PE1463/C

PUBLIC PETITIONS COMMITTEE
Scottish Parliament, T3.40,
Edinburgh, EH99 1SP, Scotland

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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 dessicated 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 insensitive[110] 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 lab[113] and the needle stick[114] 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/dL[115] 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 **r**equiring 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.

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