from the mean—**95%—almost all**—of a group of “apparently healthy” adults. The subjects were usually laboratory employees and their friends and relatives, and were **not screened for symptoms** of deficiency. Only the **lowest 2.5%** of this unscreened adult population is defined as “low”. Therefore, a physician routinely tells a patient with symptoms of a hormone deficiency and “low-normal” level, say at the 5th percentile, that his/her symptoms cannot be caused by a hormone deficiency, even though 95% of adults have higher levels! This reference-range-based approach works to detect **diseases** of the endocrine glands, which are rare, but fails entirely to detect **dysfunction** of the endocrine system with its resultant sub-optimal hormone levels and effects. Relative hormone deficiencies are quite common due to age-related deterioration, chronic stress, unhealthy lifestyles, environmental toxins, genetic abnormalities, etc. The insensitivity of this reference range endocrinology is evident in breadth of the ranges—the lower and upper limits differ by **factors of 2 up to 5!** One can double, triple or quadruple a person's “low-normal” hormone level and still be within the range! In my experience such changes in hormone levels bring remarkable improvements, and many studies do show marked differences in quality of life and health with higher vs. lower hormone levels within the population ranges. Also, individuals can vary greatly in their hormonal needs. So why don't endocrinologists offer a symptomatic patient with “low-normal” levels a **trial of hormone supplementation**—to see if higher “normal” levels relieve their symptoms? In addition to their disease-orientation, I find that they are unaware of the literature on the benefits of higher thyroid, testosterone, DHEA, estradiol, and progesterone levels within the population ranges,¹ and they hold many false beliefs about possible harms of hormone optimization.²

Absurd TSH-T4 Reference Range Thyroidology: Thyroid hormone increases the energy production and therefore the activity of every tissue and organ in the human body. “Hypothyroidism” is inadequate thyroid hormone effect leading to fatigue, achiness, weight gain, constipation, poor cognition, cold extremities, high cholesterol levels, atherosclerosis,^{3,4} depression, anxiety, and myriad other symptoms and disorders. **T3** is the active thyroid hormone, and most of it is produced by conversion from inactive **T4**. The most sensitive indicators of T3-effect in the tissues are the patient's signs and symptoms; the next best tests are the free T4 and free T3 levels in the blood. However, endocrinologists essentially ignore both of these in favor of the TSH level. This is illogical. **Thyroid stimulating hormone (TSH) is not a thyroid hormone**; it is secreted by the pituitary gland to stimulate the thyroid gland. The TSH

level does not tell us what the thyroid hormone levels are in any given patient, nor how much T3-effect there is in the rest of the body. The TSH level helps only to determine the **cause** of the hypo- or hyperthyroidism. This use of any pituitary-stimulating hormone level as a surrogate for the end-hormone's levels and effects is akin to believing that one's home-heating thermostat works perfectly even as the house gets colder and colder. The control of TSH secretion is highly complex; more likely to be dysfunctional than the thyroid gland. Deficient luteinizing hormone secretion by the pituitary gland is the most common cause of low testosterone in men. This **"Immaculate TSH" delusion corrupts all of thyroidology**.⁵ "Euthyroidism" is now equated with "normal TSH test"! Since they believe that the TSH is always "right", they assume that almost all hypothyroidism is primary—due to failure of the gland as evidenced by a high TSH. Thus the "standard of practice" requires **only a TSH test** to "rule out" hypothyroidism. Official guidelines actually **warn** physicians **not to treat** any patient, no matter how symptomatic, unless the diagnosis is "biochemically confirmed"⁶--unless the TSH is high. A "low" free T4 should trigger a diagnosis of hypothyroidism, but is often ignored if the TSH is normal. In my experience, patients with hypothyroid symptoms usually have a normal TSH but a low or low-normal free T4, and do benefit from treatment. Others have reported the same.⁷

Worse, endocrinologists use the TSH test to guide treatment! Official guidelines state that the **goal** of thyroid replacement therapy is a **normal TSH**; which assumes that TSH secretion is perfect and the TSH was "high" in the first place. Again, "clinical criteria"—the patient's **signs and symptoms—are to be ignored!**^{8,9} Endocrinologists apparently believe that the hypothalamic-pituitary system evolved to help them determine how much levothyroxine a person should swallow every morning! Nonsense; studies have repeatedly shown that even in the case of thyroid gland failure **TSH-normalizing T4 therapy does not restore quality of life or health**.^{10,11,12} It leaves free T3 levels lower than in healthy persons.^{13,14,15,16} After thyroid gland removal, TSH-suppressing T4 doses are often required to restore the patient's free T3 to its pre-operative level.¹⁷ Realizing that "TSH normalization" is not sufficient, one guideline recommends that the TSH be reduced to the low end of its range.¹⁸ The Royal College of Physicians and some experts go farther and admit that a physician can prescribe **TSH-suppressing** doses of T4 if there are no signs or symptoms of hyperthyroidism and the **free T3** is normal.^{19,20,21} In a landmark study of clinical thyroidology in Scotland, the only one of its kind, the levothyroxine dose was adjusted by specialists according to clinical criteria—the patients' signs and symptoms. The resulting treatment TSH levels were often undetectable and the free T4 higher than usual. Only the free T3 corresponded well with the untreated range and with clinical effects.²² In spite of these facts, this **grossly insensitive, ineffective TSH-based diagnosis and treatment scheme** remains "standard practice". In my experience, patients on TSH-normalizing levothyroxine doses often remain highly symptomatic and have rather low free T3 and free T4 levels. They routinely respond well to T4/T3 optimization that leaves the TSH suppressed. Doctors fear giving TSH-suppressing doses because they will be accused of overtreating the patient. They also fear being sued if the patient develops atrial fibrillation or bone loss. These are underlying medical conditions that are exacerbated by **any** increase in thyroid levels—from hypothyroid to hyperthyroid.^{23,24} The solution is not to leave everyone hypothyroid, but to treat the underlying problem. Effective thyroidology requires leadership that is now conspicuously absent.

Since the TSH cannot be used for diagnosis or for treatment, the physician must order **free T4 and free T3 levels**. However, their reference ranges are **contaminated** by the "Immaculate TSH" doctrine. To save time and money, laboratories (at least in the US) include physician-ordered thyroid tests in their reference ranges—if the TSH is normal.²⁵ So untreated and treated **hypothyroid patients** are included and resulting free T4 ranges have lower limits of only **0.6 or 0.8ng/dl** (7.7 or 10.3pmol/L) and upper limits of 1.8-2.2ng/dl! With these low ranges, persons with both a low-normal free T4 **and** free T3 can be extremely hypothyroid.²⁶ Rigorous studies of adult non-patients, without screening for symptoms, yield a narrower 95%-inclusive free T4 range of **1.0 to 1.6ng/dl** (12.9–20.6 pmol/L).^{27,28,29}

However, even this tighter free T4 range is still just an arbitrary statistical treatment of a group of unscreened adults. Persons differ in their need for thyroid hormone;^{30,31} the 5th or even 50th percentile may not be sufficient for some. Many persons I see with hypothyroid symptoms have free T4 levels between 1.0 and 1.2ng/dl. Persons also vary in their **conversion of T4 to T3** and in other mechanisms required for thyroid hormone action (e.g. polymorphisms of deiodinase enzymes, receptor proteins, transport proteins, intracellular effector proteins, etc.). Persons on T4-only therapy often have high reverse T3 levels. **Reverse T3** reduces T4-to-T3 conversion,³² so higher levels have an anti-thyroid effect. TSH stimulates T4-to-T3 conversion,^{33,34,35} so the lower TSH on oral replacement therapy reduces thyroid action throughout the body. For this reason, and because the thyroid gland naturally secretes some T3, thyroid replacement therapy should usually **include T3** (liothyronine). **Natural desiccated thyroid** is a practical and effective T4/T3 combination product that also contains metabolically active T2.³⁶ Endocrinologists have performed studies of T4-T3 combinations and proclaimed "no benefit"; but the studies were corrupted by the "Immaculate TSH" doctrine and treatment was not individualized.³⁷ Many persons have a genetic defect in T4-to-T3 conversion,³⁸ helping to explain why some patients require T3-only therapy to feel and function well. **Thyroidology must be clinical**: the physician must work with the patient to find the most effective thyroid replacement regimen.

Failure to Diagnose Cortisol Deficiency: Sufficient cortisol is necessary to cope with the physical and emotional demands of life and to prevent excessive inflammation. Cortisol-deficient persons lack mental and physical vigor. They have fatigue, pain, irritability, depression, anxiety, insomnia, hypoglycemia and cognitive dysfunction ("brain fog").

They are prone to allergies, environmental sensitivities, and autoimmune diseases. Symptoms wax and wane unpredictably. Women have lower cortisol levels and effects than men.^{39,40,41,42,43,44} Estrogen both lowers cortisol production and inactivates cortisol in the tissues,^{45,46,47} explaining why women have symptoms of cortisol deficiency when estrogen levels are high in the menstrual cycle (premenstrual syndrome and dysphoric disorder).^{48,49,50} Cortisol has anti-estrogen effects in the endometrium;⁵¹ lower saliva cortisol levels are seen in women with endometriosis and chronic pelvic pain.^{52,53} Cortisol deficiency has been linked to excessive vomiting during pregnancy^{54,55,56} and post-partum depression.^{57,58,59,60} Cortisol deficiency is a sufficient explanation for marked **female predominance** in chronic fatigue syndrome,^{61,62,63,64} fibromyalgia,^{65,66,67} post-traumatic stress disorder,^{68,69,70,71} anxiety, atypical depression.^{72,73} and autoimmune diseases.^{74,75,76,77,78,79} Cortisol/steroid therapy improves these disorders. Unable to diagnose cortisol deficiency, physicians treat the symptoms (fatigue, fibromyalgia, depression, anxiety, etc.) with **anti-depressants** that, unknown to them, raise cortisol levels.^{80,81,82,83,84,85,86,87,88} Exercise,⁸⁹ nicotine,^{90,91} coffee,⁹² marijuana,^{93,94,95} ecstasy,^{96,97} and amphetamines^{98,99} raise cortisol levels temporarily, bringing some relief. All steroids, the **anti-inflammatory glucocorticoids** like prednisone, Medrol, etc., are altered versions of cortisol; their use is a form of endocrine therapy. The problems caused by these cortisol substitutes have made doctors loathe to diagnose or treat cortisol deficiency. A full understanding of cortisol will revolutionize the practice of medicine, and vastly improve the care of women.

The current approach to the diagnosis of cortisol deficiency is **extremely insensitive**. Endocrinologists don't even view cortisol deficiency as a distinct problem; they are only taught about **severe adrenal insufficiency (AI)** caused by **disease**—Addison's disease and hypothalamic-pituitary damage. They deny the possibility of any lesser degrees of cortisol deficiency caused by **dysfunction** of the hypothalamic-pituitary-adrenal system. However, cortisol deficiency is quite common; called "adrenal fatigue" in the lay press. The most sensitive laboratory test for cortisol deficiency is **the diurnal saliva cortisol profile**. Saliva testing best reveals the free, biologically active cortisol levels throughout a normal day.^{100,101,102,103,104,105} Endocrinologists don't order saliva testing to look for cortisol deficiency; even if they did the reference ranges include "undetectable" as "normal". Actually, an AM saliva cortisol level below 1.5 to 1.8 mcg/dL suggests cortisol deficiency, and many persons with proven AI have higher levels.^{106,107,108,109} A morning saliva cortisol level is insensitive¹¹⁰ because AM cortisol levels are raised by the awakening and light reflexes,^{111,112} which are absent the rest of the day. If a physician suspects cortisol deficiency, he'll perform an **AM cortisol blood level**. This test is even less sensitive because the drive to the lab¹¹³ and the needle stick¹¹⁴ raise cortisol levels. Also, the AM cortisol reference range is far too broad, typically **5 to 25mcg/dL**. In fact, cortisol deficiency is common in symptomatic persons with AM levels less than 12mcg/dL¹¹⁵ or 14.5mcg/dL.¹¹⁶ When a physician refers a patient with suspected AI to an endocrinologist, he/she performs an **ACTH stimulation test**. This grossly unphysiological test detects only the **nearly complete destruction** or atrophy of the adrenal glands; it cannot detect **partial** primary-secondary cortisol deficiency,^{117,118,119} which is far more common. DHEA is another vital adrenal hormone,¹²⁰ and a low serum DHEAS level can help identify patients with partial AI,^{121,122} but again the reference range is far too broad (60 to 300mcg/dL). DHEAS can even be mid-range or high in some persons with isolated cortisol deficiency. Cortisol deficiency may exist even though **all tests** are apparently **normal**;¹²³ one reason being that cortisol can be inactivated and activated within tissues by 11-beta hydroxysteroid dehydrogenase enzymes. More than any other hormone, the diagnosis and treatment of cortisol deficiency must be **clinical**. Useful indicators of cortisol deficiency include a negative reaction to thyroid hormone replacement (worsening of cortisol deficiency), and improved mood and energy when on "steroids". Every symptomatic patient deserves a trial of hydrocortisone—bioidentical cortisol. No other hormone brings such rapid and dramatic improvements. If cortisol supplementation is beneficial it should be continued. Cortisol replacement therapy is **safe** long-term in clinically-adjusted doses if **DHEA** is also replaced.¹²⁴

Failure to Replace Ovarian Hormones: Not only do women suffer from thyroid and cortisol deficiency much more than men, but they suffer a **catastrophic loss** of ovarian sex steroids at **menopause**. Estradiol, progesterone, and testosterone are not just sex hormones, they are essential to the health of every tissue in the human body, including the brain. Estradiol deficiency causes fatigue, depression, vaginal dryness, sexual dysfunction, hot flashes and insomnia. It causes rapid bone loss and promotes atherosclerosis^{125,126,127,128} and Alzheimer's dementia.^{129,130,131} Tragically, women are being denied **medically-necessary** sex steroid replacement for one reason—the cardiovascular events and breast cancers caused by the drug PremPro.^{132,133} Endocrine associations endorsed this combination of horse urine estrogens and an invented progestin for decades; now they parrot **the pharmaceutical corporation lie** that bioidentical (human) estradiol and progesterone carry the **same risks as** Prempro, birth control pills, and all other hormone-like drugs. However, estradiol taken transdermally does not increase the incidence of blood clots, strokes or heart attacks as do oral Premarin and birth control pills.^{134,135} Progesterone does not increase breast cancer risk as do Provera and other progestins.^{136,137,138} Estradiol replacement with sufficient progesterone may even decrease the risk of breast cancer.¹³⁹ Adding testosterone to estradiol-progesterone replacement may help further reduce breast cancer incidence.^{140,141} Testosterone declines with age in women, and estradiol replacement further lowers free testosterone levels,¹⁴² so testosterone should also be restored to youthful levels in women to improve muscle strength, bone density, mood and libido.^{143,144}

Recommendations for Parliamentary Action: To fix any problem, one must identify and eliminate the cause(s). Every academic-professional group is resistant to change. However, I believe that the failures I have identified would have been found and corrected within the profession if not for the pervasive **influence of the pharmaceutical industry**. Endocrine professional associations, journals, conferences, and guideline-writing committees are funded by drug companies. Pharmaceutical corporations corrupt endocrine practice by imposing their own paradigm. Whereas **natural scientific medicine** seeks to identify and correct the cause—the hormone deficiency, nutrient deficiency, toxin, infection, or other biochemical disorder—**pharmaceutical medicine** instead encourages doctors to simply **name** the symptom or disorder and prescribe invented molecules (drugs) that suppress the symptoms or signs (e.g. chronic fatigue syndrome, fibromyalgia, depression, insomnia, bipolar disorder, essential hypertension, hyperlipidemia, etc.). The existence of this pharmaceutical paradigm with its alternative diagnosis and treatment scheme reduces the physician's motivation to search for the cause. Endocrinology has also been especially corrupted by **pharmaceutical hormone substitutes**. The many problems caused by these hormone-like drugs have created the impression that hormones are dangerous. Notice too, that physicians can prescribe any drug or number of drugs to patients without fear, but if they prescribe hormones outside of restrictive reference-range-based guidelines they must fear losing their license! *Cui bono?* Not the patients.

It is not parliament's responsibility to tell physicians how to practice medicine. Parliament must, however, protect its citizens from the overwhelming power of government-chartered corporations and assure that its citizens have access to effective endocrine diagnosis and therapy. To these ends I recommend that the parliament:

- 1. Ask the General Medical Council and endocrine associations** to review their guidelines for the diagnosis and treatment of hormone deficiencies with the goal of optimizing the patients' quality of life and long-term health.
- 2. Isolate the practice of endocrinology from the pharmaceutical industry** by requiring that all endocrine professional medical organizations, guideline committees and journals have **zero** pharmaceutical company funding.¹⁴⁵ Close the "revolving door" loophole by requiring that endocrinologists, as a precondition for having such leadership roles, agree that they will **never** accept any pharmaceutical money or employment. The sole exception shall be for work related to bioidentical hormone products.
- 3. Prohibit pharmaceutical direct-to-consumer advertising** because it manipulates the population into pushing their doctors into the pharmaceutical paradigm, rather than finding and correcting the cause.
- 4. Provide accurate prescribing information to physicians and patients.** Instruct the Medicines and Healthcare Products Regulatory Agency (MHRA) to stop confounding hormones with drugs. Hormones are natural to the body and essential for health, they are not drugs and do not have "side effects"! Only drugs should be presumed to have unknown deleterious effects until proven otherwise. The prescribing information for bioidentical hormone products should include only that information that is relevant to that hormone and hormone product. It must not include "drug class" warnings as it does now—all the side effects ever seen with any hormone-like drugs delivered by any route. The prescribing information should also explain what problems can occur with the hormone product and why (e.g. overdosing, route of administration, hormone imbalance, etc.). It should provide sufficient guidance to enable the physician to optimize the patients' hormone levels and effects and insure proper balance with other hormones (e.g. replace progesterone with estradiol, DHEA with hydrocortisone). All hormone-like drugs (estrogens, progestins, birth control pills, glucocorticoids, androgens, etc.) must carry a **warning** that they are similar to, but are not human hormones; they do not have the same benefits and do have deleterious effects.
- 5. Assure the availability of bioidentical hormone products** to physicians and patients in Scotland. Require the MHRA to create a streamlined approval process for bioidentical hormone products, as they should be presumed safe and effective until proven otherwise (e.g. natural dessicated thyroid, slow-release hydrocortisone tablets, slow-release aldosterone tablets, injectables, implants, infusion pumps, etc.).
- 6. Assure meaningful reporting of endocrine test results.** Laboratories and the medical profession have **failed** to deal with the many problems involved.¹⁴⁶ Parliament should direct the MHRA to require laboratories to clearly identify all reference ranges as either adjudicated-diagnostic ranges or as 2.5-to-97.5% population ranges. In gathering subjects for hormone reference range determinations, laboratories must **carefully screen** for any signs or symptoms of hormone deficiency or excess. Laboratories must never use physician-ordered tests except to produce treatment ranges. Where possible, laboratories should use the medical literature and input from clinicians to provide meaningful diagnostic ranges, not just population ranges. For thyroid tests, laboratories should include separate treatment ranges for levothyroxine-treated patients. (e.g. as produced by Fraser et al.¹⁴⁷)
- 7. Remove professional barriers to the practice of clinical endocrinology.** Instruct the General Medical Council that it **must not prosecute** any physician for practicing clinical endocrinology; for not following conventional endocrine guidelines (e.g. for treating a patient with "normal" labs, suppressing the TSH, prescribing hydrocortisone without a failed ACTH stimulation test, etc.). Clinically-adjusted bioidentical hormone treatment must be presumed safe until proven otherwise; the medical council or board bears the burden of proof that a physician is harming patients.
- 8. Preserve patients' endocrine freedom:** their right to elect, and the physician to prescribe, any endocrine treatment that improves their quality of life, in spite of theoretical or even real concerns about long-term health consequences.

- 1 Lindner, H., "The Evidence" <http://hormonerestoration.com/Evidence.html>, collected abstracts with comments, listed by hormone and disorder.
- 2 Lindner, H., Why Docs Don't Get It, <http://hormonerestoration.com/Docs.html>.
- 3 Perk M, O'Neill BJ. The effect of thyroid hormone therapy on angiographic coronary artery disease progression. *Can J Cardiol.* 1997 Mar;13(3):273-6.
- 4 Auer J, Berent R, Weber T, Lassnig E, Eber B. Thyroid function is associated with presence and severity of coronary atherosclerosis. *Clin Cardiol.* 2003 Dec;26(12):569-73.
- 5 Lindner, H., Against TSH-T4 Reference Range Thyroidology: The Case for Clinical Thyroidology, <http://hormonerestoration.com/files/TSHWrngtree.pdf>.
- 6 Clinical Practice Guidelines for hypothyroidism in adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association, <https://www.aace.com/files/final-file-hypo-guidelines.pdf>, Recommendation 29.
- 7 Skinner GRB, Holmes D, Ahmad A, Davies JA, Benitez J, Clinical Response to Thyroxine Sodium in Clinically Hypothyroid but Biochemically Euthyroid Patients, *J Nutr Environ Med* 2000 Jun;10 (2):115-124.
- 8 Ref. 5, p.31.
- 9 Lindner, H. The Non-Clinical ATA/AACE 2012 Hypothyroidism Guidelines, <http://hormonerestoration.com/files/ResponsetoGuidelines.pdf>.
- 10 Saravanan P, Chau WF, Roberts N, Vedhara K, Greenwood R, Dayan CM 2002 Psychological well-being in patients on 'adequate' doses of l-thyroxine: results of a large, controlled community-based questionnaire study. *Clin Endocrinol (Oxf)* 57:577-85.
- 11 Wekking EM, Appelhof BC, Fliers E, Schene AH, Huyser J, Tijssen JG, Wiersinga WM. Cognitive functioning and well-being in euthyroid patients on thyroxine replacement therapy for primary hypothyroidism. *Eur J Endocrinol.* 2005 Dec;153(6):747-53.
- 12 Samuels MH, Schuff KG, Carlson NE, Carello P, Janowsky JS Health status, psychological symptoms, mood, and cognition in L-thyroxine-treated hypothyroid subjects. *Thyroid* 2007, 17:249-58.
- 13 Woeber KA 2002 Levothyroxine therapy and serum free thyroxine and free triiodothyronine concentrations. *J Endocrinol Invest* 25:106-9.
- 14 Mortoglou A, Candiloros H The serum triiodothyronine to thyroxine (T3/T4) ratio in various thyroid disorders and after Levothyroxine replacement therapy. *Hormones* 2004, 3:120-6.
- 15 Ito M, Miyauchi A, Morita S, Kudo T, Nishihara E, Kihara M, Takamura Y, Ito Y, Kobayashi K, Miya A, Kubota S, Amino N. TSH-suppressive doses of levothyroxine are required to achieve preoperative native serum triiodothyronine levels in patients who have undergone total thyroidectomy. *Eur J Endocrinol.* 2012 Sep;167(3):373-8.
- 16 Hoermann R, Midgley JE, Larisch R, Dietrich JW. Is pituitary TSH an adequate measure of thyroid hormone-controlled homeostasis during thyroxine treatment? *Eur J Endocrinol.* 2013 Jan 17;168(2):271-80.
- 17 Gullo D, Latina A, Frasca F, Le Moli R, Pellegriti G, Vigneri R. Levothyroxine monotherapy cannot guarantee euthyroidism in all athyreotic patients. *PLoS One.* 2011;6(8):e22552.
- 18 Demers LM, Spencer CA. Laboratory medicine practice guidelines: laboratory support for the diagnosis and monitoring of thyroid disease. *Clin Endocrinol (Oxf).* 2003 Feb;58(2):138-40.
- 19 Vanderpump MJ., Ahlquist JO., Franklyn JA., Clayton RN., on behalf of a working group of the Research Unit of the Royal College of Physicians of London, the Endocrinology and Diabetes Committee of the Royal College of Physicians of London, and the Society for Endocrinology. Consensus statement for good practice and audit measures in the management of hypothyroidism and hyperthyroidism. *BMJ* 1996;313:539-44.
- 20 Toft, A.D, Becker, J.D., Thyroid function tests and hypothyroidism, *BMJ* 2003;326:295-296.
- 21 O'Reilly DS., Thyroid hormone replacement: an iatrogenic problem. *Int J Clin Pract.* 2010 Jun;64(7):991-4.
- 22 Fraser WD, Biggart EM, O'Reilly DS, Gray HW, McKillop JH, Thomson JA. Are biochemical tests of thyroid function of any value in monitoring patients receiving thyroxine replacement? *Br Med J (Clin Res Ed).* 1986 Sep 27;293(6550):808-10.
- 23 Gammage MD, Parle JV, Holder RL, Roberts LM, Hobbs FD, Wilson S, Sheppard MC, Franklyn JA. Association between serum free thyroxine concentration and atrial fibrillation. *Arch Intern Med.* 2007 May 14;167(9):928-34.
- 24 Coindre JM, David JP, Rivière L, Goussot JF, Roger P, de Mascarel A, Meunier PJ 1986 Bone loss in hypothyroidism with hormone replacement. A histomorphometric study. *Arch Intern Med* 146:48-53.
- 25 Personal communications with chief scientists at major and local laboratories
- 26 Mallipedhi A, Vali H, Okosieme O. Myxedema coma in a patient with subclinical hypothyroidism. *Thyroid.* 2011 Jan;21(1):87-9.
- 27 Personal communication with laboratory director of Walter Reed Army Medical Center, 2009.
- 28 Kratzsch J, Fiedler GM, Leichtle A, Brügge M, Buchbinder S, Otto L, Sabri O, Matthes G, Thiery J. New reference intervals for thyrotropin and thyroid hormones based on National Academy of Clinical Biochemistry criteria and regular ultrasonography of the thyroid. *Clin Chem.* 2005 Aug;51(8):1480-6.
- 29 Takeda K, Mishiba M, Sugiura H, Nakajima A, Kohama M, Hiramatsu S. Evaluated reference intervals for serum free thyroxine and thyrotropin using the conventional outliner rejection test without regard to presence of thyroid antibodies and prevalence of thyroid dysfunction in Japanese subjects. *Endocr J.* 2009;56(9):1059-66.
- 30 Nagayama I, Yamamoto K, Saito K, Kuzuya T, Saito T. Subject-based reference values in thyroid function tests. *Endocr J.* 1993 Oct;40(5):557-62.
- 31 Andersen S, Pedersen KM, Bruun NH, Laurberg P. Narrow individual variations in serum T(4) and T(3) in normal subjects: a clue to the understanding of subclinical thyroid disease. *J Clin Endocrinol Metab.* 2002 Mar;87(3):1068-72.
- 32 Chopra IJ. Endocrinology. A study of extrathyroidal conversion of thyroxine (T4) to 3,3',5'-triiodothyronine (T3) in vitro. 1977 Aug;101(2):453-63.
- 33 Kabadi UM 1993 Role of thyrotropin in triiodothyronine generation in hypothyroidism. *Thyroidology* 5:41-7.
- 34 Russell W, Harrison RF, Smith N, Darzy K, Shalet S, Weetman AP, Ross RJ. Free triiodothyronine has a distinct circadian rhythm that is delayed but parallels thyrotropin levels. *J Clin Endocrinol Metab.* 2008 Jun;93(6):2300-6.
- 35 Kabadi UM Role of thyrotropin in metabolism of thyroid hormones in nonthyroidal tissues. *Metabolism* 2006, 55:748-50.
- 36 Cioffi F, Lanni A, Goglia F. Thyroid hormones, mitochondrial bioenergetics and lipid handling. *Curr Opin Endocrinol Diabetes Obes.* 2010 Oct;17(5):402-7.
- 37 Lindner, H., Against TSH-T4 Reference Range Thyroidology: The Case for Clinical Thyroidology, see Sect. 9 and the appendix. <http://hormonerestoration.com/files/TSHWrngtree.pdf>.
- 38 Panicker V, Saravanan P, Vaidya B, Evans J, Hattersley AT, Frayling TM, Dayan CM. Common variation in the DIO2 gene predicts baseline psychological well-being and response to combination thyroxine plus triiodothyronine therapy in hypothyroid patients. *J Clin Endocrinol Metab.* 2009 May;94(5):1623-9.
- 39 Purnell JQ, Brandon DD, Isabelle LM, Loriaux DL, Samuels MH. Association of 24-hour cortisol production rates, cortisol-binding globulin, and plasma-free cortisol levels with body composition, leptin levels, and aging in adult men and women. *J Clin Endocrinol Metab.* 2004 Jan;89(1):281-7.
- 40 Weykamp CW, Penders TJ, Schmidt NA, Borburgh AJ, van de Calseyde JF, Wolthers BJ. Steroid profile for urine: reference values. *Clin Chem.* 1989 Dec;35(12):2281-4.
- 41 Vierhapper H, Nowotny P, Waldhäusl W. Sex-specific differences in cortisol production rates in humans. *Metabolism.* 1998 Aug;47(8):974-6.

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- 42 Roca CA, Schmidt PJ, Deuster PA, Danaceau MA, Altemus M, Putnam K, Chrousos GP, Nieman LK, Rubinow DR. Sex-related differences in stimulated hypothalamic-pituitary-adrenal axis during induced gonadal suppression. *J Clin Endocrinol Metab.* 2005 Jul;90(7):4224-31.
- 43 Kudielka BM, Buske-Kirschbaum A, Hellhammer DH, Kirschbaum C. HPA axis responses to laboratory psychosocial stress in healthy elderly adults, younger adults, and children: impact of age and gender. *Psychoneuroendocrinology.* 2004 Jan;29(1):83-98.
- 44 Takai N, Yamaguchi M, Aragaki T, Eto K, Uchihashi K, Nishikawa Y. Gender-specific differences in salivary biomarker responses to acute psychological stress. *Ann N Y Acad Sci.* 2007 Mar;1098:510-5.
- 45 Gell JS, Oh J, Rainey WE, Carr BR. Effect of estradiol on DHEAS production in the human adrenocortical cell line, H295R. *J Soc Gynecol Investig.* 1998 May-Jun;5(3):144-8.
- 46 Cohen PG. Estradiol induced inhibition of 11beta-hydroxysteroid dehydrogenase 1: an explanation for the postmenopausal hormone replacement therapy effects. *Med Hypotheses.* 2005;64(5):989-91.
- 47 Ligeiro de Oliveira AP, Oliveira-Filho RM, da Silva ZL, Borelli P, Tavares de Lima W. Regulation of allergic lung inflammation in rats: interaction between estradiol and corticosterone. *Neuroimmunomodulation.* 2004;11(1):20-7.
- 48 Girdler SS, Pedersen CA, Straneva PA, Leserman J, Stanwyck CL, Benjamin S, Light KC. Dysregulation of cardiovascular and neuroendocrine responses to stress in premenstrual dysphoric disorder. *Psychiatry Res.* 1998 Nov 16;81(2):163-78.
- 49 Oda Y. [Influences of premenstrual syndrome on daily psychological states and salivary cortisol level]. *Shinrigaku Kenkyu.* 2005 Dec;76(5):426-35.
- 50 Odber J, Cawood EH, Bancroft J. Salivary cortisol in women with and without perimenstrual mood changes. *J Psychosom Res.* 1998 Dec;45(6):557-68.
- 51 Gunin AG, Mashin IN, Zakharov DA. Proliferation, mitosis orientation and morphogenetic changes in the uterus of mice following chronic treatment with both estrogen and glucocorticoid hormones. *J Endocrinol.* 2001 Apr;169(1):23-31.
- 52 Petrelluzzi KF, Garcia MC, Petta CA, Grassi-Kassisse DM, Spadari-Bratfisch RC. Salivary cortisol concentrations, stress and quality of life in women with endometriosis and chronic pelvic pain. *Stress.* 2008;11(5):390-7.
- 53 Heim C, Ehler U, Hanker JP, Hellhammer DH. Abuse-related posttraumatic stress disorder and alterations of the hypothalamic-pituitary-adrenal axis in women with chronic pelvic pain. *Psychosom Med.* 1998 May-Jun;60(3):309-18.
- 54 Jarnfelt-Samsioe A. Nausea and vomiting in pregnancy: a review. *Obstet Gynecol Surv.* 1987 Jul;42(7):422-7.
- 55 Bondok RS, El Sharnouby NM, Eid HE, Abd Elmaksoud AM. Pulsed steroid therapy is an effective treatment for intractable hyperemesis gravidarum. *Crit Care Med.* 2006 Nov;34(11):2781-3.
- 56 Nelson-Piercy C, Fayers P, de Swiet M. Randomised, double-blind, placebo-controlled trial of corticosteroids for the treatment of hyperemesis gravidarum. *BJOG.* 2001 Jan;108(1):9-15.
- 57 Kalantaridou SN, Makrigiannakis A, Zoumakis E, Chrousos GP. Stress and the female reproductive system. *J Reprod Immunol.* 2004 Jun;62(1-2):61-8.
- 58 Mastorakos G, Ilias I. Maternal hypothalamic-pituitary-adrenal axis in pregnancy and the postpartum period. *Postpartum-related disorders.* *Ann N Y Acad Sci.* 2000;900:95-106.
- 59 Kammerer M, Taylor A, Glover V. The HPA axis and perinatal depression: a hypothesis. *Arch Womens Ment Health.* 2006 Jul;9(4):187-96.
- 60 Groer MW, Morgan K. Immune, health and endocrine characteristics of depressed postpartum mothers. *Psychoneuroendocrinology.* 2007 Feb;32(2):133-9.
- 61 Gur A, Cevik R, Nas K, Colpan L, Sarac S. Cortisol and hypothalamic-pituitary-gonadal axis hormones in follicular-phase women with fibromyalgia and chronic fatigue syndrome and effect of depressive symptoms on these hormones. *Arthritis Res Ther.* 2004;6(3):R232-8.
- 62 Jerjes WK, Cleare AJ, Wessely S, Wood PJ, Taylor NF. Diurnal patterns of salivary cortisol and cortisone output in chronic fatigue syndrome. *J Affect Disord.* 2005 Aug;87(2-3):299-304.
- 63 Strickland P, Morriss R, Wearden A, Deakin B. A comparison of salivary cortisol in chronic fatigue syndrome, community depression and healthy controls. *J Affect Disord.* 1998 Jan;47(1-3):191-4.
- 64 Jerjes WK, Peters TJ, Taylor NF, Wood PJ, Wessely S, Cleare AJ. Diurnal excretion of urinary cortisol, cortisone, and cortisol metabolites in chronic fatigue syndrome. *J Psychosom Res.* 2006 Feb;60(2):145-53.
- 65 McBeth J, Chiu YH, Silman AJ, Ray D, Morriss R, Dickens C, Gupta A, Macfarlane GJ. Hypothalamic-pituitary-adrenal stress axis function and the relationship with chronic widespread pain and its antecedents. *Arthritis Res Ther.* 2005;7(5):R992-R1000.
- 66 Gur A, Cevik R, Nas K, Colpan L, Sarac S. Cortisol and hypothalamic-pituitary-gonadal axis hormones in follicular-phase women with fibromyalgia and chronic fatigue syndrome and effect of depressive symptoms on these hormones. *Arthritis Res Ther.* 2004;6(3):R232-8.
- 67 Gur A, Cevik R, Sarac AJ, Colpan L, Em S. Hypothalamic-pituitary-gonadal axis and cortisol in young women with primary fibromyalgia: the potential roles of depression, fatigue, and sleep disturbance in the occurrence of hypocortisolism. *Ann Rheum Dis.* 2004 Nov;63(11):1504-6.
- 68 Heim C, Ehler U, Hellhammer DH. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology.* 2000 Jan;25(1):1-35.
- 69 Yehuda R, Southwick SM, Nussbaum G, Wahby V, Giller EL Jr, Mason JW. Low urinary cortisol excretion in patients with posttraumatic stress disorder. *J Nerv Ment Dis.* 1990 Jun;178(6):366-9.
- 70 Gill J, Vythilingam M, Page GG. Low cortisol, high DHEA, and high levels of stimulated TNF-alpha, and IL-6 in women with PTSD. *J Trauma Stress.* 2008 Dec;21(6):530-9.
- 71 Morris MC, Compas BE, Garber J. Relations among posttraumatic stress disorder, comorbid major depression, and HPA function: a systematic review and meta-analysis. *Clin Psychol Rev.* 2012 Jun;26(4):301-15.
- 72 Stewart JW, Quitkin FM, McGrath PJ, Klein DF. Defining the boundaries of atypical depression: evidence from the HPA axis supports course of illness distinctions. *J Affect Disord.* 2005 Jun;86(2-3):161-7.
- 73 Levitan RD, Vaccarino FJ, Brown GM, Kennedy SH. Low-dose dexamethasone challenge in women with atypical major depression: pilot study. *J Psychiatry Neurosci.* 2002 Jan;27(1):47-51.
- 74 Johnson EO, Kostandi M, Moutsopoulos HM. Hypothalamic-pituitary-adrenal axis function in Sjögren's syndrome: mechanisms of neuroendocrine and immune system homeostasis. *Ann N Y Acad Sci.* 2006 Nov;1088:41-51.
- 75 Cutolo M, Sulli A, Pizzorni C, Secchi ME, Soldano S, Seriola B, Straub RH, Otsa K, Maestroni GJ. Circadian rhythms: glucocorticoids and arthritis. *Ann N Y Acad Sci.* 2006 Jun;1069:289-99.
- 76 Demir H, Tanriverdi F, Ozoğul N, Caliş M, Kirnap M, Durak AC, Keleştimur F. Evaluation of the hypothalamic-pituitary-adrenal axis in untreated patients with polymyalgia rheumatica and healthy controls. *Scand J Rheum.* 2006 May-Jun;35(3):217-23.
- 77 Kebapçılar L, Bilgir O, Alacacioglu A, Yildiz Y, Taylan A, Gunaydin R, Yuksel A, Karaca B, Sari I. Impaired hypothalamo-pituitary-adrenal axis in patients with ankylosing spondylitis. *J Endocrinol Invest.* 2010 Jan;33(1):42-7.
- 78 Gudbjornsson B, Skogseid B, Oberg K, Wide L, Hallgren R. Intact adrenocorticotrophic hormone secretion but impaired cortisol response in patients with active rheumatoid arthritis. Effect of glucocorticoids. *J Rheumatol.* 1996 Apr;23(4):596-602.

-
- 79 Chikanza IC, Petrou P, Kingsley G, Chrousos G, Panayi GS. Defective hypothalamic response to immune and inflammatory stimuli in patients with rheumatoid arthritis. *Arthritis Rheum.* 1992 Nov;35(11):1281-8.
- 80 Raison CL, Miller AH. When not enough is too much: the role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. *Am J Psychiatry.* 2003 Sep;160(9):1554-65.
- 81 Pariante CM, Thomas SA, Lovestone S, Makoff A, Kerwin RW. Do antidepressants regulate how cortisol affects the brain? *Psychoneuroendocrinology.* 2004 May;29(4):423-47.
- 82 McGinn LK, Asnis GM, Rubinson E., Biological and clinical validation of atypical depression. *Psych Res.* 1996 Mar 29;60(2-3):191-8.
- 83 Kier A, Han J, Jacobson L. Chronic treatment with the monoamine oxidase inhibitor phenelzine increases hypothalamic-pituitary-adrenocortical activity in male C57BL/6 mice: relevance to atypical depression. *Endocrinology.* 2005 Mar;146(3):1338-47.
- 84 Sagud M, Pivac N, Muck-Seler D, Jakovljevic M, Mihaljevic-Peles A, Korsic M. Effects of sertraline treatment on plasma cortisol, prolactin and thyroid hormones in female depressed patients. *Neuropsychobiology.* 2002;45(3):139-43.
- 85 Ahrens T, Frankhauser P, Lederbogen F, Deuschle M. Effect of single-dose sertraline on the hypothalamus-pituitary-adrenal system, autonomic nervous system, and platelet function. *J Clin Psychopharmacol.* 2007 Dec;27(6):602-6.
- 86 Schlösser R, Wetzel H, Dörr H, Rossbach W, Hiemke C, Benkert O. Effects of subchronic paroxetine administration on night-time endocrinological profiles in healthy male volunteers. *Psychoneuroendocrinology.* 2000 May;25(4):377-88.
- 87 Hawken ER, Owen JA, Hudson RW, Delva NJ. Specific effects of escitalopram on neuroendocrine response. *Psychopharmacology (Berl).* 2009 Nov;207(1):27-34.
- 88 Briscoe VJ, Ertl AC, Tate DB, Dawling S, Davis SN. Effects of a selective serotonin reuptake inhibitor, fluoxetine, on counterregulatory responses to hypoglycemia in healthy individuals. *Diabetes.* 2008 Sep;57(9):2453-60.
- 89 Garde AH, Persson R, Hansen AM, Osterberg K, Orbaek P, Eek F, Karlson B. Effects of lifestyle factors on concentrations of salivary cortisol in healthy individuals. *Scand J Clin Lab Invest.* 2008 Nov 4:1-9.
- 90 Mendelson JH, Sholar MB, Goletiani N, Siegel AJ, Mello NK. Effects of low- and high-nicotine cigarette smoking on mood states and the HPA axis in men. *Neuropsychopharmacology.* 2005 Sep;30(9):1751-63.
- 91 Wilkins JN, Carlson HE, Van Vunakis H, Hill MA, Gritz E, Jarvik ME. Nicotine from cigarette smoking increases circulating levels of cortisol, growth hormone, and prolactin in male chronic smokers. *Psychopharmacology (Berl).* 1982;78(4):305-8.
- 92 Lovallo WR, Al'Absi M, Blick K, Whitsett TL, Wilson MF. Stress-like adrenocorticotropin responses to caffeine in young healthy men. *Pharmacol Biochem Behav.* 1996 Nov;55(3):365-9.
- 93 Cone EJ, Johnson RE, Moore JD, Roache JD. Acute effects of smoking marijuana on hormones, subjective effects and performance in male human subjects. *Pharmacol Biochem Behav.* 1986 Jun;24(6):1749-54.
- 94 Murphy LL, Muñoz RM, Adrian BA, Villanúa MA. Function of cannabinoid receptors in the neuroendocrine regulation of hormone secretion. *Neurobiol Dis.* 1998 Dec;5(6 Pt B):432-46.
- 95 Ranganathan M, Braley G, Pittman B, Cooper T, Perry E, Krystal J, D'Souza DC. The effects of cannabinoids on serum cortisol and prolactin in humans. *Psychopharmacology (Berl).* 2009 May;203(4):737-44.
- 96 Parrott AC, Lock J, Conner AC, Kissling C, Thome J. Dance clubbing on MDMA and during abstinence from Ecstasy/MDMA: prospective neuroendocrine and psychobiological changes. *Neuropsychobiology.* 2008;57(4):165-80.
- 97 Harris DS, Baggott M, Mendelson JH, Mendelson JE, Jones RT. Subjective and hormonal effects of 3,4-methylenedioxymethamphetamine (MDMA) in humans. *Psychopharmacology (Berl).* 2002 Aug;162(4):396-405.
- 98 Jacobs D, Silverstone T, Rees L. The neuroendocrine response to oral dextroamphetamine in normal subjects. *Int Clin Psychopharmacol.* 1989 Apr;4(2):135-47.
- 99 Fehm HL, Holl R, Steiner K, Klein E, Voigt KH. Evidence for ACTH-unrelated mechanisms in the regulation of cortisol secretion in man. *Klin Wochenschr.* 1984 Jan 2;62(1):19-24.
- 100 Dorn LD, Lucke JF, Loucks TL, Berga SL. Salivary cortisol reflects serum cortisol: analysis of circadian profiles. *Ann Clin Biochem.* 2007 May;44(Pt 3):281-4.
- 101 Arafah BM, Nishiyama FJ, Tlaygeh H, Hejal R. Measurement of salivary cortisol concentration in the assessment of adrenal function in critically ill subjects: a surrogate marker of the circulating free cortisol. *J Clin Endocrinol Metab.* 2007 Aug;92(8):2965-71.
- 102 Laudat MH, Cerdas S, Fournier C, Guiban D, Guilhaume B, Luton JP. Salivary cortisol measurement: a practical approach to assess pituitary-adrenal function. *J Clin Endocrinol Metab.* 1988 Feb;66(2):343-8.
- 103 Gozansky WS, Lynn JS, Laudenslager ML, Kohrt WM. Salivary cortisol determined by enzyme immunoassay is preferable to serum total cortisol for assessment of dynamic hypothalamic-pituitary-adrenal axis activity. *Clin Endocrinol (Oxf).* 2005 Sep;63(3):336-41.
- 104 Vining RF, McGinley RA, Maksvytis JJ, Ho KY. Salivary cortisol: a better measure of adrenal cortical function than serum cortisol. *Ann Clin Biochem.* 1983 Nov;20 (Pt 6):329-35.
- 105 Umeda T, Hiramatsu R, Iwaoka T, Shimada T, Miura F, Sato T. Use of saliva for monitoring unbound free cortisol levels in serum. *Clin Chim Acta.* 1981 Mar 5;110(2-3):245-53.
- 106 Restituto P, Galofré JC, Gil MJ, Mugueta C, Santos S, Monreal JJ, Varo N. Advantage of salivary cortisol measurements in the diagnosis of glucocorticoid related disorders. *Clin Biochem.* 2008 Jun;41(9):688-92.
- 107 Løvås K, Husebye ES. [Salivary cortisol in adrenal diseases] *Tidsskr Nor Laegeforen.* 2007 Mar 15;127(6):730-2.
- 108 Deutschbein T, Unger N, Mann K, Petersenn S. Diagnosis of Secondary Adrenal Insufficiency: Unstimulated Early Morning Cortisol in Saliva and Serum in Comparison with the Insulin Tolerance Test. *Horm Metab Res* 2009 Nov;41(11):834-9.
- 109 Marcus-Perlman Y, Tordjman K, Greenman Y, Limor R, Shenkerman G, Osher E, Stern N. Low-dose ACTH (1 microg) salivary test: a potential alternative to the classical blood test. *Clin Endocrinol (Oxf).* 2006 Feb;64(2):215-8.
- 110 Raff H. Utility of Salivary Cortisol Measurements in Cushing's Syndrome and Adrenal Insufficiency. *J Clin Endocrinol Metab.* 2009 Oct;94(10):3647-55.
- 111 Weibel L, Follenius M, Spiegel K, Ehrhart J, Brandenberger G. Comparative effect of night and daytime sleep on the 24-hour cortisol secretory profile. *Sleep.* 1995 Sep;18(7):549-56
- 112 Leproult R, Colecchia EF, L'Hermite-Baleriaux M, Van Cauter E. Transition from dim to bright light in the morning induces an immediate elevation of cortisol levels. *J Clin Endocrinol Metab.* 2001 Jan;86(1):151-7.
- 113 Wener, R.E., Evans, G.W., The Impact of Mode and Mode Transfer on Commuter Stress, The Montclair Connection Final Report June,2004, <http://www.utrc2.org/sites/default/files/pubs/Impact-of-Mode-%26-Mode-Transfer-on-Commuter-Stress-Montclair-Connection.pdf>
- 114 Nelson N, Arbring K, Theodorsson E. Neonatal salivary cortisol in response to heelstick: method modifications enable analysis of low concentrations and small sample volumes. *Scand J Clin Lab Invest.* 2001 Jul;61(4):287-91.
- 115 Al-Aridi R, Abdelmannan D, Arafah BM. Biochemical Diagnosis of Adrenal Insufficiency: The added Value of Dehydroepiandrosterone Sulfate (DHEA-S) Measurements. *Endocr Pract.* 2010 Dec 6:1-32.

-
- 116 Greenfield JR, Samaras K. Evaluation of pituitary function in the fatigued patient: a review of 59 cases. *Eur J Endocrinol.* 2006 Jan;154(1):147-57.
- 117 Reimondo G, Bovio S, Allasino B, Terzolo M, Angeli A. Secondary hypoadrenalism. *Pituitary.* 2008;11(2):147-54.
- 118 Streeten DH, Anderson GH Jr, Bonaventura MM. The potential for serious consequences from misinterpreting normal responses to the rapid adrenocorticotropin test. *J Clin Endocrinol Metab.* 1996 Jan;81(1):285-90.
- 119 Oki K, Yamane K, Yoneda M, Nojima H, Watanabe H, Kohno N. A Case of Addison's Disease Confirmed with Low Dose Cosyntropin Stimulation Test. *Endocr J.* 2007 Dec;54(5):765-9.
- 120 Labrie F, Luu-The V, Bélanger A, Lin SX, Simard J, Pelletier G, Labrie C. Is dehydroepiandrosterone a hormone? *J Endocrinol.* 2005 Nov;187(2):169-96.
- 121 Yamaji T, Ishibashi M, Takaku F, Itabashi A, Katayama S, Ishii J. Serum dehydroepiandrosterone sulfate concentrations in secondary adrenal insufficiency. *J Clin Endocrinol Metab.* 1987 Sep;65(3):448-51.
- 122 Al-Aridi R, Abdelmannan D, Arafah BM. Biochemical Diagnosis of Adrenal Insufficiency: The added Value of Dehydroepiandrosterone Sulfate (DHEA-S) Measurements. *Endocr Pract.* 2010 Dec 6:1-32.
- 123 Ibid.
- 124 Robinzon B, Cutolo M. Should dehydroepiandrosterone replacement therapy be provided with glucocorticoids? *Rheumatology (Oxford).* 1999 Jun;38(6):488-95.
- 125 Hodis HN, Mack WJ, Lobo RA, Shoupe D, Sevanian A, Mahrer PR, Selzer RH, Liu Cr CR, Liu Ch CH, Azen SP; Estrogen in the Prevention of Atherosclerosis Trial Research Group. Estrogen in the prevention of atherosclerosis. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med.* 2001 Dec 4;135(11):939-53.
- 126 Heart, stroke and vascular diseases, Australian facts 2004, <http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=6442454948>, p.27
- 127 Mack WJ, Slater CC, Xiang M, Shoupe D, Lobo RA, Hodis HN. Elevated subclinical atherosclerosis associated with oophorectomy is related to time since menopause rather than type of menopause. *Fertil Steril.* 2004 Aug;82(2):391-7.
- 128 Mendelsohn ME. Protective effects of estrogen on the cardiovascular system. *Am J Cardiol.* 2002 Jun 20;89(12A):12E-17E; discussion 17E-18E.
- 129 Zandi PP, Carlson MC, Plassman BL, Welsh-Bohmer KA, Mayer LS, Steffens DC, Breitner JC; Cache County Memory Study Investigators. Hormone replacement therapy and incidence of Alzheimer disease in older women: the Cache County Study. *JAMA.* 2002 Nov 6;288(17):2123-9.
- 130 Kawas C, Resnick S, Morrison A, et al. A prospective study of estrogen replacement therapy and the risk of developing Alzheimer's disease: The Baltimore Longitudinal Study of Aging. *Neurology* 1997;48:1517-1521.
- 131 Paganini-Hill A, Henderson VW. Estrogen replacement therapy and risk of Alzheimer's disease. *Arch Intern Med* 1996;156:2213-2217.
- 132 The Necessity and Safety of Bioidentical Sex Steroid Replacement in Women, <http://hormonerestoration.com/files/AUBOB.pdf>
- 133 Simon J. Lies, damn lies and statistics: a jaundiced view of the Women's Health Initiative (WHI) and where we are with hormone therapy (HT) and estrogen therapy (ET) today. *Climacteric* 2005;8(Suppl 2):1-2
- 134 Canonico M, Oger E, Plu-Bureau G, Conard J, Meyer G, Levesque H, Trillot N, Barrellier MT, Wahl D, Emmerich J, Scarabin PY; Estrogen and Thromboembolism Risk (ESTHER) Study Group. Hormone therapy and venous thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study. *Circulation.* 2007 Feb 20;115(7):840-5.
- 135 Canonico M, Plu-Bureau G, Lowe GD, Scarabin PY. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. *BMJ.* 2008 May 31;336(7655):1227-31.
- 136 Campagnoli C, Clavel-Chapelon F, Kaaks R, Peris C, Berrino F. Progestins and progesterone in hormone replacement therapy and the risk of breast cancer. *J Steroid Biochem Mol Biol.* 2005 Jul;96(2):95-108.
- 137 de Lignières B, de Vathaire F, Fournier S, Urbinelli R, Allaert F, Le MG, Kuttent F. Combined hormone replacement therapy and risk of breast cancer in a French cohort study of 3175 women. *Climacteric.* 2002 Dec;5(4):332-40.
- 138 L'hermite M, Simoncini T, Fuller S, Genazzani AR. Could transdermal estradiol + progesterone be a safer postmenopausal HRT? A review. *Maturitas.* 2008 Jul-Aug;60(3-4):185-201.
- 139 Espié M, Daures JP, Chevallier T, Mares P, Micheletti MC, De Reilhac P. Breast cancer incidence and hormone replacement therapy: results from the MISSION study, prospective phase. *Gynecol Endocrinol.* 2007 Jul;23(7):391-7.
- 140 Hoffling M, Hirschberg A, Skoog L, B Von Schoultz B. Testosterone addition may inhibit estrogen-progestogen induced breast cell proliferation. *Climacteric* 2005;8(Suppl 2):1-2
- 141 Dimitrakakis C, Zhou J, Wang J, Belanger A, LaBrie F, Cheng C, Powell D, Bondy C. A physiologic role for testosterone in limiting estrogenic stimulation of the breast. *Menopause.* 2003 Jul-Aug;10(4):292-8.
- 142 Casson PR, Elkind-Hirsch KE, Buster JE, Hornsby PJ, Carson SA, Snabes MC. Effect of postmenopausal estrogen replacement on circulating androgens. *Obstet Gynecol.* 1997 Dec;90(6):995-8.
- 143 Barrett-Connor E, Young R, Notelovitz M, Sullivan J, Wiita B, Yang HM, Nolan J. A two-year, double-blind comparison of estrogen-androgen and conjugated estrogens in surgically menopausal women. Effects on bone mineral density, symptoms and lipid profiles. *J Reprod Med.* 1999 Dec;44(12):1012-20.
- 144 Davis SR, van der Mooren MJ, van Lunsen RH, Lopes P, Ribot C, Rees M, Moufarege A, Rodenberg C, Buch A, Purdie DW. Efficacy and safety of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. *Menopause.* 2006 May-Jun;13(3):387-96.
- 145 Professional Medical Associations and Their Relationships With Industry: A Proposal for Controlling Conflict of Interest," *JAMA*, April 1 <http://jama.jamanetwork.com/article.aspx?articleid=183670>
- 146 Henny J, Petitclerc C, Fuentes-Arderiu X, Petersen PH, Queraltó JM, Schiele F, Siest G. Need for revisiting the concept of reference values. *Clin Chem Lab Med.* 2000 Jul;38(7):589-95.
- 147 Fraser WD, Biggart EM, O'Reilly DS, Gray HW, McKillop JH, Thomson JA. Are biochemical tests of thyroid function of any value in monitoring patients receiving thyroxine replacement? *Br Med J (Clin Res Ed).* 1986 Sep 27;293(6550):808-10.