The Diagnosis and Treatment of Thyroid and Cortisol Deficiencies
Including Hormonal Treatment of Rheumatic Diseases

Relax: this presentation is available online
Topics

- **Bioidentical** Hormones are Best
- Hormone Loss with Age
- Restorative Endocrinology
- Hypometabolism: **Thyroid** and **Cortisol** Deficiency
- **Cortisol** and **DHEA** in Rheumatic Diseases
- **Hormone D** and Fish oil
- Sex hormone replacement for Women and Men
Hormones

- Parts of our integrated neuro-endocrine-immune system
- Travel via blood to all cells
- **Control** cells’ proliferation, differentiation, protein synthesis, metabolic rate, etc.
- The most **powerful** molecules in biology
- **Optimal** levels and effects are essential for **health** and **quality of life**
Drug companies have patented ~5 to 200 variations of each molecule.
Bioidentical Hormones are not Drugs

Correct molecular structure—same action at receptors, same metabolism and elimination

Non-toxic:
- No side effects, only effects
- No interactions with drugs
- No allergic reactions

Safe and Beneficial in physiological levels/balance

Negative effects: Due to excessive dose, wrong delivery method, or imbalance with other hormones
Bioidentical Hormone Restoration is Best Medical Practice

- If a hormone is low, restore optimal levels!
  - Type 1 Diabetes: bioidentical insulin
  - Hypothyroidism: bioidentical T4 (Synthroid, Levoxyl)
  - Growth hormone deficiency: bioidentical GH
  - Adrenal insufficiency: cortisol (hydrocortisone)
  - Non-bioidenticals: Menopause, autoimmune dz, allergy

The Controversies:
- How do we diagnose deficiency?
- How do we decide which dose is right?
- What do we do about deficiencies due to aging?
What about Losses due to Aging?

DHEA ↔ DHEA-S
Thyropause

Fig. 7. Age-dependent variations in serum FT₃ concentration in healthy human subjects up to centenarians [Modified from S. Mariotti et al.: J Clin Endocrinol Metab 77:1130–1134, 1993 (147), with publisher’s permission. © The Endocrine Society.]

Fig. 8. Age-dependent variations in serum TSH concentration in healthy human subjects up to centenarians [Modified from S. Mariotti et al.: J Clin Endocrinol Metab 77:1130–1134, 1993 (147), with publisher’s permission. © The Endocrine Society.]

80% decline

TSH response to low T4 (2.7-3.2µg/dL)

Carle, Thyroid. 2007 Feb;17(2):139-44
Growth Hormone (GH)
Somatopause

Clinical Chemistry 48, No. 12, 2002
Andropause

Testosterone in Men

Baltimore Longitudinal Study of Aging (BLSA). Harman et al., 2001
Steroid Loss in Women >> Men

Men

Women

Testosterone

Progesterone average

Young
Old

Men

Women

DHEA-S 5,000,000 pg/ml
Cortisol 100,000 pg/ml

50% loss

90% Loss

Less estrogen than old men!
Common View

- Persistence of youthful levels of hormones would cause more heart attacks and cancers as we age (?)

- The loss of hormones is adaptive—helps us to live longer (?)

- Fits the Pharmaceutical Agenda: Take drugs for every symptom and disorder caused by hormone loss (!?!)


Against the Common View

- **Aging** is a natural self-destruct program that kicks in around age 25 in humans.

- Obesity, high blood pressure, diabetes, heart attacks, autoimmune diseases, and many cancers increase years after hormone deficiencies set in and occur more often in those with lower levels!

- **Aging** and the loss of hormones due to aging are both natural and bad for you!

- Studies of balanced hormone restoration show the expected youthful benefits and improvements in these disorders—and no proof of harm!!
Why Docs Don’t Get It:
Reference Range Endocrinology

“Normal” ranges are not optimal ranges!
- Include 95% of tested persons of same decade in age
- Subjects not screened for symptoms of hormone deficiency
- Only some are diagnostic ranges (glucose, cholesterol)

Docs assume that all ranges are diagnostic!
- Male free testosterone: 35 – 155 pg/ml 5x!
- Female free testosterone: 0.0 - 2.2 pg/ml ∞!
- Thyroid - Free T4: 0.6 - 1.8 ng/dl 3x!
- AM serum cortisol 5 – 25 mcg/dl 5x!

“Normal” result → no hormonal dx/rx → drugs
Reference Range Endocrinology

For thyroid: TSH-normal **symptomatic** patients
No screening for symptoms for any hormone

Hormone effects vary continuously with concentration!

- Hormone Level
- FT4 ng/dL

- Too little
- Disease

- 95% of unscreened pop. →
  - "Everything is Normal"
  - "No Thyroid Disease"

- Too much
- Disease

"Too much" Disease
"Too little" Disease
Intelligent Endocrinology

Tighter optimal range based on non-patients, symptom-screening, and physiological research

Individualized diagnosis and treatment

Narrower FT4 range seen in non-patients

Anti-Endocrinology

- **Do not provide estradiol or estradiol with progesterone to women** with ovarian failure except to relieve symptoms, and only for 5 years or until the usual age of menopause.¹

- **Do not to provide any testosterone to women**, no matter how low their levels or what symptoms they have, except temporarily for the purpose of improving sexual desire.²

- **Do not provide testosterone to men**, regardless of their symptoms, unless their free testosterone levels are “unequivocably low” (below the population ranges of 35-155pg/ml or 8.5-24pg/ml), on repeated testing. If low, restore the level to mid-range.³

- **Do not provide DHEA to any person** no matter how low their levels, even if low due to disease or due to physician-prescribed glucocorticoid therapy.⁴


Anti-Thyroidology

- **Do not diagnose hypothyroidism if the TSH is normal**, regardless of symptoms or signs. If the TSH is high, provide only enough inactive levothyroxine to normalize the TSH (0.5 to 4.5mIU/L), all regardless of symptoms, signs, FT4 or FT3 levels.

- **Do not diagnose central (TSH-normal) hypothyroidism** unless there is obvious disease of the hypothalamic-pituitary system and the FT4 is low. If diagnosed, provide only enough levothyroxine to raise the FT4 level into the upper half of the range, again regardless of signs, symptoms and FT3 levels.

- **Do not test for or prescribe the active thyroid hormone, T3**. If the FT3 level is low, do not treat, regardless of symptoms.

Do not provide cortisol to any person unless the AM serum cortisol is repeatedly below the reference range (5-25mcg/dL) and he/she fails an ACTH stimulation test, again regardless of symptoms.

Do not provide growth hormone to any adult unless the IGF-1 is repeatedly below the reference range (e.g. 80-200mcg/dL) and the person fails not one but two stimulation tests, again regardless of symptoms or signs.


New Paradigm: Restorative Endocrinology

- Endocrine glands and hypothalamic-pituitary control systems deteriorate with age.

- Our bodies cease to regulate our hormones for optimal health.

- Partial hormone deficiencies are harmful.

- The restoration of youthful/optimal and hormone levels is:
  - Essential to preventative medicine
  - Essential to the treatment of all disease
  - Essential to our quality of Life!
Fatigue, Depression, Pain
Thyroid and Cortisol Deficiencies

- Thyroid sets throttle, cortisol delivers the fuel.
- Thyroid determines **metabolic rate** in every tissue.
- Lack of either leads to hypometabolism.
- Health and quality of life require **optimal** levels of both!
- Conventional tests and ranges are insensitive.
- Irrational fear of thyroid and cortisol supplementation
- Underdiagnosed, undertreated—Docs prescribe **pharmaceuticals** instead (SSRIs, amphetamines, anti-seizure drugs, anti-psychotics, sedatives, etc.)
Hypothyroidism

- Mental fog, poor concentration, depression
- Fatigue, need for excessive sleep
- Cold extremities, always feels cold
- Aches and pains
- Hair loss; dry, coarse scalp hair
- Weight gain
- Constipation
- Ankle swelling, facial puffiness
- High cholesterol, increased atherosclerosis
Diagnosing Hypothyroidism

**First:** symptoms and physical signs (high cholest., low pulse)

**Second:** relatively low free $T_4$ and free $T_3$ levels—even if within the laboratory reference range (“normal”)
- Laboratory FT4 reference range 0.8 to 1.8 ng/dL, FT3 2.0 to 4.4 pg/ml
- **Non-patient** FT4 reference range 1.0 to 1.7 ng/dL, FT3 2.5 to 4.3 pg/ml

**Third:** TSH level—indirect, fallible test, useful only to determine the cause of hypothyroidism.

Ultimate Proof of Diagnosis: Favorable response to therapeutic trial of T4/T3 thyroid optimization

Pharmaceutical medicine relies on TSH only—has it backwards!
Normal TSH—No Correlation with FT4

TSH-normal FT4 values: 3 to 29!

Untreated inpatients and outpatients referred for evaluation of thyroid disorders
Restorative Thyroidology

“Standard” Treatment: Inactive T₄ (Levoxyl, Synthroid) to “normalize” the TSH level.

Inadequate, resulting in lower free T₃ levels, persistence of symptoms

Give T₄ plus T₃ (NDT or levothyroxine+liothyronine)

Adjust dose according to symptoms and free T₄ and free T₃ levels.

The TSH tst is USELESS for both diagnosis or treatment!

Cortisol

- Foundation of the hormonal system—all other major hormones counteract cortisol

- Our body’s natural “steroid”—anti-inflammatory

- **We need** more cortisol with **stress, inflammation, and disease.**

- **Too much**—Diabetes, HTN, belly fat, osteoporosis

- **Too little**—fatigue, depression, aches & pains, anxiety, hypoglycemia, insomnia, inflammation

- Modulates the immune system—prevents and controls **allergies** and **autoimmune diseases**
Cortisol Deficiency

- Fatigue—“Adrenal Fatigue”
- Depression
- Aches & pains
- Anxiety, irritability
- Can’t cope with stress or exertion
- Insomnia—frequent awakening
- Severe PMS, PMDD
- Hypoglycemia
- Allergies, autoimmune diseases

Marked Variability: good days, bad days
Cortisol Deficiency

- Serum cortisol and ACTH stimulation tests are insensitive.

- Clue: Feels much better on prednisone, often needs steroids for allergies, illnesses, etc.

- Should be assumed in anyone whose condition improves with glucocorticoids ("steroids")—they are altered cortisol molecules.

- Unrecognized: Docs only know Addison’s Disease (near total adrenal gland failure).
Diagnosis of Cortisol Deficiency

**Symptoms** and low saliva cortisol levels, often low DHEAS

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**Testosterone, Free and Total**

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<td>Free Testosterone (Direct)</td>
<td>&lt;0.2</td>
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<td>pg/mL</td>
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**DHEA-Sulfate**

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**Cortisol**

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<td>Cortisol PM 2.3 - 11.9</td>
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Cortisol Restoration

- Use hydrocortisone (cortisol), 2-4 doses /day
- Dose must be adjusted by symptoms. (usually 10 to 50mg/day)
- Safe in physiological doses and balance with other hormones
- Cortisol replacement suppresses DHEA levels, must replace to prevent bone loss, increased blood sugar, muscle weakness, easy bruising, etc.
- Must maintain thyroid/cortisol balance.
- Must optimize sex hormones

See Dr. William Jeffries' Safe Uses of Cortisol
DHEA:  
The Other Adrenal Hormone

- Most abundant steroid hormone; yet ignored
- Cells make testosterone and estradiol from it
- Levels decline with age, stress and disease
- Lower levels assoc. with \(\uparrow\) disease, \(\uparrow\) mortality
- Balances and counteracts cortisol’s effects
- Reduces pain and inflammation
- Improves immune system function
- Improves fertility and sexual function in women
DHEA Restoration

- **Improves** blood sugar control, **lowers** insulin levels, and **counteracts** negative effects of diabetes
  

- **25mg/day improves mood, fatigue and joint pain in elderly men.**
  

- **Improves sexuality in postmenopausal women.**
  

- **Alleviates depression**
  

- **Reduces pain—restores natural endorphins**
  
DHEA Replacement

- Best taken sublingually 1-2x/day
- Life Extension dissolve-in-the-mouth 25mg tablets (www.lef.org)
- 12.5-25mg/day for women
- 25 to 50mg/day for men.
- Women may experience pimples, oily skin initially
- Start with low dose and work up gradually
Rheumatic Diseases

- **Autoimmune**—the body attacks its own tissues as if they are foreign invaders.

- Excessive **inflammation** in various tissues

- The body needs higher-than-normal **cortisol** levels to combat inflammation, reduce immune hyperactivity, and control the disease.
Adrenal Hormones and Rheumatic Diseases

**Rheumatic diseases assoc. with ↓HPA activity, lower cortisol levels, and relative adrenal insufficiency**


**Cortisol receptor isoforms and polymorphisms assoc. with autoimmune disease.**


**Low DHEAS found years before onset of RA, and in all rheumatic diseases.**


**Stress is a trigger of autoimmune disease.**


**Low cortisol levels in fibromyalgia, chronic pain.**

The Female Dilemma

Female/Male ratios:

- **Autoimmune:** RA 3:1, SLE 9:1, PMR 2:1, Sjögrens 18:1, Hashimotos /Graves thyroiditis 5:1, Mult. Sclerosis 3:1,
- **Non-immune:** Chronic fatigue 4:1, Depression 2:1, Anxiety 3:2, Fibromyalgia 8:1

Women make 1/2 as much cortisol as men.

Vierhapper H, Metabolism. 1998 Aug;47(8):974-6

Women release less cortisol under stress


Estradiol lowers cortisol levels and opposes cortisol throughout the body.


Anti-depressants often prescribed—they increase cortisol levels and effects.

Sagud M, Neuropsychobiology. 2002;45(3):139-43
Glucocorticoids ("Steroids")

Cortisol (hydrocortisone)

Methylprednisolone (5x) Medrol®

Dexamethasone (70x) Decadron®

Prednisone (4x)
Steroid Treatment

Docs don’t realize that glucocorticoid treatment is a form of hormone replacement.

Docs do not check cortisol levels or replace DHEA.

Prednisone ≤7.5mg, Medrol ≤6mg are replacement doses.

Low-dose prednisone (≤7.5mg/d) generally safe.

Excess steroid without DHEA → bone loss, infections, diabetes, weight gain, high blood pressure, moon face.

Hydrocortisone preferred; most benefits, least negative effects. Short-acting, long-acting tablets under development (Duocort®).
DHEA for Rheumatic Diseases

- **All patients on steroids should be given** DHEA

- **Increases** bone density with ≤10mg of prednisone
  Mease PJ,. J Rheumatol. 2005 Apr;32(4):616-21

- **Improves** mood and energy in patients on steroids
  Hunt PJ, Clin Endocrinol Metab. 2000 Dec;85(12):4650-6

- **Increases** natural killer cell number and activity

- **Reduces** inflammatory markers (IL-6, TNF-α)
  Daynes RA, J Immunol 1993 Jun 15;150(12):5219-30
DHEA for SLE

- SLE patients have very low DHEAS levels
- Prasterone® is DHEA by prescription
- Increases IL-2 and reduces SLE disease activity
  
  Petri MA, Arthritis Rheum. 2004 Sep;50(9):2858-68

- Suppresses IL-10--reduces autoantibody production in Lupus
  
  Chang DM, Ann Rheum Dis. 2004 Dec;63(12):1623-6

- Allows reduction in steroid dose.
  

- Improves well-being, sexuality, and cognition in women with Lupus or adrenal insufficiency
  
TNF-α and Adrenal Hormones

- TNF-α is an inflammatory cytokine that is elevated in autoimmune diseases.

- TNF-α suppresses cortisol and DHEAS production → more inflammation, vicious cycle.

- Higher cortisol and DHEAS levels suppress TNF-α levels.

- Anti-TNF-α drugs (Enbrel, Remicade, Humira) increase cortisol and DHEAS levels.

  Straub RH, Arthritis Rheum. 2008 Apr;58(4):976-84
  Ernestam S, J Rheumatol. 2007 Jul;34(7):1451-8
Vitamin D=Hormone D

- A powerful hormone with anti-inflammatory effects

- Vit. D levels are low in SLE patients, contributing to inflammation. Vit. D improves immune system abnormalities.
  

- Higher Vit. D levels assoc. with lower TNF-α.
  
  Peterson CA, J Inflamm (Lond). 2008 Jul 24;5:10

- Levels must be >30ng/ml for significant benefit

- Optimal levels 55-70ng/ml, usually requires 4000IU Vit. D3 daily from all sources

- D3 much more effective than D2 (pharmaceutical)
Fish Oils—Omega-3 Fatty Acids

- Decrease the production of inflammatory eicosanoids, cytokines, and reactive oxygen species.

- Reduce TNF-α levels.

- Improve SLE disease activity and have cardiovascular benefits.
  Duffy EM, J Rheumatol. 2004 Aug;31(8):1551-6

- Proven beneficial in Rheumatoid Arthritis.

- Dose: 1500 to 3000mg EPA +DHA daily

- Resveratrol lowers IL-6, TNF-α, and CRP.
  Ghanim H Clin Endocrinol Metab. 2010 Jun 9.
Sex Hormones in Autoimmune Diseases

- Low testosterone and progesterone levels seen in men and women with RA.

- Testosterone and progesterone immunosuppressive

  Wilder RL. J Rheumatol Suppl. 1996 Mar;44:10-2
  Schust DJ, Hum Reprod. 1996 May;11(5):980-5

- RA and MS improve during pregnancy (high progesterone), worsen with breast feeding (low progesterone).

- Higher testosterone levels helpful in autoimmune diseases that affect women>men

- Estrogen and testosterone beneficial in MS.

  Gold SM, Prog Brain Res. 2009;175:239-51
Not Just “Sex Hormones”

Estradiol, progesterone, testosterone and DHEA are required for the function, growth, and maintenance, of all tissues in both sexes!

- Maintain brain function and health—neurosteroids affect mood, cognition, memory, pain, etc.
- Maintain the immune system—progesterone and testosterone are mild immunosuppressants
- Maintain connective tissue: skin, hair, bone, muscle
- Improve insulin sensitivity: prevent diabetes, fatty liver
- Reduce blood pressure—improve endothelial function
- Prevent atherosclerosis (plaques in arteries)
Testosterone Restoration for Men

- Improves mood and sociability
- Restores energy and ambition
- Improves cognition, probably protects against Alzheimer’s disease
- Increases libido and sexual performance
- Increases muscle and bone mass
- Reduces abdominal fat, improves insulin sensitivity, lowers blood pressure—counteracts metabolic syndrome (Syndrome X)

Testosterone and the Heart

- **Low** testosterone levels correlate with **coronary artery disease** and **stroke**
  - Arterioscler Thromb. 1994; 14:701-706
  - Eur Heart J 2000; 21; 890–4
  - Int J Cardiol. 1998 Jan 31;63(2):161-4

- **Testosterone dilates** coronary arteries—improves angina

- **T increases** heart muscle size, strength

- **T decreases** fibrinogen levels—prevents blood clots
  - Endocr Res. 2005;31(4):335-44
Testosterone and the Prostate

- **Lower testosterone** levels increase the risk of prostate cancer.  
  J Natl Cancer Inst. 2008 Feb 6;100(3):170-83  
  Morgenthaler A, Urology 2006;68:1263-7

- **Low testosterone** associated with more aggressive prostate cancers  
  Slater S, Drugs Aging 2000 Dec;17(6):431-9

- **Testosterone** supplementation does not increase the risk of prostate cancer.  

- **Testosterone** is a prostate growth factor, but does not promote prostate cancer.

- **Prostate cancer** growth can be **temporarily** slowed only by eliminating all testosterone from the body.

Read *Testosterone for Life*, Dr. Abraham Morgentaler
Female Andropause

- Young woman’s free testosterone level is 2x her free estradiol.
- DHEAS declines with age—main source of androgen effect and 50% of circulating testosterone in women.
- Female testosterone levels decline 50% between age 20 and 45.
- Oral estrogens and birth control pills reduce free testosterone and DHEAS levels.
Women Need Testosterone

- **Improves** energy, mood, and mental function
- **Improves** sexual desire and sensation
- **Increases** muscle and tissue strength
- **Opposes** estradiol-induced breast stimulation and reduces risk of breast cancer
- **With estradiol**, increases bone density
  - J Reprod Med. 1999 Dec;44(12):1012-20
Natural Treatment of Rheumatic Diseases

- Diagnose and treat cortisol deficiency

- Hydrocortisone is safe long-term in physiologically necessary doses (20-50mg) IF given with DHEA and sex hormone restoration.

- Prednisone is the 2nd choice, may provide better anti-inflammatory effect.

- Optimize sex hormone levels in women and men

- Optimize Hormone D levels and fish oil intake

- If necessary, pharmaceuticals in consultation with your rheumatologist
For More Information

- *The Hormone Solution—Stay Younger Longer*  Thierry Hertoghe, MD
- *The Miracle of Natural Hormones*  David Brownstein, MD
- *How to Achieve Healthy Aging—Look, Live, and Feel Fantastic After 40*  Neal Rouzier, MD

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