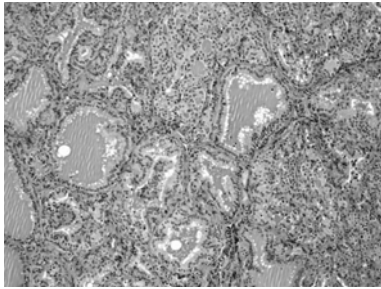
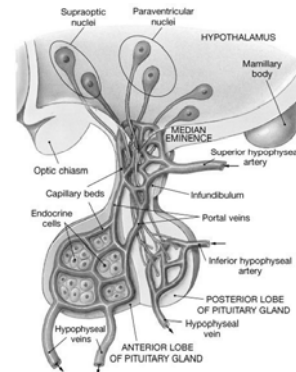


Thyroid Stimulating Hormone (Challenges)

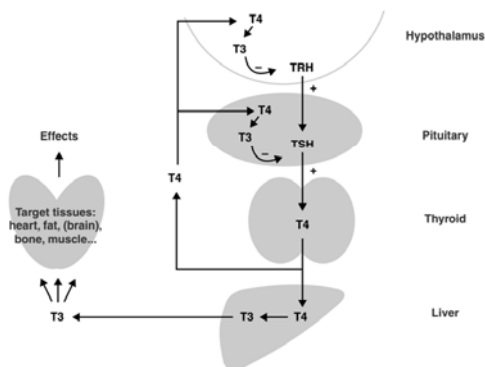


Mohammad Reza Bakhtiari *DCLS, PhD*

TSH Source



Hypothalamus-pituitary-thyroid-peripheral tissues axis



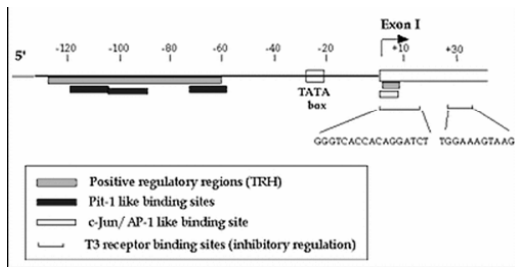
TSH Structure

Hetero



- TSH (28-30kDa) is a glycoprotein and consists of two subunits:
- The α (*alpha*) subunit
 - The gene is located on chromosome 6
 - The α chain has a 92-amino acid sequence.
 - nearly identical to hCG, LH, and FSH.
 - The α subunit is thought to be the effector region responsible for stimulation of adenylate cyclase (involved the generation of cAMP).
- The β (*beta*) subunit (TSHB):
 - The gene is located on 1
 - The β chain has a 118-amino acid sequence.
 - unique to TSH, and therefore determines its receptor specificity
- TSH secreted throughout life, particularly reaches high levels during the periods of rapid growth and development.

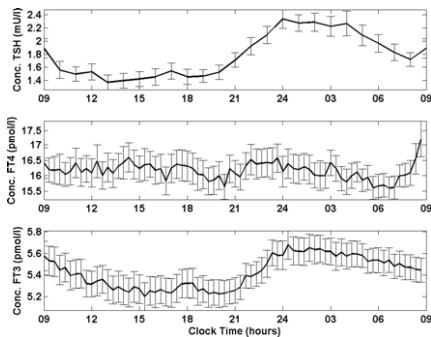
Regulatory regions of hTSH β gene



Important TSH Assay Issues

1. TSH Diurnal Rhythm
2. TSH Variability
3. Log-linear Relationship
4. Equilibrium Time
5. Antibody Interference
6. Method Dependency
7. TSH Reference Intervals
8. Pregnancy
9. Drugs
10. NTI

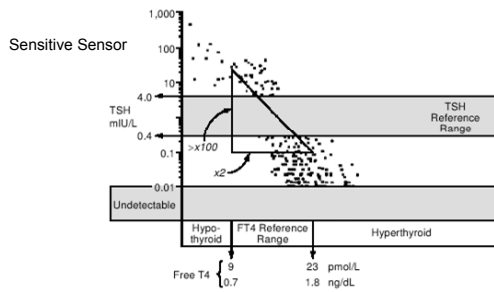
TSH Diurnal Rhythm



TSH Variability

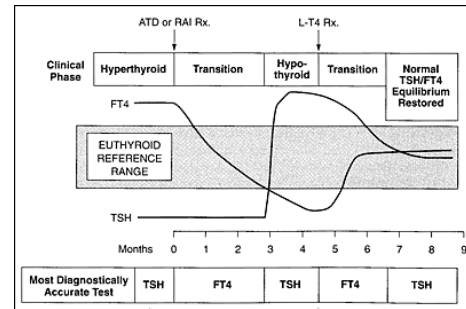
- Inter individual Variation: High 32%
- Intra individual Variation: Moderate 20%
- A wide population-based RI
- Serial determination in a person: $\geq \Delta 0.7$ mIU/L

Log-linear Relationship



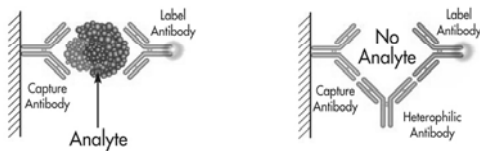
Equilibrium Time

Slow-back Sensor



Laboratory support for the diagnosis and monitoring of thyroid disease. *Thyroid 2003; 13:1-126.*

Antibody Interference False High TSH



TSH Assay Interference

(Heterophilic Antibodies Sources)

- Exposure to animals (e.g. animal technicians, veterinarians, animal handlers)
- Alternate animal contact therapy (e.g. thymic cells, sheep cells, embryonic cells)
- Exposure to animal products (e.g. food preparation)
- Special diets (e.g. cheese)
- Deliberate immunization (e.g. therapies, vaccinations, certain imaging treatments)
- Blood transfusions
- Autoimmune diseases
- Dialysis
- Patent medicines (OKT3)
- Maternal transfer
- Cardiac Myopathy
- G.I. Disease (E. Coli)
- **Rheumatoid factors can also act as heterophilic antibodies**

<http://scantibodies.com/nbr.html>

Antibody Interference

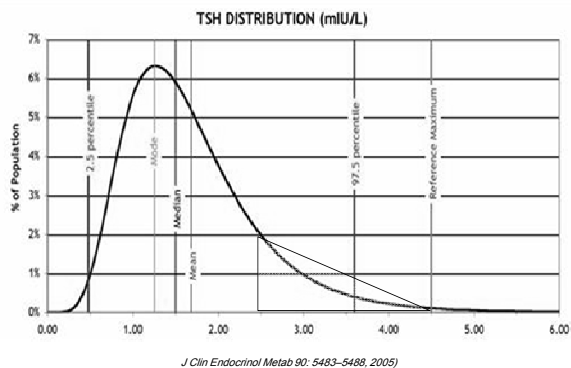
False LOW or High TSH

- TSH Auto Antibodies
- Measurement of Auto Abs

Method Dependency

- TSH Molecule Heterogeneity
- 10 % Variation among assays
 - Same method for TSH monitoring
- Reference Interval also method dependent
 - Applied only for the same method

TSH Reference Intervals

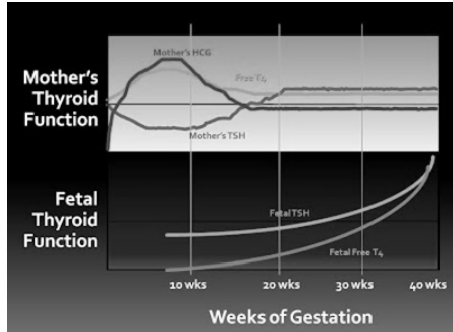


TSH Reference Intervals

- Higher prevalence of Abs for TSH 3.0 – 5.0 (Ab test)
- Progression to Overt Hypothyroidism
 - 2.5 %/year if Ab-
 - 4.5 %/year if Ab+
- Some proposed the upper cutoff= 3 or even 2.5 mIU/L
- 2004 Consensus: 0.45 – 4.5
- Still Controversial
- But Age Specific RI: for >70 years up to 6.0
- But Pregnancy RI according to ATA:
 - 1st T: 0.1 – 2.5
 - 2nd T: 0.2 – 3.0
 - 3rd T: 0.3 – 3.0

J Clin Endocrinol Metab 90: 5483–5488, 2005

Pregnancy Induced TFTs Changed

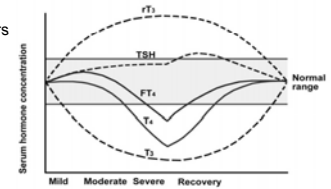


Non Thyroidal Illness (NTI)

Euthyroid sick syndrome

Some Examples

- Gastrointestinal diseases
- Pulmonary diseases
- Cardiovascular diseases
- Renal diseases
- Infiltrative and metabolic disorders
- Inflammatory conditions
- Myocardial infarction
- Starvation
- Sepsis
- Burns
- Trauma
- Surgery
- Malignancy
- Bone marrow transplantation



Drug Effects on TFTs

Table II. Effects of some drugs on thyroid function tests

Cause	Drugs	Effects
Inhibit thyroid hormone synthesis or release from the thyroid gland	Lithium, sulfonyleureas	↓ FT ₄ , ↓ FT ₃ , ↑ TSH
Decreases triiodothyronine hormone production by inhibiting peripheral conversion of FT ₄ to FT ₃	Glucocorticoids, propranolol, amiodarone, propylthiouracil	↓ FT ₃ leads to ↑ FT ₄
Stimulate TSH secretion	Iodine, lithium, dopamine antagonists, cimetidine	↑ TSH
Inhibit TSH secretion	Glucocorticoids, dopamine agonists, somatostatin	↓ TSH
Inhibit T ₄ and T ₃ binding to transport proteins	Phenytoin, sulfonyleureas, diazepam, furosemide, salicylates	↑ FT ₄ , ↑ FT ₃
Inhibit gastrointestinal absorption of ingested thyroid hormones for those on thyroid treatment	Cholestyramine, leucine sulfate, aluminum hydroxide, and secalate	↓ FT ₄ , ↑ TSH


The South African Medicines Formulary (SAMF), Vol 24, No 7 (2006)

In a case of Discordant or Anomalous Results (Conclusion)

After review of the clinical context, the following steps are helpful in evaluating anomalous thyroid results:

- Review of the medication history.
- Confirmation of serum TSH by an alternative method that identifies the degree of TSH suppression.
- Follow-up sampling to establish whether the abnormality is transient or persistent.
- An alternative estimation of serum free T₄, avoiding one-step methods that are known to frequently give spurious results, especially during critical illness.
- Measurement of serum total T₄ to establish whether the serum free T₄ estimate is disproportionately high or low, due to a pre-analytical or method-dependent artefact.
- Evaluation of the sample for possible heterophilic antibody interference; note that there are no established criteria that rule out such interference.
- Investigation of propositus and family members for evidence of unusual binding abnormalities or hormone resistance.

Clin Biochem Rev Vol 24 November 2003



Thank you for your Attention

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