Review of thyroid function

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If it helps, thyroid function and testing is hard for everyone – clinical scientists, physicians, researchers, etc. So don’t feel left out.

Introduction
What does the thyroid do and is it important?

Short answers: a lot and oh my, yes.

- T3 and T4 control the basal metabolic rate (energy).
  - Control of Body temperature
  - Pulse rate, cardiac output and other cardiac functions
  - Glucose metabolism, fat metabolism, protein degradation in tissues such as muscles and
  - Brain function (alertness, forgetfulness, balance, decision making, levels of concentration, etc.)
  - Growth in children; change in bone density in adults
  - and more
How does it do this?

It makes and stores to be released on demand three major compounds:

- Triiodothyronine ($T_3$)
- Tetraiodothyronine (thyroxine or $T_4$)
- Calcitonin (not going to mention again)
How

The thyroid hormones use iodine in their synthesis. This is the only place of important iodine concentration.

Iodine is found in:
- fish (such as cod and tuna),
- seaweed,
- shrimp and other seafood,
- enriched pasta,
- Dairy products (milk, eggs, etc.),
- beef,
- Bread made with iodized salt,
- iodized salt

Absorbed in the GI tract and stored in the thyroid.
Step 3

- A complicated feedback loop

- The brain makes a hormone called thyrotropin releasing factor (TRH). This stimulates the pituitary gland.

- The pituitary gland then makes the thyroid stimulating hormone (TSH). This tells the thyroid to make and release T3 and T4.
**Thyroid function**

- **TRH** – made in the brain in response to nerve signals (think cold/hot temperatures).
  - Stimulates
- **TSH** – made in the pituitary gland stimulates
- **T₃** and **T₄** – made in the thyroid
TRH responds to both the internal (ex., fever, dieting, emotional stress, inflammation, etc.) and external (temperature, stress, change in lifestyle) environments.

TSH stimulates the production of $T_3$ and $T_4$ until the need is met and then shut off.

If the need is not met (because the thyroid is not responding for some reason), then there is an increase in TSH.
Testing for most common situations

- **TRH testing is usually not done.**
  - Too low a concentration
  - Too difficult to interpret due to external issues

- **TSH testing is most often done**
  - Direct relationship with thyroid control
  - Can be used in diagnosis and monitoring therapy

- **T4 and T3 testing (comes in two forms free and bound)**
  - Are most important in diagnosis
  - But, by themselves, cannot discern if the problem resides in the thyroid or in the pituitary (lack of TSH production)
Testing for most common situations

**Typical**
- $\uparrow$TSH causes $\uparrow T_3$ and $T_4$
- $\downarrow$TSH causes $\downarrow T_3$ and $\downarrow T_4$

**Hyperthyroid**
- $\downarrow$TSH no TSH control $\uparrow T_3$ and $T_4$

**Hypothyroid**
- $\uparrow$TSH no response $\downarrow T_3$ and $\downarrow T_4$
Are there other weird situations?

Sure

Pituitary disease (source of TSH) can suppress TSH so it looks as if the thyroid is not working when it is simply not being stimulated.

\[ \downarrow \text{TSH} \quad \text{causes} \quad \downarrow \text{T}_3 \quad \text{and} \quad \downarrow \text{T}_4 \]

Medication such as some dopamine stimulating agents or cranial radiation can suppress TRH. Since we don’t test for this, this determination requires a physician to interpret.

\[ \downarrow \text{TRH} \quad \text{causes} \quad \downarrow \text{TSH} \quad \text{causes} \quad \downarrow \text{T}_3 \quad \text{and} \quad \downarrow \text{T}_4 \]
Are there other weird situations?

Sure

Hormones

- Need a binding protein to store the compound
- Need another binding protein to carry the hormone to the designated sites of action.
- Need correctly constructed binding sites on the target cells

- If any of these do not work correctly, then there are can too much or too little hormone action at the cell level.
- If there is a binding protein problem, can test for free $T_3$ & $T_4$

And this list can go on.
Are there other weird situations?

Most hormones need storage and carrier proteins.

- The major protein that stores the inactive T3 and the more active T4 is called thyroxin-binding globulin.
- Globulins are antigenic so it is possible to develop antibodies to the globulin. Hormones are made but not active since they are bound to damaged TBG. This results in a deficiency of T3 and T4 and causes an increase in TSH.
  - Can look a lot like hypothyroidism but isn’t.
  - Indeed the thyroid can be overworked if severe.

- TBG can be increased in liver disease and pregnancy.
  - Can look a lot like hyperthyroidism.
Are there other weird situations?

Most hormones need enzymes to be stored and liberated on need. Interference with these enzymes can cause problems.

- **Thyroid peroxidase antibodies**
  - **Hashimoto’s Disease** - This is an autoimmune disease and the most common cause of [hypothyroidism](#).
  - **Grave’s Disease** - This is also an autoimmune disease and the most common cause of [hyperthyroidism](#).
Most physicians will check the TSH on patients who have other conditions since the relationship between disease-states and the ability of the TRH, TSH, T3 and T4 to function correctly is very sensitive.
As people age, the relationship between the pituitary and thyroid gland can become compromised so as one ages, it is possible to have a hypothyroid condition which will enhance or mask a lot of signs and symptoms seen in other conditions, causing delays in diagnosis and treatment.