Overcoming Thyroid Disorders

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Chronic fatigue | Fibromyalgia | Graves' disease | Hashimoto's disease | Hypothyroidism

David Brownstein, M.D.

"The superior physician helps before the early budding of the disease... The inferior physician begins to help when the disease has already developed."

> Yellow Emperor s Classic of Internal Medicine Huang Ti Nei Ching Su Wen 2697-2597 BC

History of Thyroid Replacement Therapy

• China

- Reference to treating goiter with burnt sponge and seaweed in 1600 BCE
 - Earlier writings (~2700 BCE)
- 239 BCE Master Lu's Spring and Autumn Annals:
 - "In places where there is too much light water, there is much baldness and goiter."
- 6th century CE, Chinese were treating cretins with sheep thyroid

History of Thyroid Replacement Therapy

- Western medicine recognized the relationship between goiter and iodine deficiency in the 19th century
 - It was not until the late 1800's (1891) the effective treatment of subcutaneous injections of thyroid extract was reported by George Murray in England

"Forty percent of the American people—four of every ten children and adults—today are suffering needlessly and many are dying for lack of an ingredient vital for health. Is the ingredient unknown? No. Or unavailable? No. For years, medicine has recognized the role of the deficiency in some areas of health and disease and has had clues to its great importance in many other areas. But the knowledge too often has not been used—and still is not being used—because of the unreliability of laboratory tests that have failed to show the deficiency even when doctors could see its manifestations clearly enough in patients before them. And while laboratory tests have erred and have misled both doctors and patients, patients have suffered."

Overcoming Thyroid Disorders

- Hypothyroidism
- Poor T4 Converters and Thyroid Hormone Resistance
- Fibromyalgia and Chronic Fatigue Syndrome
- Hyperthyroidism and Autoimmune Disorders
- Natural Hormones
- Diet
- Detoxification
- Coagulation Disorders

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Thyroid Hormone

- Affects every cell in body
- Cannot achieve optimum health without a properly functioning thyroid gland
- Hypothyroidism may be the most commonly missed diagnosis today
- 60% of the population may have undiagnosed thyroid illness.





Thyroid and Other Endocrine Imbalances

- Allergies
- Anxiety
- Arthritis
- Cancer
- Candida
- Chronic Fatigue
- Coronary Artery Disease
- Cystic breasts
- Cystic ovaries
- **Depression**
- Diabetes

- Endometriosis
- Gout
- Hypertension
- Hypotension
- Infertility
- Mental Disorders
- Multiple Sclerosis
- Obesity
- **P.M.S.**
- Psoriasis

Subclinical Hypothyroidism and Ischemic Heart Disease

- 97 subjects with SCH (TSH 6.0-15mIU/L) v. euthyroid controls (2279)
 - 20 years of follow-up
- SCH associated with a 76% increase in IHD
- SCH associated with a 79% increase in mortality from IHD

When subclinical hypothyroid patients treated with thyroid hormone, there was no difference seen.

Subclinical Hypothyroidism and Risk of CHD and Mortality

35 year study. 55,287 participants with 542,294 person-years of follow-up.

- Risk of CHD:
 - TSH 4.5 to 6.9_{mtu/L}: Neutral
 - TSH 7.0-9.9: 17% increase
 - TSH 10-19.9: 89% increase

• Risk of CHD Mortality:

- TSH 4.5 to 6.9_{mTU/L}: 9% increase
- TSH 7.0-9.9: 42% increase
- TSH 10-19.9: 58% increase

SCH and Endothelial Dysfunction

- 27 Patients with SCH compared to 22 healthy controls
 - Endothelial function (brachial artery doppler US)
 - Results:

Compared to the control group, patients with SH showed significant reduced flow-mediated diameter. After thyroid hormone therapy, flow improved. "We suggest that thyroid hormone replacement therapy may help to prevent atherosclerosis in {SCH} patients.

Hypothyroidism and Atherosclerosis

- TSH receptor is expressed on coronary arteries and adipocytes
 - Elevated TSH may directly affect endothelial function of coronary arteries or fat cells
 - Induce ischemic heart disease in hypothyroidism.

Psychomotor Development in Children and Thyroid Levels

- 86 Children assessed at 12, 18 and 24 months
- Results:
 - Maternal serum FT4 levels in first trimester of pregnancy was the major determinant in psychomotor development at 18 and 24 months

210% increase in mild-to-severe delay in FT4 <25th percentile

IQ and Maternal Hypothyroidism

- Children of mothers with untreated hypothyroidism v. mothers without hypothyroidism
- IQ scores were 7 points lowered in children of untreated mothers
- 19% of untreated mothers had children with IQ <85 compared with 5% of others

Hypothyroidism and Oxidative Stress

- 20 hypothyroid subjects v. 20 controls
- Comparing oxidative stress markers
- Results:
 - TC, LDL cholesterol, trigycerides, thiobarbituric acid reactive substances, SOD, catalase were significantly higher in hypothyroid group.

"...hypothyroidism is associated with an increase in oxidative stress..."

Fetal Death and Maternal Thyroid Function (2)

- In fetal loss group compared to the unaffected group:
 - Increase in TSH: 1.33 v. 1.007MoM
 - Decrease in median FT4: 0.958 v. 0.992MoM
 - Increase in incidence of TSH above 97.5th percentile: 5.9% v. 2.5%
 - Decrease in FT4 below 2.5th percentile: 5.0% v.
 2.5%



- Acne
- Arthritis
- Arteriosclerosis
- Constipation
- Cold Extremities
- Decreased hearing
- **Depression**
- Eczema
- Fatigue (A.M. Fatigue)
- Headaches
- Hypercholesterol
- Hypertension

- Hypotension
- Infertility
- Mental Impairment
- Menstrual disorders
- Ovarian cysts
- Parasthesias
- PMS
- Poor memory
- Psoriasis
- Recurrent infections
- Slowed movements
- Voice hoarseness

Physical Exam Signs

- Anemia
- Dry skin
- Edema
- Goiter
- Hair loss
- Hypertension

- Hypotension
- Macroglossia
- Periorbital edema
- Poor eyebrow growth
- Puffy face
- Sluggish reflexes

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- 1993 WHO estimated that global goiter prevalence was 12%
 - 655 million people in 110 countries

WHO/UNICEF/ICCIDD. Assessment of Iodine Deficiency Disorders and Monitoring Their Elimination. A Guide for Program Managers. 3rd ed. Geneva: WHO, 2007 Best Pract Res Endocrinol Metab 2010; 24: 1–11.

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- Blood Tests
 - TSH, T4 free, T3 free, Reverse T3, TPO and thyroglobulin Ab's
- 24 Hour urine testing
- Serum Ferritin
- Serum B12 (<450pc/ml)
 - Clinical Pearls, March 1997, Vol. 7, No. 3.

TSH: All in the Timing

- 42 Subjects
 - 20 SCH
 - 22 with primary hypothyroidism
 - 16 with Hashimoto's and 6 post-surgical
 - TSH levels were lowered in afternoon compared to morning in 41 of 42 subjects
 - TSH in morning: 5.83mU/L v. 2.18 mU/L in afternoon

An afternoon TSH level would miss a diagnosis of hypothyroidism



Median TSH levels

	Morning	Afternoon
SCH	5.83	3.79
Primary Hypothyroid	3.27	2.18

Thyroid Gland Examination Alters Blood Tests

- Thyroid gland palpation performed
- Blood levels obtained before and two hours postpalpation
- Results: Increases in TT3, FT3, FT4, TG
 - No change with TSH and TT4



"Thyroid function tests cannot be interpreted in a vacuum. Nonthyroidal disease and certain drugs affect these tests. A suppressed TSH in a critically ill patient might indicate sick euthyroid syndrome. {The decision to treat} should be individualized. There is no sense in waiting three years to treat a patient with a persistent TSH >5 if the patient is clearly symptomatic, TPO titer is elevated and a goiter is present. In summary, we should...discard rigid guidelines that are driven mainly by cost containment."



Thyroid **T4** ► Reverse T3 **T3 Effects On Body**



- Reverse T3 competes with both T3 and T4 for transporters and receptors
- Reverse T3 inactivates and degrades Deiodianse 1 and 2
 - Converts T4 to T3 and degrades RT3



- Iodine
- Liver detox
- T3 preparations
- Cortisol or adrenal support

TSH is a Poor Test

"The biological effects of thyroid hormones at the peripheral tissues- and not TSH concentrations- reflect the clinical severity of hypothyroidism. A judicious initiation of (thyroid hormone) treatment should be guided by clinical and metabolic presentation and thyroid hormone concentrations and not by serum TSH concentrations."

What About Low TSH Levels?

- 428 Korean subjects
- 65 Years and older
- 5 year evaluation of thyroid function and development of dementia or MCI



Baseline Normal Subjects

	Non-Progressive Group	Progression Group	
TSH (mIU/L)	2.24	1.78	
Baseline MCI Subjects			
	Non-Progressive Group	Progression Group	
TSH (mIU/L)	2.26	1.42	

There was no difference in baseline T4 levels, however, lower AST and ALT levels observed in the progression groups.

J. Clin. Endoc. And Metab. Doi:10.1210/jc.2013-3385. accepted Nov. 18, 2013


"TSH above 2.0mU/L is a risk factor for future development of hypothyroidism, especially when TPO is detected. This is true even in the absence of thyroid antibodies. Ultimately, the diagnosis and efficacy of treating subclinical hypothyroidism should not be based on the TSH reference range alone, but should integrate the degree of TSH elevation with patient-specific risk factors and the concentration of TPO antibodies."



"We should acknowledge that TSH is not a good indicator of the adequacy of thyroxine replacement. We should prescribe sufficient thyroxine to restore the patient to a clinically euthyroid state, while maintaining T3 within the reference range."



Framingham study. 2407 participants followed for 3.5 years.

- Women:
 - Weight increased by 2.3kg for every 1-unit increment in TSH concentration
- Men:
 - Weight increased by 1.1kg for every 1-unit increment in TSH concentration

"Change in serum TSH concentrations over time (within reference range) was strongly and linearly associated with weight gain."

Thyroid Function and Alzheimer's Disease

- 209 Participants
- 12.7 years follow-up
- Women in the lowest (<1.0mIU/L) and highest (>2.1 mIU/L) of serum TSH concentration had increased risk of Alzheimer's disease compared to those in middle tertile (0.5-2.1mIU/L)
- Lowest tertile: 239% increase
- Highest tertile: 215% increase.

TSH, Cognitive Impairment

- 495 elderly residents
- TSH v. cognitive impairment
- TSH<0.5mIU/L associated with a 712% increase in cognitive impairment

How To Check The Basal Body Temperature

- Shake thermometer down at night or use a basal thermometer
- In A.M., take axillary temperature before arising
- Menstruating women should take their temperatures on days 2-4 of cycle
- Normal axillary temperature is 97.8-98.2 Fahrenheit

Diagnosing Hypothyroidism

- History
- Physical exam
- Basal Body Temperatures
- Blood Tests.

Don't Rely Solely on Lab Tests

"Are not the feelings of the patients often as clinically valuable as the other findings? In no case can we wholly discount them. A good laboratory report is cold comfort to a patient whose symptoms remain unchanged, and the doctor can repeat such reports until he is blue in the face, but they will not help his patient much if unaccompanied by controlled symptoms and changed feelings. The successful physician is the one who knows best how to make his patients feel better."

Comparing Thyroid Medications

Desiccated Thyroid

- T1
- T2
- T3
- T4
- Calcitonin
- Diuretic Effect
- Selenium

Levothyroxine SodiumT4

Interference with Absorption of L-thyroxine

- Ferrous sulphate
- Aluminum-containing antacids
- Raloxifene
- Bile acid sequestrants
- Calcium carbonate
- PPI's

Other Thyroid Rx. Choices

- Nature-Throid and Westhroid
 - Corn-free, desiccated thyroid hormone
- Compounded Desiccated Thyroid Hormone
 - No fillers
 - Adjust dosage
- Compounded T3
 - Slow release
 - No fillers

Desiccated Thyroid Treatment

- Adults: Start at 1/2 grain
- Elderly, heart disease history: Start at ¹/₄ grain and go slowly
- Monitor basal temperatures, lab work, physical exam signs and symptoms.

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Thyroid Hormone Resistance

- Target tissues of body have reduced responsiveness to thyroid hormone
 - First described in 1967
- Can occur with adequate production of thyroid hormone
- Analogous to adult onset diabetes

Laboratory tests will be inaccurate!

— Thyroid Hormone Resistance

- Genetic anomalies of thyroid hormone receptors
- Autoimmune, oxidative, or toxic damage to thyroid-hormone receptors
- Competitive binding to thyroid-hormone receptors by pollutants, food additives, etc.



- Bind to TH receptors and Estrogen receptors
- Food containers, baby bottles, re-usable water bottles, metal food cans
 - Dental sealant
 - Antagonize TH receptor activation

Over 6 billion pounds of BPA produced and over 100 tons released into the atmosphere worldwide annually.

Clin. Endocrin. And Metab. 2002:87:5185-90 Endocrine Reviews. 2009;30:75-95 PLOS One.. 9.27.11



- BPA inhibited the regulation of most T3dependant responsive genes
- Affected T3 signaling pathways during metamorphosis

"BPA represents a serious risk for human development through disruption of T3 signaling pathways."

Triclosan and Thyroid

- Antibacterial agent (chlorinated, organic molecule similar to Bisphenol A) found in many household products
 - Toothpaste, mouthwash, soap, deodorant, shaving cream, cleaning supplies, kitchen utensils, trash bags, clothing, bedding, children's toys

Triclosan and Thyroid₂₀

- Newborn rats fed varying amounts of triclosan for 31 days
- Results: Decrease in T4 concentrations with increasing concentrations
- Significant increases in liver weights with higher doses



- Inhibit TPO catalysed iodination
 - Daidzein and genistein
 - Inhibits intracellular thyroid hormone production
 - Soy products, peas, beans, nuts, grain products, coffee, and tea
 - Avg. 3.1mg dietary isoflavones consumed by 35% of U.S. adults daily
 - Adolescents diagnosed with Graves' or Hashimoto's more likely to be fed soy formula as infants

Organochlorine Pesticides

- Activates hepatic uridine diphosphate glucuronyltransferases (UDPTG's)
 - Increases T4 metabolism
 - Can result in euthryoid goiter or hypothyroidism



- 4-MBC and octylmehtoxycinnamate (OMC) decrease 5' deiodinase activity
 - Found in wastewater treatment plants
 - Bioaccumulation in fish and human milk



- Contaminant of drinking water
 - Nitrogen fertilizers
 - High levels found in green leafy and root vegetables
 - Organic lettuce found to have less nitrate as compared to conventional lettuce

Compared to women in the lowest quartile of nitrate intake from public water supplies, those in the highest quartile were found to have a 2.2x increase risk of thyroid cancer.

> ESPA J. 2008;689:1-79 Food Addit. Contam. 2006;23:1283 Epidem. Vol. 21, N. 3. May 2010



- Rats fed iodine-sufficient v. iodine deficient diet
- After 2.5 months, no difference in TH
- After 24 hours of perchlorate exposure:
 - Both T3 and T4 lowered significantly in iodinedeficient rats, not iodine-sufficient rats
 - After two weeks of perchlorate exposure, iodinesufficient rats had lowered T4 and T3 levels

Estrogen Therapy and Thyroid Replacement

- Oral estrogen therapy results in increased binding of thyroid hormone
 - Increased TBG

This increased TBG effect not observed with transdermal estrogen therapy.









Lowered T3 Levels in Elderly Associated With:

- Lowered attention
- Depression
- Increased mortality
- Lowered ability to perform activities of daily living.

T4 to T3 Inhibitors

Nutrient Deficiencies

- Iodine
- Iron
- Selenium
- Zinc
- Vitamin A
- Vitamin B2
- Vitamin B3
- Vitamin B6
- Vitamin B12

Medications

- Amiodarone
- Beta Blockers
- Birth Control Pills
- Iodinated Contrast Agents
- Lithium
- Methimazole
- Phenytoin
- Propylthiouracil
- SSRI
- Theophylline

Vitamin B-12 for Health



Anemia | Brain Fog | Bursitis | Depression | Fatigue | Fibromyalgia | Heart Disease

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T4 to T3 Inhibitors (2)

- Aging
- Alcohol
- Alpha-Lipoic Acid
- Arsenic
- BPA
- Chemotherapy
- Cigarette Smoking
- Cruciferous Vegetables
- Diabetes
- Fasting
- Fluoride

- Growth Hormone Deficiency
- Hemochromatosis
- Lead
- Low Adrenal State
- Mercury
- Pesticides
- Soy
- Stress
- Sunscreen
- Surgery
- Radiation

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- Stress
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- Surgery
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Water Fluoridation Promotes Hypothyroidism

- Cross sectional study design
 - Hypothyroidism prevalence correlated with fluoride in drinking water
 - Conclusion: Compared to non-fluoridated areas, fluoridated areas had significantly more hypothyroidism

T4 to T3 Inhibitors

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Medications

- Amiodarone
- Beta Blockers
- Birth Control Pills
- Iodinated Contrast Agents
- Lithium
- Methimazole
- Phenytoin
- Propylthiouracil
- SSRI
- Theophylline



- Shell fish, crabs, kidney, liver and Brazil nuts
- As compared to other organs, thyroid has highest concentration of selenium


Selenoproteins

- Glutathione peroxidase
 - Reduces H₂0₂
 - Antioxidant, anti-inflammatory
 - Decreases phospholipid hydroperoxides
 - Moderates apoptosis
- Thioredoxin peroxidase
 - Found in mitochondria
 - Regulates cellular redox level, cell development and proliferation
- Iodothyronine deiodianase
 - Conversion of T4 into T3 or rT3
 - Local (intracellular) T3 production

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- Zinc
- Vitamin A
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- Vitamin B6
- Vitamin B12

Medications

- Beta Blockers
- Birth Control Pills
- Estrogen
- Iodinated Contrast Agents
- Lithium
- Phenytoin
- Theophylline

National Health and Nutrition Survey

 1971-2000 NHANES showed iodine levels declined 50% in the United States



National Health and Nutrition Survey

- 1971-2000 NHANES showed <u>iodine levels</u> declined 50% in the United States
- During this time, <u>increased incidence</u> of:
 - Thyroid illnesses (hypo, autoimmune, cancer)
 - Cancers of the breast, prostate, endometrium and ovaries
- All of the above conditions can be caused by iodine deficiency.



Chronic fatigue | Fibromyalgia | Graves' disease | Hashimoto's disease | Hypothyroidism

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