Hypothyroidism and Subclinical Hypothyroidism
Testing and Treatment
1 hours CME/ CE

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Financial Disclosure: Co-owner Restorative Formulations
Either can be fatal

- Abnormally high metabolism
- Abnormally low metabolism

Thyroid system

- Largely determines metabolic rate which is crucial for optimal health
Purpose of T3 is to set the speed of DNA transcription, the speed of life

- Corepressor (CoR) is displaced
- Coactivator (CoA) is recruited
- DNA transcription is accelerated

Kliewer SA, Umesono K, Mangelsdorf DJ, Evans RM (January 1992). "Retinoid X receptor interacts with nuclear receptors in retinoic acid, thyroid hormone and vitamin D3 signalling". Nature 355 (6359): 446–9. doi:10.1038/355446a0. PMID 1310351
Body temperature and metabolic rate track each other

Mouse’s core body temperature (blue line), oxygen consumption (pink line)

Swoap SJ. The pharmacology and molecular mechanisms underlying temperature regulation and torpor. Biochem Parmacol. 2008 Oct1;76(7):817-824

• When body temperature goes up metabolic rate goes up, when temperature goes down metabolic rate goes down, independent of any form of regulation or any other factors.

• Metabolic rate is proportional to temperature in all life forms (mammals, birds, reptiles, amphibians, fish, plants, bacteria) [mass-, temp-adjusted universal metabolic rate]

• Metabolic rate is proportional to temperature in cold-blooded or warm-blooded animals (whether the temperature sets the metabolic rate or the metabolic regulation sets the temperature).

If the temperature is low, is it a Supply problem or a peripheral Conversion/utilization problem?

Thyroid hormone blood tests don’t measure thyroid hormone expression because they don’t measure body temperature

80% of T3 is produced and regulated intracellularly in a time-specific and tissue-specific fashion.

This regulation and control is invisible to blood tests.
Ubiquitin Proteasome Pathway

Key regulatory system for protein levels

Ubiquitin is found in every cell

E1 activates ubiquitin for attachment to E2

E2 transports ubiquitin to E3 for attachment to targeted protein

Process repeats until chain of at least 4 ubiquitin

Targeted and tagged protein is recognized and digested by proteosome and amino acids are recycled

This is the key pathway that regulates the activity of D2 which converts T4 to T3
T4 and rT3 both accelerate the destruction of type II deiodinase (D2), decreasing the half-life of D2 by as much as 50%, slowing the conversion of T4 to T3.

This can explain why many patients don’t feel well on T4-containing medicine.

Some people feel better on herbs than on T4.

• With good T4 to T3 conversion, T4 medicine may improve a patient’s temperature (expression).
• With poor T4 to T3 conversion, T4 medicine and RT3 may make conversion worse.
• I don’t recommend T4-containing medicine until a patient’s temperature is normal.
Patient comes in with symptoms of low thyroid function or slow metabolism

- Fatigue
- Fibromyalgia
- Depression
- Weight gain
- Migraines
- PMS
- Irritability
- Fluid retention
- Hair loss
- Dry skin, Dry hair
- Insomnia

- Low body temperature confirms slow metabolism
- What is the TSH? High TSH = Hypothyroidism or Iodine
- What was TSH before starting thyroid medicine, if on it?
TSH can sometimes go up significantly (10-100+ mIU/L) just by adding iodine (>6 mg/day)

- If TSH goes up, T3 and T4 don’t go down, temperature goes up, and patient feels better then **not hypothyroidism**.

- If patient remains on the iodine, TSH usually normalizes in 6–12 months, but sometimes longer.

- If patient weans off iodine, tests TSH usually normalizes in several weeks.

- Iodine is high value nutrient, TSH up-regulated to stimulate NIS.

- In a few: rash, palp’s, potentiation of thyroid meds.

* http://www.inchem.org/documents/jecfa/jecmono/v024je11.htm
If TSH is >8 mIU/L...

Not on thyroid medicine:

• Ask about iodine intake.
• Consider checking anti-TPO antibodies.
• Consider clearing thyroid pathways with T3 before NDT.
• Consider starting patient on 30-60 mg of NDT according to temperature and symptoms.
• Consider herbal thyroid, adrenal, and nutrient support.

On thyroid medicine:

• If on a lot of T4 for a long time, consider clearing thyroid pathways completely by weaning T4 and using T3 only for a time
• Otherwise, consider increasing thyroid medicine dose.
• Consider herbal thyroid, adrenal, and nutrient support.
Subclinical Hypothyroidism if T4 is normal

If TSH is 4-7 mIU/L...
Not on thyroid medicine:
• Consider therapeutic trial of herbs and nutrients instead of T4-containing medicine. Titrating anti-inflammatory herbs and nutrients according to body temperature (guggul, blue flag, ashwagandha, iodine, selenium)
• Consider checking anti-TPO antibodies/ immune support herbs (Rosemary, Cordyceps, Rehmannia)
• Then, consider treating with T3, T4, or both

On thyroid medicine:
• Consider reducing T4-containing dose, maybe in half
• Consider adding herbs and nutrients to support conversion
• If on a lot of T4 for a long time, consider clearing thyroid pathways completely by using T3 only for a time, instead of T4
If TSH is < 4 mIU/L...

**Not on thyroid medicine:**

- Consider therapeutic trial of herbs and nutrients titrated according to body temperature.
- Consider treating with T3 instead of, or in addition to herbs and nutrients. T3 can be increased 7.5 mcg BID, each day if patient is without complaints and pulse is < 100 b/m, up to about 75 mcg BID.

**On thyroid medicine:**

- If TSH was < 5 mIU/L before starting medicine, consider switching to T4 therapy to T3 only to normalize temperature before gradually weaning.
- Consider adding herbs and nutrients to support conversion
Interactions with thyroid medicine

- T4 and T3 naturally occur in the body.
- Different medicines can affect absorption, sex hormone binding globulin, and dosing medicine to titrate by TSH.
- However, we can manage therapy according to temperature and symptoms.

Contraindications for thyroid medicine

- Thyroid hormone is necessary for life.
- The side effects of T3 are mainly cardiovascular and more short-term than long-term.
- Angina
- T3 has a short half-life, dropping metabolism could puzzle doctors of unconscious ICU patient cut off from medicine.
Iodine controversy in Hashimoto’s Thyroiditis

Oxidative stress > less reduced glutathione > more $H_2O_2$ in cell > more oxidized iodine in cell > more damage > more autoimmunity

GSH = Reduced glutathione, GS-SG = Oxidized glutathione, GPX = Glutathione peroxidase, TPO = Thyroid peroxidase
Selenium increases GPX which reduces $\text{H}_2\text{O}_2$ inside follicular cell, increasing GSH

Selenium, a component of selenocysteine is found in all three deiodinases as well as GPX

- Iodine increases thyroid autoimmunity in specially bred mice, however, iodine plus selenium reduces it

- Selenium increased plasma glutathione peroxidase by 21% and TPO antibody decreased by 76%. When Se stopped, glutathione peroxidase dropped and TPO markedly climbed.

Above 1mg/d, iodolactone made from arachidonic acid

\[
\text{Iodine + arachidonic acid} \xrightarrow{TPO} 6\text{-iodolactone}
\]

6-iodolactone (6-IL)

- Key regulator of apoptosis and cellular proliferation in the thyroid. Studies on 6-iodolactone are usually done with dosage ranges over 6 mg/day of iodine
- Other iodolipids such as iodohexadecanal have been shown to suppress thyroid function in at least 4 other ways providing thyroid auto regulation
- Similar iodinated lipids form in the breast via Lactoperoxidase (LPO)
- Without iodine > inflammation > cysts > nodules > hyperplasia > cancer in various tissues (thyroid, breast, prostate)
6-iodolactone, key mediator of antitumoral properties of iodine.

Nava-Villalba M¹, Aceves C².
6 ways iodolipids affect the thyroid

Above 1 mg/d iodide ceases to function as a substrate for hormonogenesis. Iodine nourishes the thyroid gland to make thyroid hormone, and calms or rests the thyroid to help prevent overproduction of thyroid hormone and damage.

1. inhibition of H2O2 generation by dual oxidases, thereby blocking iodide oxidation and organification

2. suppression of sodium-iodide symporter (NIS) expression, stopping the entry of iodide and lowering the intracellular iodide concentration;

3. inhibition of thyroid hormone secretion.

In high concentrations of iodide, additional mechanisms are also observed, like

4. reduction of thyroid blood flow, (12mg/day)

5. inhibition of thyroid growth,

6. induction of apoptosis. Difference between necrosis and apoptosis can be seen and (fragmentation of DNA and other findings in apoptosis)
Impact of iodine deficiency on thyroid system

- Hypothyroidism
- Hyperplasia / Nodules
- Thyroid Cancer
- Hashimoto’s Thyroiditis

“…there is little doubt that increasing dietary iodine intake will limit goiter and thyroid nodule formation, the formation of differentiated thyroid cancer, and possible further dedifferentiation to anaplastic thyroid carcinoma.”


**Iodine and anaplastic thyroid carcinoma.**

**Smyth PP.**
TPO levels with herbal and nutrient support

• Small percentage of people can have TPO go up with iodine supplementation.

• On the other hand, up to 70% of people can normalize their temperatures with the combination of iodine + selenium + herbs (thyroid, adaptogens). 95% of the time TPO antibodies go down, not up.
• T4 to T3 conversion are reduced with stress fasting and illness.
• Heavy metals and other toxins also disrupt thyroid function

Bianco AC, Nunes MT, et al. The Role of Glucocorticoids in the Stress-Induced Reduction of Extrathyroidal 3,5,3'-Triiodothyronine Generation in Rats. Endocrinology. 1987;120(3):1033
Schimmel M. Thyroidal and Peripheral Production of Thyroid Hormones. Annals of Internal Medicine 1977;87:760-768
Workup for low thyroid symptoms and low body temperature

• History and physical exam. Lifestyle, nutrition, exercise, stress, depression, heavy metal or toxin exposures.
• Comprehensive metabolic panel > rule out kidney disease, diabetes, liver problems, etc.
• Complete blood counts > rule out anemia, infection, leukemia, and so on.
• TSH > rule out primary hypothyroidism
• Consider ferritin (preferably above 70 ng/L, TPO is heme dependent)
• Consider food allergy testing (inflammation can inhibit thyroid expression)
• Consider adrenal fatigue
• EKG, good baseline to have
• If no better explanation for the symptoms and temperature, impaired transport/conversion/resistance of thyroid hormones may also be considered.

Yu J, Koenig RJ. Regulation of hepatocyte thyroxine 5’-deiodinase by T3 and nuclear receptor coactivators as a model of the sick euthyroid syndrome. J Biol Chem. 2000 Dec 8;245(49):38293-301
Typical lifestyle stressors

- Childbirth
- Divorce
- Death of a loved one
- Job or family stress
- Surgery or Accidents
- Heavy metal toxicity (e.g., mercury)
- Bromine, Fluorine, Chlorine; especially a mixture of compounds that contain these
Lifestyle measures for low body temperature

I suggest:

- Stress-reduction, declutter, simplify
- Regular, moderate exercise, especially short sprints
- Detoxification, sauna
- Organic foods (to avoid pesticides and toxins)
- Avoid gluten, aspartame, excess alcohol
- Get adequate rest, good multi-vitamin and nutrition
- Iodine (12 - 48 mg/d) + Selenium (100 - 800 mcg / d)
- Zinc (12 - 48 mg/d)
- Vitamin D balances humoral and cellular immune function
- Iron
- B12 (1 mg/d) important in digestion, blood cell formation, other
- Tyrosine
- Certain thyroid (dose according to body temperature) and adrenal support
- Botanicals
- Improved gut health > consider resting the gut
- Fat loss to reduce inflammation
- Eating organically
Guggul (Commiphora Myrrha)

- Contains ketosteroids that support iodine uptake and T4 to T3 conversion.
- Supports healthy cholesterol levels. Decreases total serum lipids, cholesterol, triglycerides, and beta lipoproteins and increases all thyroid functions.


Bladderwrack (Fucus Vesiculosis, Kelp)

- Good source of iodine and other substrates.
- Contains diiodotyrosine (2 DIT join to make T4).
- Non-iodine compounds in seaweed may also be very helpful in thyroid related disorders such as Hashimoto’s thyroiditis.
- Used for centuries in Asian cultures for both hypo and hyper.

Blue Flag (Iris Versicolor)

- Used extensively from 1830–1940 to treat thyroid disorders
- Late 1800’s made into a pharmaceutical called Iridin for hypothyroidism
- Commercially used to detoxify toxic land
- Traditionally used to “move sluggish body fluids”

Triphala Fruit (Amla, Bellerin myrobalan, Chebulic myrobalan)

- Used for centuries as anti-inflammatory and other
- Thyroid most susceptible to inflammation
Botanical Adrenal Support

- Very important in thyroid disorders and treatment
- Help normalize endocrine function, resistance to stress
- Support for stamina as well as mental and immune function
- Thyroid and Adrenal go together like two players on the same team. When one struggles the other is taxed as well
- Adrenal support can often help people tolerate T3 therapy
Adrenal Support Herbs

• Siberian Ginseng (Eleutherococcus senticocus) – helps optimize adrenal response. Excellent for stress-related exhaustion and emotional disturbances.

• Ashwagandha (Withania somnifera)

• Holy Basil (Ocimum sanctum) – helps to normalize hyperglycemia, corticosterones, and adrenal hypertrophy from chronic stress. GABAergic, calming

• Rose Root (Rhodiola rosea) – adaptogen and anti-stress herb. Increases serotonin and endorphins, mood

• Licorice – Glycerrhizic acid decreases the breakdown of cortisol which can bind to mineralocorticoid receptors and increase blood pressure. Also been used in the treatment of hepatitis, and viral illnesses such as EBV
Immune Support Herbs

• Rehmannia – Helps balance immune function and B and T cell biosynthesis.

• Cordyceps – Fungus, antioxidant, immune-modulating, protects liver.

• Rosemary (Rosmarinic acid) – Rosmarinic acid is a polyphenol that helps balance immune function by inducing apoptosis of activated T cells and neutrophils without affecting T cells or neutrophils in their resting state. May be helpful in T-cell leukemia, RA, Lupus, SLE, Ulcerative Colitis, Crohn’s, MS. Neuroprotective.

• Turmeric – Neuroprotective and neuroregenerative, anti-inflammatory, anti-oxidant, promotes healthy vasculature.
People don’t have hypothyroid symptoms without having a low body temperature.
• 9 obese patients and 12 lean controls in Italy. Morning temperature is the same. One degree F split during day.

**Figure 1.** Twenty-hour body core temperature profiles (±SEM) in obese (n = 9; 2 females) and lean subjects (n = 12; 2 females). Grey panel represents the dark period. The values of BcT recorded every 2 min are averaged every 15 min.
The temperature does fluctuate during the day.
How to measure body temperature

• By mouth, with a Galinstan (liquid metal consisting of gallium, indium, and tin) thermometer.
• 3 times a day, 3 hours apart, starting 3 hours after waking
• For several days for diagnosis (temperature runs higher between ovulation and menstruation).
• You can also encourage your patients to check their temperatures when they feel their best and when they feel their worst, so they can see the correlation.
• Symptoms can occur T<98.6F and more often with T<98F

Disorders such as ... hypothyroidism must be excluded before a diagnosis of PMS can be considered.
Hypothyroidism and hyperthyroidism in anxiety disorders revisited: new data and literature review

Thyroid function should be checked in patients with Panic Disorder and Generalized Anxiety Disorder
Hypothyroidism is also associated with:

- Migraine headache
- Carpal tunnel syndrome
- Depression
- Hair loss
- Irritable bowel syndrome
- Fibromyalgia
- Obesity
- Mental fog
- Low sex drive


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