Metabolism

- Define Metabolism
  - The sum of the physical and chemical processes in an organism by which its material substance is produced, maintained, and destroyed, and by which energy is made available.
  - Anabolism requires energy to build complex tissue
  - Catabolism releases energy, involves the breakdown of complex tissue to simpler components.

Active Metabolism

- Hormonal regulators of metabolism
  - Thyroid Hormone: Triiodothyronine - T3
  - Estrogen/progesterone
  - DHEA
  - Growth Hormone
  - Testosterone
  - Cortisol
  - Leptin
  - Epinephrine / Norepinephrine
  - Non-hormonal cellular cytokines

Metabolism, Basal metabolism

- The basal metabolic rate (BMR) is a measurement of energy required to keep the system functioning at rest.
- Measured in calories, metabolic rates increase with exertion, stress, fear, and illness
- Thyroid hormones help regulate BMR
  - How is the your thyroid involved?

Thyroid Definitions

- Hypothyroid – When the thyroid gland does not produce enough thyroid hormone
- Hyperthyroid – When an overactive thyroid produces an excessive amount of thyroid hormone
- Normothyroid – Like Goldilocks and the third bed.

Thyroid Cascade

- Biological definition: A system in which the system responds in an opposite direction to the perturbation.
  - T4 and T3 come from the thyroid gland
  - These hormones feedback to pituitary and hypothalamus gland
  - This reduces the TSH and TRH production
  - DIO enzymes may also be involved in cellular feedback of some type – more on this…
Somato-what?
- Somatostatin (aka Growth Hormone Inhibiting Hormone, GHIH) is the compensatory hormone to somatotropin, (aka Growth Hormone, GH)
- Somatostatin secreted from the Hypothalamus goes to inhibit TSH and GH
- Somatostatin secreted from the pancreas inhibits insulin and glucagon and pancreas secretions
- Somatostatin is secreted from the digestive tract cells and suppresses digestive hormones, enzymes and mesenteric blood flow

Somatostatin respect
- The checks and balances of thyroid function are well beyond the oversimplified

TRH $\rightarrow$ TSH $\rightarrow$ T4 & T3 $\rightarrow$ T3/rT3

Thyroid Definitions
- Hypothyroid – When the thyroid gland does not produce enough thyroid hormone
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TSH $\rightarrow$ T4 & T3
Reference ranges for thyroid function
- TSH: 0.3-3.5 mIU/mL
- Free T4: 0.7-1.9 ng/dL
- Free T3: 2.3-4.2 pg/mL

Other tests that claim value
- TRH stimulation test
- Free T3/rT3 ratio
- Basal Body Temperature

TRH Stimulation Test
- Hypothalamic TRH stimulates Pituitary TSH
- There is speculation that some might have a hyper-responsive pituitary, so TSH elevation is inadequate for desired thyroid hormone secretion
- Telltale /Practical sign—High norm TSH with Low T4
- TRH is unsubstantiated and unlikely to return as a screening test for hypothyroidism.

Free T3/rT3 Ratio
- Depending upon the reference range of your lab – the desirable number is different.
- Proponent claim that the higher the ratio, the better.
- Presumes the more active T3, compared to inactive rT3.

Basal Body Temperature
- Our basal body temperature is one expression of our cellular metabolism, and theories were established many years ago that oversimplified our complex thermodynamic regulation and hormonal and chemical cascade
- Hypothyroid became the scapegoat.
While thyroid hormones do influence metabolic function and temperature, they are, (perhaps the lesser) among many hormones and messenger molecules involved in this regulation, including sex hormones, leptin, epinephrine, norepinephrine, and cytokines.


Hypothalamus

**Hypothalamus**

Perihypothalamus

Thyroid

Pituitary

Peripheral Tissue

- DIO2 dependent T4 → T3
- DIO3 dependent: T4 + T3 → rT3 / T2

Doctrine of Viz Medicatrix Naturaee

*The Healing Power of Nature is the inherent self-organizing and healing process of living systems which establishes, maintains and restores health.*

*It is the goal of the physician and each of us as individuals to recognize and understand this ordered and intelligent healing process within ourselves.*

- RM

Prevalence of hypothyroid using TSH

- Over 25,000 had their TSH tested
- 9.5% of those tested were above the reference range (0.3-5.1).
- 60% of those that were on thyroid prescriptive treatment still had TSH outside the reference range.

- Data: The Colorado thyroid disease prevalence study.

Who develops hypothyroidism

- Women represent about 75% of those diagnosed with hypothyroidism.
  - Greater hormonal variation/stress throughout a woman's life
  - Greater incidence of auto-antibodies

Men are rarely tested for hypothyroidism.

Men represent less than 10% of people treated for hypothyroid, yet 25% who have it

- Gender difference are similar for hyperthyroid.

Who develops hypothyroidism

- Data: The Colorado thyroid disease prevalence study.

TSH → T4 & T3

- It is generally observed that thyroid hormone sensitivity, reflected by a low normal TSH is desirable.

**TSH**

**TSH & Endothelial Inflammation**

- Impaired endothelial function, suggesting early-stage atherosclerosis, may be more prevalent in female hypothyroid patients and in people with TSH levels in the upper part of the reference range (3.3-3.7)


TSH & CHD Severity

- Low but clinically normal thyroid function is associated with more severe coronary and carotid atherosclerosis and increased carotid artery intima media thickness

- Measured by TSH in patients with cardiac-related chest pain

- Yun KH, et al. Relationship of thyroid stimulating hormones with coronary atherosclerosis in aging patients. Int J Cardiol 2007;123 (1) 56-60
TSH & Blood Pressure/Lipids
- Linear and positive associations between thyrotropin (TSH) levels within the reference range and BP and less favorable serum lipid profiles in people with higher thyrotropin levels have been reported.

TSH & CHD mortality in women
- This study shows that CHD mortality increases in women with increasing levels of thyrotropin (TSH) within the reference range (0.5-3.5).
  - This study failed to separate the CHD risk related to the insulin-resistance found commonly in those with elevated TSH - RMP.

TSH & Weight - BMI
- It has been suggested that thyrotropin (TSH) levels within the reference range may be positively associated with body mass index.

Let's Prescribe T4 to lower CHD?
- Not so fast!
  - Deficient environments: increased thyroid and nodules in iodine deficient environments.
  - "Hypo-thyroid and "sub-clinical hypothyroidism is likely related to the present IR."
  - Fernandez-Real et al. Thyroid function is intrinsically linked to insulin sensitivity and endothelium-dependent vasodilation in healthy young people. J Clin Endocrinol Metab 2006;91(9): 3317-3324.

Maybe TSH doesn't indicate thyroid function:
- Then what is being measured with higher TSH levels?
  - **INSULIN RESISTANCE**
  - Increased TSH levels are negatively associated with insulin sensitivity.
  - Fernandez-Real et al. Thyroid function is intrinsically linked to insulin sensitivity and endothelium-dependent vasodilation in healthy young people. J Clin Endocrinol Metab 2006;91(9): 3317-3324.

High TSH and Insulin Resistance
- The association is clear.
  - Evolutionary theory: Both conditions are similarly advantageous under similar environmental circumstances.
  - But which comes first?
    - Hypo-thyroid \(\rightarrow\) IR
    - IR \(\rightarrow\) hypo-thyroid

Insulin Resistance \(\rightarrow\) Higher TSH
- TSH levels were much higher in those with a MetS diagnosis.
  - IR was causally linked to the onset of enlarged thyroid and nodules in iodine deficient environments.
  - Measured as thyroid growth and nodules.
  - Measured as elevations in TSH.

CHD with high TSH is due to IR
- After a decade of associating high TSH to high CHD risk...
  - "CHD risk related to "hypothyroidism" and "sub-clinical hypothyroidism" is likely related to the present IR."

Subclinical hypothyroid & TSH
- Clinical trials to date have not consistently shown a beneficial effect of T4 treatment on serum lipids in "subclinical hypothyroid".
  - "Insulin resistance may be a contributing reason for abnormal lipid values."
TSH – a case of mistaken identity
- TSH likely rises secondary to insulin resistance. But it is not all from the top down!
- Peripheral conversion of thyroid hormone is likely more important than the thyroid cascade.
- → Enter DIO 1, 2 & 3.

DIO's & Peripheral Conversion
DIO = Iodothyronine Deiodinase
- Peripheral Tissue
  - DIO2 dependent: T4 → T3
  - DIO3 dependent: T4 → T3 & T3 → rT3 / T2
- T3 levels are 98% dependent upon these peripheral activators/deactivators

What are the DIO enzymes?
- The iodothyronine deiodinases (DIO) are selenocysteine-containing enzymes:
  - DIO1 is the least active
  - DIO2 is the primary intracellular activator of T3
  - DIO3 can prevent activation and/or deactivate T3
  - DIO3 enzyme irreversibly inactivates T3, or prevents T4 being activated, by removal of an inner ring iodine atom to generate T2 or rT3 respectively

DIO Enzymes are now seen as 1º
- The discovery of these new roles and mechanisms for the deiodinases indicates that tissue-specific deiodination plays a much broader role than once thought, involving developmental biology and metabolism.

Does T3 measure your metabolism
- It remains unclear which T3-responsive energetic processes are most relevant for the determination of basal metabolic rate
  - Bile acids increase post-prandially in the serum
  - BA’s signal the TGR5 receptor that secretes glp-1 and activate DIO2 in brown adipose tissue and muscle.
  - Ruh-roh! Another drug for type 2 DM that raises insulin? "These properties position TGR5 as an attractive and "drugable" mechanism for those with MetS"

Thyroid & Bile Acids & Insulin
In summary:
- After eating, when Bile acids release, there is an activation of T3, thereby raising tissue metabolic rates
  - the opposite of fasting/anorexia where T3 levels drop
- Bile acids stimulate the gut receptor that raises insulin.
  - Excess elevation of insulin is one of the first steps in insulin resistance!

DIO3/DIO2 & Insulin Resistance
- Deiodinase enzymes regulate:
  - Tissue-specific regulation of thyroid hormone metabolism via local and central control
  - Local adjustments to thyroid hormone action
  - Target gene transcription patterns
- There is a subsequent regulation of glucose homeostasis and insulin sensitivity.

What Slows T3 Metabolism?
- Negative caloric balance
- Intensive Exercise
- Elevations in stress neurotransmitters & elevations in serum cortisol.
- Many meds, surgeries & chronic illness
- Diabetes and insulin resistance
Why Slow T3 Metabolism?

- Preservation Theory: As you age, exercise, light stress, restrict calories, and respond to daily stresses, your thyroid activity compensates to help “preserve your capital.”
- Adaptive theory: As active metabolism is dominant during demanding exercise, T3 is metabolically most important.
- Inflammatory theory: DIO2 which activates T3 enhances cellular activity and thereby increases the cellular inflammatory response.

Preservation: TSH & Longevity

- Results simply indicate that those with the higher TSH and lower Free T4 and Free T3 levels were more likely to live the longest.
- Those with positive thyroid peroxidase antibodies were the exceptions.
- Therefore proper thyroid treatment should be initiated sooner if either finding is present.

Preservation: TSH & Longevity

- Elderly individuals with abnormally high levels of thyrotropin (TSH) do not experience adverse effects and may have a prolonged life span.
- In people over age 65, subclinical hypothyroidism is not associated with impairment of physical and cognitive function or depression.

Thyroid & Aging/Longevity

Who were the exceptions?

- Those with higher TSH levels (>8 mIU/L)
- Those with positive thyroid peroxidase antibodies

- Therefore proper thyroid treatment should be initiated sooner if either finding is present.

Preservation: T3 & Cal. Restriction

- Men & Women: 1800, 2400, 2800 kcal diet
- Calorically restrictive (CR) diets are associated with prolonged life span.
- In the 1800 kcal group, Free T3 levels were more likely to live the longest.
- Men & Women: 1800, 2400, 2800 kcal diet
- Results simply indicate that those with higher TSH and lower Free T4 and Free T3 levels were more likely to live the longest.

Preservation: T3 & Cal. Restriction

- Exercise! Your Active Metabolism

- Adaptive theory – as active metabolism is dominant during demanding exercise, T3 dependent resting metabolism can take a back seat.
- Thyroid Research 2013

Adaptive Theory: All Exercise

- Initially almost all hormones increase with the onset of better circulation.
- TSH, T4, FT4, FT3, Total T3 all increase.
- After 5’, as intensity increases, the TSH and T4 continue to stay elevated, but the T3 hormones decrease back to baseline.
- Adaptive theory: Aerobic ex.

Adaptive Theory: Aerobic ex.

- Basal metabolic rate unchanged after aerobic exercise x 12 weeks.
- Benefits: Free fatty acids were elevated in the exercise group, from the muscles utilization of fats for energy.
- The VO2Max for the exercisers improved.
- Circulating Free-Thyroxine (FT4) levels decreased in the exercise group!

Adaptive Theory: Aerobic ex.

- Exercise in Heat Slows Thyroid

- Elite Swimmers 120-140 pulse for 35 minutes.
- In 68, 78, 88 degree F water
- Free T3 and T3 did not change.
Adaptive Theory: Conditioning
- Athletes ran 75 km and 45 km.
- Pre & post workout T4, T3, TSH & rT3 levels.
- Younger and better-conditioned runners had stable T4, TSH, T3 levels.
- Older and less-conditioned athletes reacted to the stressful exert with decreased T4, T3 & TSH.
- The response was seen as exhaustion reaction.

Adaptive Theory: Stressful exer.
- Intensive exercise (II) was 90% of VO2 max while 90% at 40% VO2 max for 45'.
- Steady endurance exercise (SEE) was 45 min at 60-65% of VO2 max.
- Free T4, Free T3, Reverse T3 and cortisol.
- All hormones were up immediately post-exertion.
- 12 hours after: only II group had a persistent elevation of Reverse T3 and diminished Free T3.

Stress – A Model of Adaptation
- When extreme stress is placed upon the body...
- Increase in plasma cortisol & catecholamine.
- Over time, physical results in a reduction of pituitary-adrenal activation in response to exercise & stress.
- Although, highly trained athletes exhibit clinical mild hypercortisolism at baseline... AND...
- the proinflammatory cytokine, IL-6 is also activated.

The Thyroid Scapegoat
- Terms like “Sick”, “Bad”, “Hypo-” & “Depressed”, all present an unfortunate fall-guy.
- The findings/symptoms that lead a clinician or researcher to one of these terms can inappropriately label the thyroid gland with a disease that is, in fact, your brilliant adaptation.
- All too often, the researcher to one of these terms can easily fall-guy.

Tests That Signal Thyroid Problems
- TSH >6.0 mU/mL.
- If TPO Antibodies are elevated [Ref range <10]
- Past age 45, some hypothyroid findings on blood tests might be tolerable.
- Past age 65, some hypothyroid findings on blood tests might be tolerable.
- Although, highly trained athletes exhibit clinical mild hypercortisolism at baseline...

Insulin Resistance: The Blood Code
1. Complete Blood Count
2. Comprehensive Metabolic Panel
3. HgbA1C
4. Serum Insulin
5. Lipid Panel
6. Optional Vitamin D, Ferritin, CRP

“I have been and still am a seeker, but I have ceased to question stars and books; I have begun to listen to the teaching my blood whispers to me.”
Hermann Hesse, from Demian
The Blood Code – Step One

Dietary changes to implement
- Reduce CHO intake to your set-tolerance and replace with dietary fats and vegetables. Your CHO tolerance can be found at BloodCode.com.
- Reduce simple sugar and fructose.
- Assure micronutrient intake and adequate protein as building blocks for thyroid hormones and activators.
- Address underlying insulin resistance. The other side of the diet coin is fitness...
Implement Fitness – Daily!

Improve overall conditioning so stress is better tolerated. Not just stress from exercise, but from EVERYTHING.

If you need convincing, read


Implement Fitness – Daily!

Nutrient Needs for Thyroid balance

Nutrient Supplementation is to prevent deficiency, breach the threshold, not to treat or “normalize” your thyroid.

Iodine:
- USRDA = 120 mcg - Up to 290 mcg for lactation!
- Reasonable Adult Supplemental Range = 50-300 mcg

Selenium:
- USRDA = 50-70 mcg
- Reasonable Adult Supplemental Range = 50-200 mcg

Zinc:
- USRDA = about 10 mg - Up to 13 mg for lactation
- Reasonable Adult Supplemental Range = 10-15 mg

Vanadium – this is easy through any diet.
- USRDA = not established (diet contains 10-30 mcg)
- Adult Supplemental Range = 20 mcg-100 mcg

Iodine and TSH/DIO2 Too much?

- Iodine was given (rats) at normal, 3-fold, 6-fold, 10-fold, 50-fold quantities.
- Measurement of TSH levels and DIO2 levels and gene expressions in Blood and pituitary
- From 8 weeks onward in the study the 10-fold and 50-fold iodine uptake inhibits pituitary D2 activity and induces elevation of TSH levels.


Food Sources of Iodine

- Seaweed, whole or sheet, per 5 gram 10 - 2,400
- Cod, baked, 3 ounces 99
- Figues, dried, whole, 1 cup 75
- Iodized salt, fine, 1.5 g (1/4 tsp) 71
- Milk, 1 cup 56
- Shrimp, 3 ounces 35
- Sardines, 1 can 35
- Egg, 1 large 24
- There is no substantial iodine in red meats

Food Sources of Selenium

- Brazil nuts (6-8 nuts) 544
- Tuna, light, canned, 3 ounces 68
- Cod, cooked, 3 ounces 32
- Turkey, light meat,3 oz 27
- Baked, egg, 4 inch 27
- Chicken breast, meat only, 3 oz 24
- Beef chuck roast, 3 ounces 23
- Sunflower seed kernels, dry, 1 oz 23
- Ground beef, cooked, broiled, 3 oz 18
- Egg, whole, hard-boiled, 1 large 15

Food Sources of Zinc

- Oysters, which are the best source of zinc. 15-200 mg per 3 ounces.
- Red meat, poultry, seafood such as crab and lobsters, All are about 10-20 mg per 3 ounces.
- Beans, nuts, whole grains, contain about 3-8 mg per cup
- Dairy products provide minimal amounts

Food Sources of Vanadium

- #1 – Radishes - 80mcg per 3 ounces
- Shellfish & Fish
- Parsley, dill, black pepper
- Mushrooms
- Olives

Thyroid – Metabolism - Health

“The doctor has been taught to be interested not in health but in disease. What the public must be taught is that health is the cure for disease.”

Prevention is not the domain of the doctor.
Your vibrant and long life comes from regularly practicing & exercising your health.

- Thank You
  Dr. Richard Maurer
  TheBloodCode.com

Richard Maurer, ND  The Blood Code (c) and Maine Metabolism