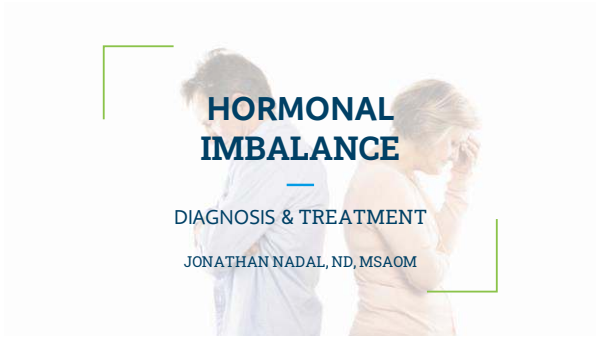


HORMONAL IMBALANCE

DIAGNOSIS & TREATMENT

JONATHAN NADAL, ND, MSAOM

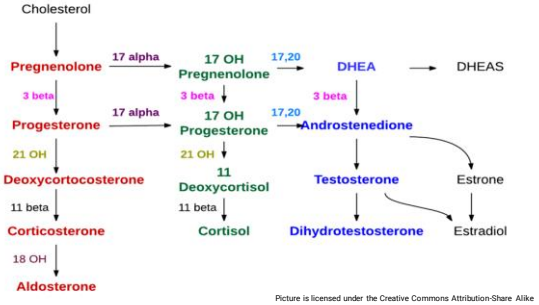
1

A review of hormones and other signaling molecules

"Cholesterol is the precursor of the five major classes of steroid hormones: progestagens, glucocorticoids, mineralocorticoids, androgens, and estrogens."

Berg JM, Tymoczko JL, Stryer L. Biochemistry. 5th edition. New York: W H Freeman; 2002. Section 26.4, Important Derivatives of Cholesterol Include Bile Salts and Steroid Hormones. Available from: https://www.ncbi.nlm.nih.gov/books/NBK22339/

2



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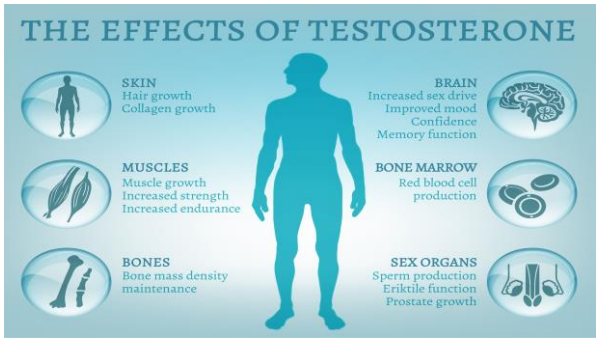

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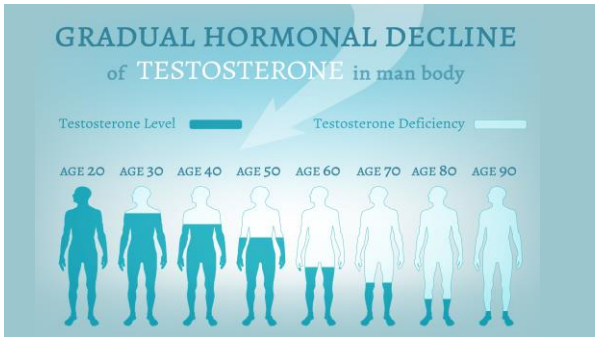


5

Symptoms of Low Testosterone in Men and Women

- Decreased energy and fatigue, decreased libido, decreased muscle mass and strength, loss of axillary and pubic hair, reduced facial hair (especially males), poor concentration and memory, depressed mood, sleep disturbance, hot flashes and sweats, increasing BMI...

6

Environmental/External Factors Causing Low Testosterone

- Xeno-estrogens: these are chemicals and toxins that have estrogen like activity in our body. There are hundreds of chemicals and medications* that are considered to be xeno-estrogens and they are common in our environment.
- Foods that increase estrogen: tofu, soy products, flax seeds, dry fruit...alcohol abuse

- Increased exposure to environmental estrogens and other environmental pollutants during fetal development and during reproductive years is suggested to be a major cause of the considerable rise in the incidence of disorders of development *and* function of the male sexual system...

Joffe M. Infertility and environmental pollutants. Br Med Bull. 2003;68:47- 70.

7

Integrative Medical Approach to Low Testosterone

Herb:

Panax ginseng (Korean ginseng)

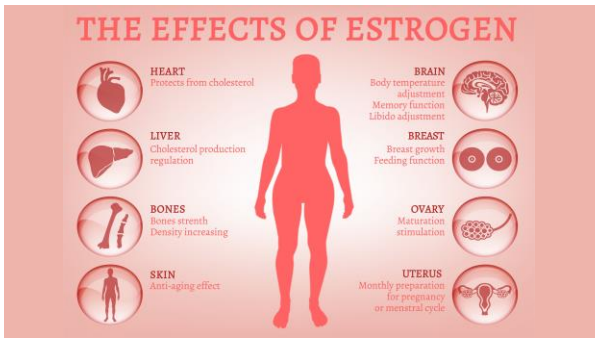
• High-quality crude ginseng root: 1.5 to 2 g/day

Nutrient:

"Zinc is perhaps the most important trace mineral for male sexual function and is found in high concentrations within the prostate and testes; particularly high amounts are also found in the semen..."

Wong WY, Thomas CM, Merkus JM, et al. Male factor subfertility: possible causes and the impact of nutritional factors. Fertil Steril. 2000;73: 435-442.

8



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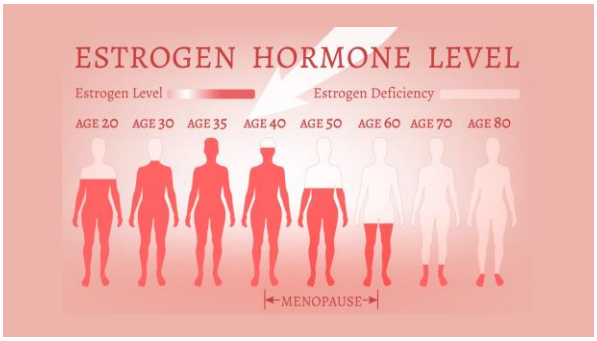


10

Symptoms of Estrogen Imbalance in Women* and Men

- *Changes in menstrual periods (frequency, duration)
- *PMS symptoms, such as breast swelling or tenderness, and bloating
- Mood swings, usually presenting as depression or anxiety
- Decreased sex drive
- Hair loss
- Thyroid imbalances
- Sleep disturbances
- Slowed metabolism and/or weight gain
- Fatigue
- Poor concentration

11

Environmental Factors (exposure or diet) on Estrogen Imbalance

- Industrial chemicals and pesticides can leach into soil and groundwater, and make their way into the food chain by building up in fish, animals, and people.
- Non-organic produce can have pesticide residues
- Some consumer products contain EDCs (endocrine disrupting chemicals) or are packaged in containers which can leach EDCs, such as household chemicals, fabrics treated with flame retardants, cosmetics, lotions, products with fragrance, and anti-bacterial soaps
- Processed foods can accumulate traces of EDCs that leach out of materials used in manufacturing, processing, transportation, and storage
- Soy-based products contain phytoestrogens, which are chemicals produced by plants that mimic estrogen
- Household dust can contain EDCs such as lead, flame retardants, and PCBs from weathering construction material or furniture

https://www.hormone.org/your-health-and-hormones/endocrine-disrupting-chemicals-edcs

12

Integrative Medical Approach to Low Estrogen

Herb: ***Cimicifuga racemosa (Black Cohosh)***
Modern clinical applications focus heavily on mitigating menopausal complaints
and regulating the estrogen cascade.
Shahin A, Ismail A, Zahran K, et al. Adding phytoestrogens to clomiphene induction in unexplained infertility patients. Biomed Online. 2008;16:580-588.

Nutrient: B Complex
It is imperative to take the B-group vitamins in a stable, combined formulation owing to their interrelation and interdependence in a number of key reactions in the body. Deficiencies of this group of vitamins are associated with a number of fertility problems...

13

Integrative Medical Approach to High Estrogen

Herbs to that help normalize hormones such as Vitex agnus-castus
Dante G and Facchinetti F. Herbal treatments for alleviating premenstrual symptoms: a systematic review. J Psychosom.Obstet.Gynaecol. 2011;32(1):42-51.

Seed cycling or at least consuming 2 tablespoons of flax seeds per day.

14

Progesterone

- Progesterone prepares the endometrium for the potential of pregnancy after ovulation. It triggers the lining to thicken to accept a fertilized egg. It also prohibits the muscle contractions in the uterus that would cause the body to reject an egg.
- Women's ovaries begin producing decreasing amounts of estrogen and progesterone around 50 years of age. Then the pituitary gland attempts to compensate by producing more follicle stimulating hormone (FSH).

- Hormone Health Network."Progesterone | Endocrine Society." Hormone.org, Endocrine Society, 27 May 2020, https://www.hormone.org/your-health-and-hormones/glands-and-hormones-a-to-z/hormones/progesterone

15

Symptoms of Progesterone Imbalance in Women and Men

- For women: abdominal pain, breast soreness, spotting between periods, vaginal dryness, depression/anxiety/mood swings, low libido, low blood sugar, headaches or migraines
- For men: erectile dysfunction, muscle loss, fatigue, memory loss or trouble concentrating

16

Integrative Medical Approach to Low Progesterone

Nutrients

Vitamin B6:

Administration of vitamin B6 at doses of 200-800 mg/day reduces blood estrogen, increases ***progesterone*** and results in improved symptoms under double-blind conditions.

Zinc:

Zince helps the pituitary gland to release follicle-stimulating hormone. This encourages ovulation and tells your ovaries to produce more progesterone, in case you become pregnant each month.

17

Environmental Factors (exposure or diet) on Progesterone Imbalance

Progesterone is a natural hormone, usually excreted in higher concentrations than estrogens, and has been detected in aqueous environments.

It is typically transformed during wastewater treatment processes and in the environment. However, minor modifications to the structure may result in transformation products (other classes of steroids) which still exhibit potent biological activity.

Jasper O. Ojoghoro, Abdul J. Chaudhary, Pablo Campo, John P. Sumpter, Mark D. Scrimshaw, Progesterone potentially degrades to potent androgens in surface waters, Science of The Total Environment, Volume 579, 2017, Pages 1876-1884

18

DHEA vs DHEA-S

DHEA-S represents the more stable index of adrenocortical activity and stress accumulated over time, whereas DHEA may better reflect the response to acute stressors. By measuring DHEA-S, it is easier to gain an understanding of the body's systemic biological reservoir of DHEA.

Kamin HS, Kertes DA: Cortisol and DHEA in Development and Psychopathology. Horm Behav 2016.
Starka L, Duskova M, Hill M: Dehydroepiandrosterone: a neuroactive steroid. J Steroid Biochem Mol Biol 2015;145:254-260.

19

Symptoms of Low DHEA in Men and Women

- **Fatigue**
- **Decreased stamina**
- **Foggy thinking**
- **Decreased muscle size**
- **Rapid aging**
- **Decreased libido**

20

Diet and Low DHEA

It is common for a lot of our patients with reactive hypoglycemia to have *some functional hypoadrenalism (ie, adrenal fatigue as apposed to true adrenalcortical insufficiency)*. These patients might benefit from eating smaller, more frequent meals and avoiding refined carbohydrates, caffeine, and alcohol.

21

Supplementing with DHEA

Considerations for dosage:

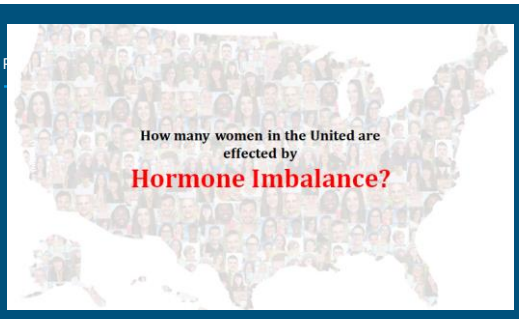
5-15 mg /day for women and 10-20 mg/day for men. Although some clinical trials have used much higher...

"In both sexes, a 100 mg daily dose of DHEA restored serum DHEA levels to those of young adults and serum DS to levels at or slightly above the young adult range."

Morales AJ, Haubrich RH, Hwang JY, Asakura H, Yen SS. The effect of six months treatment with a 100 mg daily dose of dehydroepiandrosterone (DHEA) on circulating sex steroids, body composition and muscle strength in age-advanced men and women. *Clin Endocrinol (Oxf)*. 1998;49(4):421-432.

Herbs: *Licorice root*, *Eleutherococcus senticosus (Siberian ginseng)*

22



23

24

What is the problem with

Hormone Imbalance?

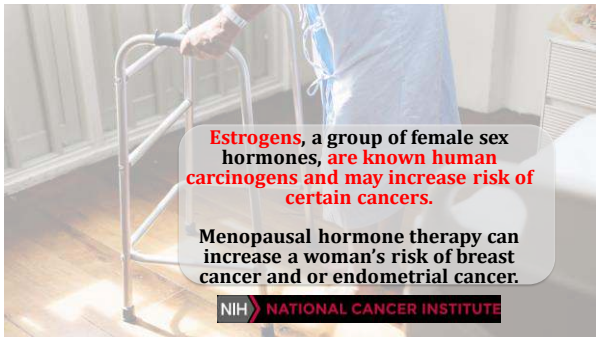
25

What is the problem with

Hormone Imbalance?

- **unexplained weight gain or weight loss**
- unexplained or excessive sweating
- **difficulty sleeping**
- changes in sensitivity to cold and heat
- very dry skin or skin rashes
- changes in blood pressure
- changes in heart rate
- brittle or weak bones
- changes in blood sugar concentration
- **irritability and anxiety**
- **unexplained and long-term fatigue**
- increased thirst
- **depression**
- **headaches**

26



27

28

Hormone imbalance can also increase your risk for diabetes.

29

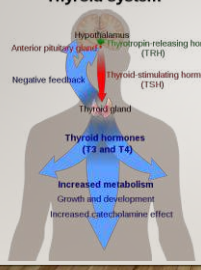
American Diabetes Association.

Every day, 3,835 people are diagnosed with diabetes type 2 in the U.S alone.

30

Lose Weight:
How Healthy Thyroid Can Lead to Healthy Weight!

31



TSH = Thyroid stimulating Hormone

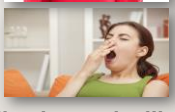
T4 = Majority of the thyroid hormone

T3 = the 'Active' Thyroid hormone!

Most doctors only check for TSH, T3, and T4.

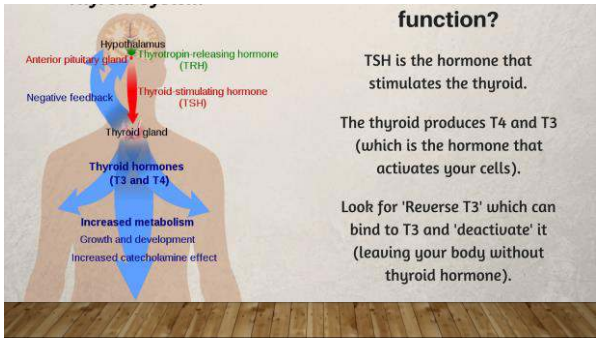
33






Patients take medication and still suffer from symptoms. Why?

34

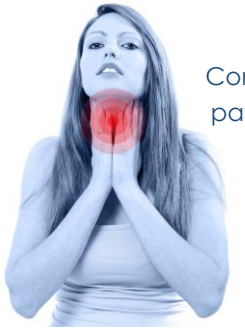


35

Diagnosis of Thyroid Conditions: What to Test?

Is TSH, T3, and T4 enough?

36



Considerations in evaluating patients in clinical practice.

37

A study published at the Department of Medicine of University of California, found that **normal levels of TSH may not be correlating with normal levels of T3.**

Levels of T3 might be lower in patients with normal TSH.

Woeber, K. A. (2002). Levothyroxine therapy and serum free thyroxine and free triiodothyronine concentrations. Journal of Endocrinological Investigation, 25(2), 106-109. doi:10.1007/bf03343972

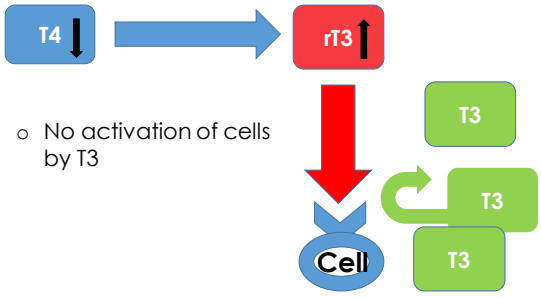
38

Reverse T3: A Strong 'Anti-T3 Hormone'

rT3 is not just an inactive metabolite, it is also **a powerful inhibitor of the conversion of T4 to T3.**

Chopra, I. J. (1977). A Study of Extrathyroidal Conversion of Thyroxine (T4) to 3,3',5-Triiodothyronine (T3) in Vitro*. Endocrinology, 101(2), 453-463. doi:10.1210/endo-101-2-453

39



- No activation of cells by T3

40

- Stress
- Trauma
- Low-calorie diet
  Inflammation
- Toxins
- Infections
- Liver/kidney dysfunction

Jones, D. (2010). Textbook of functional medicine. Gig Harbor, WA: Institute for Functional Medicine.

41

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42

- Stress
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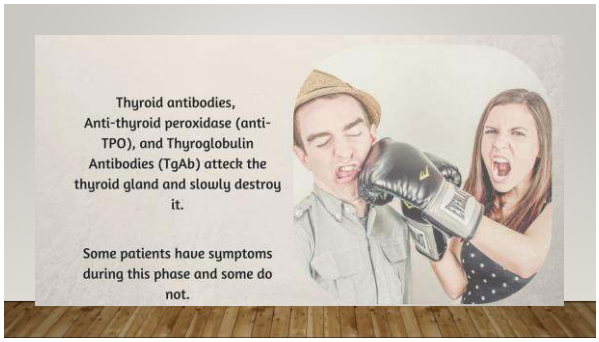
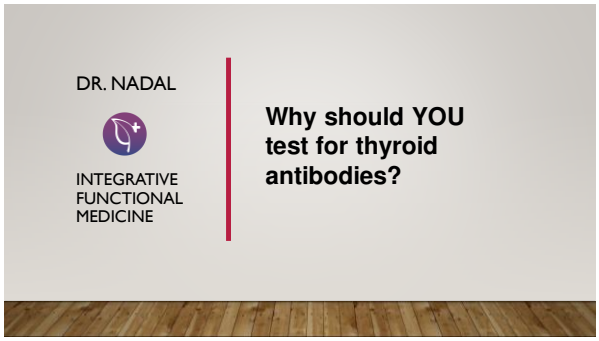
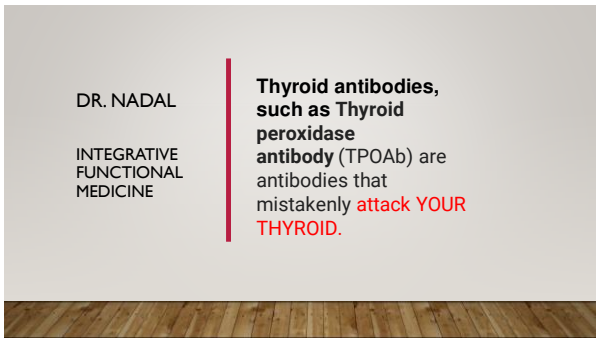
43


Thyroid antibodies, Anti-thyroid peroxidase (anti-TPO), and Thyroglobulin Antibodies (TgAb) atteck the thyroid gland and slowly destroy it.
Some patients have symptoms during this phase and some do not.

44


DR. NADAL
INTEGRATIVE FUNCTIONAL MEDICINE
Why should YOU test for thyroid antibodies?

45


DR. NADAL
INTEGRATIVE FUNCTIONAL MEDICINE
Thyroid antibodies, such as Thyroid peroxidase antibody (TPOAb) are antibodies that mistakenly attack YOUR THYROID.

46

Why should you test for thyroid antibodies?

A study that evaluate 426 women who complained of thyroid symptoms:

- dry hair
- chronic fatigue or "becoming easily fatigued"
- chronic weakness
- Dysphagia*
- Irritability
- Lack of concentration and chronic nervousness

They had normal TSH (mean between 1 and 2)

•TPO antibodies were highest in patients with six or more of the above symptoms

Ott J, R. Promberger, F. Kober, et al. Hashimoto's Thyroiditis Affects Symptom Load and Quality of Life Unrelated to Hypothyroidism: A prospective Case-Control Study in Women Undergoing Thyroidectomy for Benign Goiter. Thyroid. Feb 2011; 21(2):161-7.

47

Women with high TPO antibodies were and those with the highest BMI.

Ott J, R. Promberger, F. Kober, et al. Hashimoto's Thyroiditis Affects Symptom Load and Quality of Life Unrelated to Hypothyroidism: A prospective Case-Control Study in Women Undergoing Thyroidectomy for Benign Goiter. Thyroid. Feb 2011; 21(2):161-7.

48

Higher TPO antibodies were also associated with..

- Early pregnancy loss
- Breast cancer

Ott J, R. Promberger, F. Kober, et al. Hashimoto's Thyroiditis Affects Symptom Load and Quality of Life Unrelated to Hypothyroidism: A prospective Case-Control Study in Women Undergoing Thyroidectomy for Benign Goiter. Thyroid. Feb 2011; 21(2):161-7.

49

Thyroid Function in Fibromyalgia patients:

52.6% of patients had **Central** (hypothalamic or pituitary) hypothyroidism

10.5% of patients had **primary** (thyroidal) hypothyroidism

Lowe JC. Thyroid Status of 38 Fibromyalgia Patients. Clinical Bulletin of Myofascial Therapy. 1996;2(1):47-64. doi:10.1300/j425v02n01_07.

50

Fibromyalgia patients with 'normal' thyroid labs received a hypothyroid treatment and showed significant improvement in symptoms.

John C. Lowe MA, DC, Richard L. Garrison MD, Alan Reichman MD, Jackie Yellin BA. (1997) Triiodothyronine (T3) Treatment of Euthyroid Fibromyalgia. Clinical Bulletin of Myofascial Therapy 2:4, pages 71-88.

51

Cognitive function
&
Subclinical
Hypothyroidism

Should you treat?

52

Studies on subclinical hypothyroidism and cognitive function are contradicting. Some studies show improvement[1] with levothyroxine (T4) and some did not.[2]

1. Correia N , Mullally S , Cooke G , Tun TK , Phelan N , Feeney J , Fitzgibbon M , Boran G , O'Mara S , Gibney J 2009 Evidence for a specific defect in hippocampal memory in overt and subclinical hypothyroidism. J Clin Endocrinol Metab 94:3789–3797
2. Jorde R , Waterloo K , Storhaug H , Nyrnes A , Sundsfjord J , Jenssen TG 2006 Neuropsychological function and symptoms in subjects with subclinical hypothyroidism and the effect of thyroxine treatment. J Clin Endocrinol Metab 91:145–153

53

BRAIN
A JOURNAL OF NEUROLOGY

Patients with neuroanatomical basis for defect in working memory and subclinical hypothyroid were treated with L-T4. After 6 months working memory and fMRI results normalized.

Zhu DF , Wang ZX , Zhang DR , Pan ZL , He S , Hu XP , Chen XC , Zhou JN 2006 fMRI revealed neural substrate for reversible working memory dysfunction in subclinical hypothyroidism. Brain 129:2923–2930

54

Considerations in Treating Thyroid Imbalance

55

56

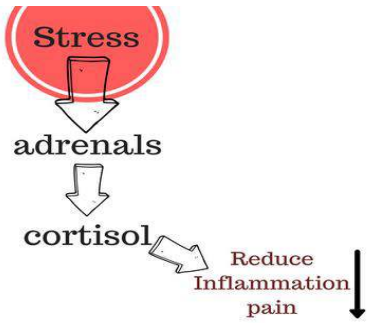
- ✓The adrenals secrete Cortisol, a powerful anti-inflammatory substance.
- ✓React to stressors like illness, injury, and even emotional or psychological stress.
- ✓Increase blood sugar.
- ✓Regulate blood pressure.
- ✓Regulating weight.

57

58


Stress
adrenals
cortisol

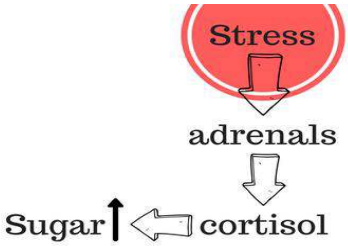
59


Stress
adrenals
cortisol
Reduce
Inflammation
pain

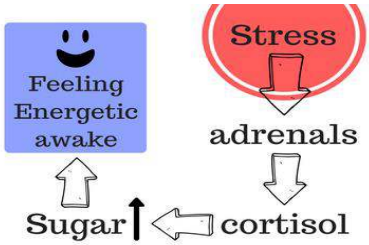
60


Stress
adrenals
cortisol

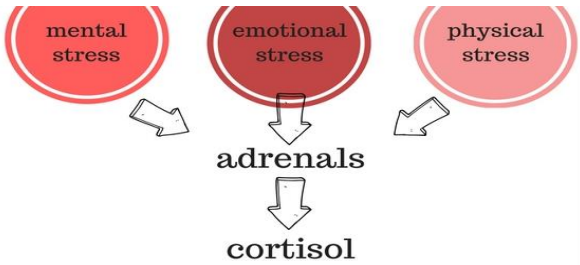
61


Stress
adrenals
Sugar
cortisol

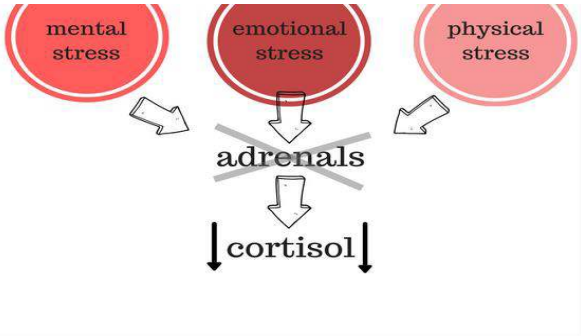
62


Feeling
Energetic
awake
Stress
adrenals
Sugar
cortisol

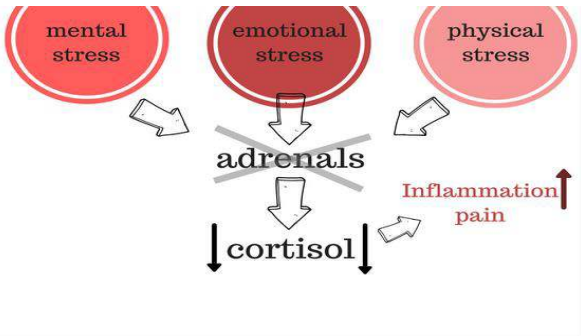
63


mental
stress
emotional
stress
physical
stress
adrenals
cortisol

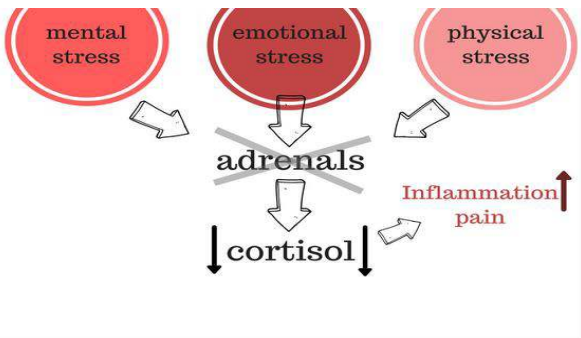
64


mental stress
emotional stress
physical stress
adrenals
cortisol

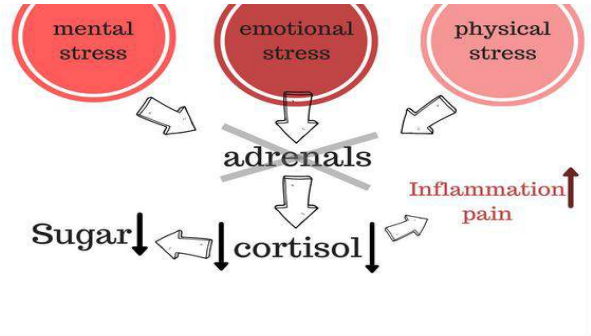
65


mental stress
emotional stress
physical stress
adrenals
Inflammation pain
cortisol

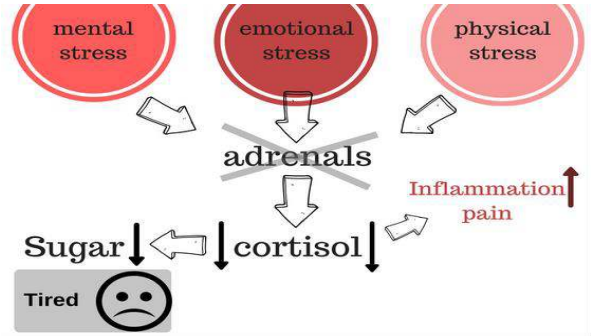
66


mental stress
emotional stress
physical stress
adrenals
Inflammation pain
cortisol

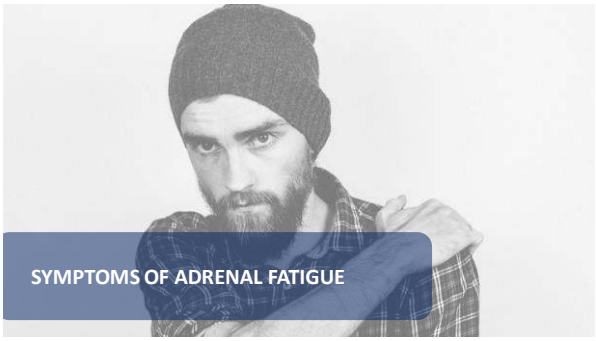
67


mental stress
emotional stress
physical stress
adrenals
Inflammation pain
Sugar
cortisol

68


mental stress
emotional stress
physical stress
adrenals
Inflammation pain
Sugar
cortisol
Tired

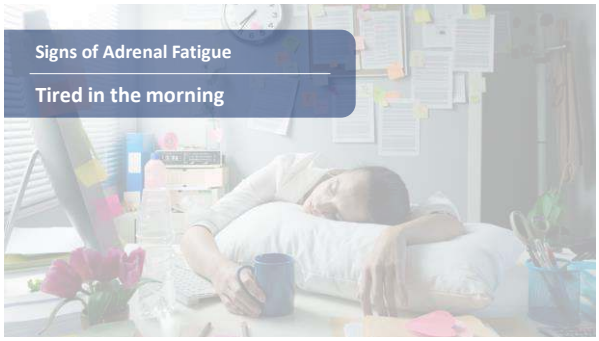
69


SYMPTOMS OF ADRENAL FATIGUE

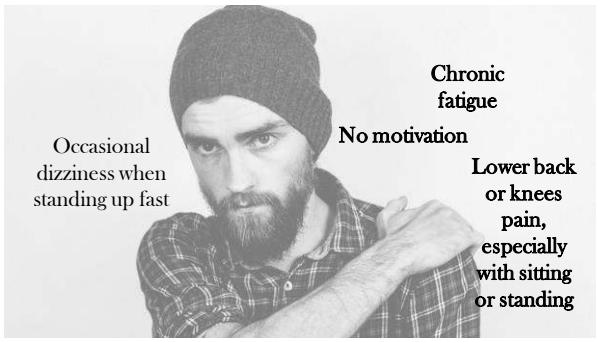
70


Signs of Adrenal Fatigue
CHRONIC LOWER BACK PAIN

71


Signs of Adrenal Fatigue
Tired in the morning

72


Occasional dizziness when standing up fast
Chronic fatigue
No motivation
Lower back or knees pain, especially with sitting or standing

73


Signs of Adrenal Fatigue
CHRONIC INFLAMMATION AND PAIN

74

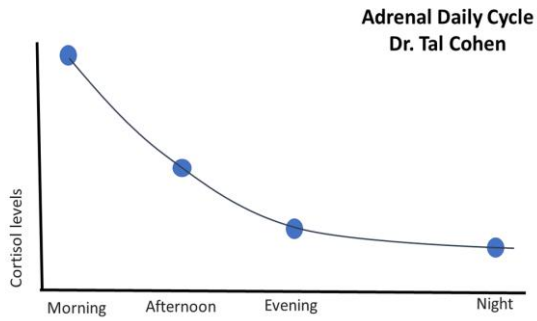

Signs of Adrenal Fatigue
FEELING STRESSED or OVERWHALMED

75


Signs of Adrenal Fatigue
FATIGUE IN THE AFTERNOON

76

77



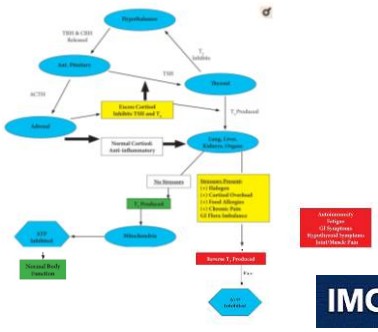
78

Treating both the Adrenal and Thyroid Outperforms Nutritional Supplementation and Medications for Autoimmune Thyroiditis

Wellwood, C., & Rardin, S. (2014). Adrenal and Thyroid Supplementation Outperforms Nutritional Supplementation and Medications for Autoimmune Thyroiditis. Integrative medicine (Encinitas, Calif.), 13(3), 41-7.

IMCJ Integrative Medicine: A Clinician's Journal

79



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80

Inflammation and the hormonal system

In chronic inflammatory diseases, a preponderance of energy expenditure pathways is switched on, leading to typical hormonal changes such as insulin/IGF-1 resistance, hypoandrogenemia, hypovitaminosis D, mild hypercortisolemia, and increased activity of the sympathetic nervous system and the renin-angiotensin-aldosterone system.

Straub RH. Interaction of the endocrine system with inflammation: a function of energy and volume regulation. *Arthritis Res Ther*. 2014;16(1):203. Published 2014 Feb 13. doi:10.1186/ar4484

81

The impact of infections on the hormonal system

Cytokines, the polypeptide mediators of the immune system, were shown to exert numerous actions on endocrine functions.

Igaz P, Falus A, Gláz E, Rácz K. Cytokines in diseases of the endocrine system. *Cell Biol Int*. 2000;24(10):663-668.

In response to a pathogen encounter, cytokines modify responsiveness of peripheral organs to endocrine signals, resulting in altered levels of blood hormones such as insulin, which promotes the ability of the body to fight infection.

Wensveen FM, Šestan M, Turk Wensveen T, Polić B. 'Beauty and the beast' in infection: How immune-endocrine interactions regulate systemic metabolism in the context of infection. *Eur J Immunol*. 2019;49(7):982-995.

82

The impact of diet on the hormonal system

High-fat and high-sugar diet in animal showed to disrupt sex hormones.

High-fat and high-sugar diet impaired estradiol, progesterone, and luteinizing hormone, surges before ovulation.

Ratio alteration of progesterone and testosterone strongly correlated with ovarian cyst formation.

Volk, K. M., Pogrebna, V. V., Roberts, J. A., Zachry, J. E., Blythe, S. N., & Toporikova, N. (2017). High-Fat, High-Sugar Diet Disrupts the Preovulatory Hormone Surge and Induces Cystic Ovaries in Cycling Female Rats. Journal of the Endocrine Society, 1(12), 1488–1505. https://doi.org/10.1210/js.2017-00305

83

The Effect of Environmental Toxins (heavy metals) on Hormonal System

"Pesticides, solvents, aromatic hydrocarbons, ***heavy metals***, and Chemical dusts have been associated with both male and female infertility."

Smith EM, Hammonds-Ehlers M, Clark MK, et al. Occupational exposures and risk of female infertility. JOEM. 1997;39:138-146.

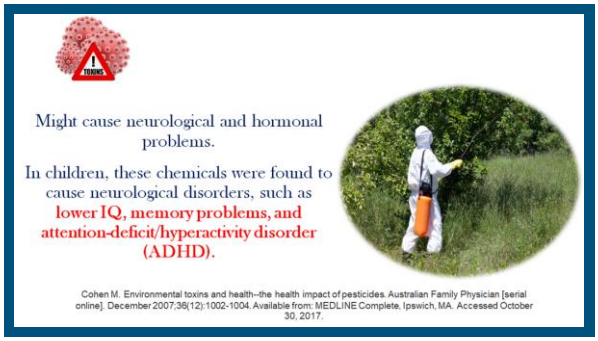
84

The Effect of Environmental Toxins (pesticides) on Hormonal System

"In addition to being neurotoxic, these compounds are profoundly immunotoxic and are often toxic to the endocrine system as well. "

Mendes J. The endocrine disrupters: a major medical challenge. Food Chem Toxicol. 2002;40:781-788.

85



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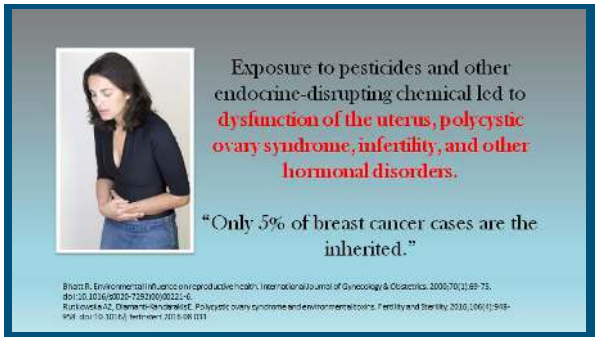

87

The Overall Effect of Environmental Toxins on the Hormonal System

The most common presentations of toxic damage to the endocrine system are:

1. Sleep disturbances or changes in energy level or mood.
2. Alterations in weight, appetite, and bowel function.
3. Sexual interest and function change; in females, any menstrual change.
4. Changes in temperature perception, sweating, or flushing.
5. Alteration of hair growth and skin texture.

88

Clinical application of lifestyle medicine for hormonal imbalance

Stress Management: both stimulating (games/ hobbies) and calming activities

Sleep: adequate and consistent, imperative for regulation of healthy circadian rhythym.

Healthy Diet: Plant based, whole food

Adequate hydration: some recommend ½ the body weight in H2O, depends on patient and any underlying conditions

Psychological wellbeing: promote feelings of safety and community

Exercise: 3-5 x/week depending on patient

89

Clinical application of nutritional medicine and diet for hormonal imbalance

"Because many Western diseases are hormone-dependent cancers, it has been postulated that the typical Western diet, compared with a vegetarian or semi-vegetarian diet, may alter hormone production, metabolism, or action at the cellular level."

Adlercreutz CH, Goldin BR, Gorbach SL, et al. Soybean phytoestrogen intake and cancer risk [published correction appears in J Nutr 1995 Jul;125(7):1960]. *J Nutr*. 1995;125(3 Suppl):757S-770S.

"Consumption of a plant-based diet can prevent the development and progression of chronic diseases that are associated with extensive neovascularization."

Fotsis T, Pepper M, Adlercreutz H, Hase T, Montesano R, Schweigerer L. Genistein, a dietary ingested isoflavonoid, inhibits cell proliferation and in vitro angiogenesis. *J Nutr*. 1995;125(3 Suppl):790S-797S.

90

Clinical application of Herbal medicine for hormonal imbalance

For Women:

- ***Cimicifuga racemosa (black cohosh)***
- ***Angelica sinensis (dang gui)***
- ***Asparagus racemosa (Shatavari)***
- ***Paeonia lactiflora (white peony)***
- ***Tribulus terrestris (Tribulus)***
- ***Vitex agnus castus (chaste berry)***

91

Clinical application of Herbal medicine for hormonal imbalance

For Men:

- ***Panax ginseng (Korean ginseng)***
- ***Pygeum africanum (Pygeum)***
- ***Tribulus terrestris (Tribulus)***
- ***Astragalus membranaceous (Astragalus)***
- ***Turnera diffusa (Damiana)***
- ***Withania somnifera (Withania)***

92