Thyroid – Thy Accelerator

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The Good Lord made an Internal Combustion Engine and we called it the Vertebrate Body. The Lord then gave the body a hormoaccelerator to burn the fuel brighter and faster by fashioning a gland that like testis, sits just underneath the skin of the neck to detect the weather temperature, and accordingly scale up or scale down its working so that every part of the body responds accordingly. Thyroid, the texts declare, is NOT indispensable for life. But *sans* thyroid, life is no life, but a burdensome dread, in a blown up edematous body, devoid of that divine spark in the eyes. Thyroid, through its so-called T_3, T_4 is the fine tuner of the pace of human life.

The Greeks of ancient times used a full body shield that had a notch at its top to accommodate the chin. Galen felt that the largest cartilage of the larynx has a similar shape, and named it the thyroid cartilage. The thyroid resting over it and the trachea, and having similar shape got similar name. And what thyroid gland poured into your circulation got christened as thyroxin.

Two Nobelists are associated with the evolution of thyroid science. Kocher of Switzerland pioneered successful thyroid surgery in 1876 and then went on to do 43,000 thyroidectomies, designing incisions and instruments, to be rightly called the Father of thyroid surgery and Nobeled in 1909, one of the few surgeons so honoured in Nobel history. The other K is Kendall of Mayo Clinic who isolated thyroxin hormone, and then worked on corticoids to earn the Nobel therefore in 1950.

Human thyroid through all the rough and tumble of life, stays on track, making the body prosper, mind sparkle, and the soul ponder. Its heady link to the hypothalamous and the pituitary is a highly delicate servomechanism that involves the thyroid itself regulating the higher centers which in turn monitor the thyroid output. Hence the commonality of T_3, T_4 and TSH in most of thyroid biochemical studies. The rewarding parts of thyroid functional hypes and hypos are the wide array of drugs/isotopes/surgery available to euthyroidize the patient. The latest *Current Diagnosis and Treatment*, 2008, now in its 47th edition, has a formidable list of psychic/somatic/therapeutic states which can make an innocent euthyroid as hyper or hypo, and more tragically treated for the same. So thyroid diagnosticians beware, for, to you your diagnosis is only a *word*, but for the patient it may turn out to a *sentence*.

A Christian in Old French is *Chretien* which ended up as *cretin*, on account of some interesting history: "The Arian refugees settled in the Pyrenees and because of their persecution retired into remote valleys. As a result of restricted diet, isolation, intermarriage, etc., as well as deficient iodine content in the food, children were often of a peculiar stunted body with backward minds -a condition later known to be associated with thyroid deficiency. The term chretien for this kind of Christian seems to have developed as a term of contempt and was applied to other children of the same kind in other localities. Paracelsus was first to point out the relation between goitrous parents and children who were cretins. Wolfgang Hoefer described cretinism in 1657. The word appeared in English in 1779." Myx-/Myxo means mucus and the condition was used by Gull in 1873 to connote "Infiltration of the tissues with a substance like mucus." In myxoedema he saw adult cretinism for he wrote "On a cretinoid state supervening in adult life in women." It was Ord who, in 1877, coined the term myxoedema to connote

"mucous dropsy" of the skin. The first definitely successful attempt at endocrine therapy of myxoedema was made by Murray in 1891, and reported in the *BMJ* in 1892 as "Remarks on the treatment of myxoedema with thyroid juice." In 1835, Graves published an account of exophthalmic goiter in *London Med Sur Journal*, which was such an admirable one that Trousseau, a great admirer of Graves, proposed that the condition (of primary hyperthyroidism, or exophthalmic goiter) be named Grave's disease.

Some parting words about thyroid tumors. Generalized thyroid enlargement, called goiter is traceable to guttur or guttural meaning the throat. Juvenal, great Roman satirical poet, wrote, in 1st centuryA.D. as to "Who wonders at goiter in the Alps?" Goitre was located in the thyroid in the 18th century. Localized enlargement of thyroid is often described as a nodule, or if nodules are multiple, as nodular goiter. They behave benignly, both structurally and functionally. We have under us a male, now of 63, who first came to us in 1981, with retrosternal highly stuck medullary carcinoma of the thyroid. It was nibbled at, at the famed Sloane Kettering, in 1982. Since then the gentleman has carried with him, and now the so-called tumor is seen at multiple places. Yet his life, his marriages, his travels go on. A medically-declared malignant thyroid can behave as providentially benign.

Thyroid Function

Abstract: Evaluation of the presence of thyroid auto-antibodies (anti-microsomal or anti-TPO antibodies) and anti-thyroglobulin (anti-Tg) may be helpful in determining the aetiology of hypothyroidism or in predicting future hypothyroidism. Anti-TPO antibody testing may also help to diagnose Hashimoto's thyroiditis as an aetiology of primary failure.

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In patients with non-thyroid disease who are severely ill, TSH secretion is decreased, T4 levels are decreased, and T3 levels are markedly decreased. In these patients, the primary abnormality is the decreased peripheral production of T3 from T4. Other abnormalities seen in patients who are critically ill include decreased TBG levels and abnormalities in the hypothalamic-pituitary axis.

The TRH stimulation test is rarely needed now because of improved TSH assays. It may still be helpful to confirm hypothyroidism based on an exaggerated TSH response in patients who have a low free T4 level and a normal TSH level. In patients with hypothalamic or pituitary thyroid dysfunction, TSH levels do not increase in appropriate relation to the low free T4 levels. The absolute levels may be in the normal or even slightly-elevated range but inappropriately low for the severity of the hypothyroid state.

Assays

Commonly asked assays for thyroid functions are:
T3, T4 and TSH and.
Free T3, Free T4 and TSH
TSH alone is enough for monitoring treatment of hypothyroidism.
Free T4 index when TSH levels are not diagnostic enough.
In most healthy patients, TSH values are 0.5-1.5

mU/L, but reference ranges vary up to 5 mU/L. TSH levels peak in the evening and are lowest in the afternoon, with marked variations due to physiologic conditions such as illness, psychiatric disorders, and low energy intake. Age guidelines for age related reference ranges for TSH

Age Reference	Range
Cord blood	2.0- 40.0 µIU/ml
1-6 days	0.4-15.0 µIU/ml
1 week to 1 year	0.4-10.0 µIU/ml
1 year and above	0.4-5.5 µIU/ml

TEST METHOD: Chemiluminiscence

If TSH levels are above the reference range, perform a surrogate assessment of free hormone levels using additional tests. A free T4 test is recommended over a total T4 test or other measurement because it is not affected by thyroid hormone binding proteins. If free T4 assays are unavailable or unreliable, a free thyroxine index (FTI) serves as a surrogate of the free hormone level. Free thyroid hormone levels can be estimated by calculating the percentage of available thyroid hormone-binding sites (T3 resin uptake) or by measuring the concentration of thyroxine-binding globulin (TBG). The FTI is the product of the T3 resin uptake and total T4 levels.

Patients with primary hypothyroidism have elevated TSH levels and decreased free-hormone levels. Patients with elevated TSH levels but normal free-hormone levels or estimates are considered to have sub-clinical hypothyroidism. Hypothyroidism is virtually the only disease that is characterized by sustained, rising TSH levels. As the TSH level increases early in the disease, an increased conversion of T4 to T3 occurs, which maintains T3 levels. In early hypothyroidism, TSH levels are increased, T4 levels are normal to low, and T3 levels are normal.

Very low TSH concentrations do not always indicate hyperthyroidism in the following conditions: Treated Gravers' disease. Euthyroid nodular goitre and some autonomous adenoma. Some systemic diseases. Certain drugs, eg high-dose corticosteroids. In hyperthyroidism, TSH may remain within the reference range in the presence of heterophilic antibodies.

DISADVANTAGES OF TSH ESTIMATION ALONE

- The measurement of TSH alone will not detect rare forms of hypothyroidism caused by pituitary dysfunction. The signs and symptoms of hypothyroidism are often minor in these cases; usually the first sign is gonadotrophin deficiency.
- No information is obtained as regards the active hormone (T4 or T3).
- In hospitalized patients with severe systemic illnesses TSH concentration may temporarily be abnormal (either decreased or increased) without coexisting thyroid disease. In these cases, the concentration of free T4 will often be close to the lower limit of the reference range.
- TSH measurements change slowly over 4 - 6 weeks. If any changes are evident, free T4 should also be measured.

HISTOLOGIC FINDINGS

- Auto-immune thyroiditis causes a decrease in intra-thyroidal iodine stores, an increased iodine turnover and defective organification.
- Chronic inflammation of the gland causes progressive destruction of the functional tissue with widespread infiltration by lymphocytes and plasma cells with epithelial cell abnormalities. In time, dense fibrosis and atrophic thyroid follicles replace the initial lymphocytic hyperplasia and vacuoles.
- Functional tissue destruction and infiltration may also be caused by previous administration of radioiodine, surgical fibrosis, metastasis, lymphomatous changes, sarcoidosis, tuberculosis, amyloidosis, cystinosis, thalassaemia, and Reidel's thyroiditis.

MONITORING REPLACEMENT THERAPY

- TSH is the most important test to be used. It is acceptable to have TSH concentration close to the lower limit of the reference range, if free T4 is within the reference range and the patient has no symptoms of hyperthyroidism.

- When the treatment for hypothyroidism has been established, measurements every few years will suffice.
- The increased risk of auto-immune diseases must be borne in mind.
- Thyroxine medication must not be taken on the morning of the day when free T4 and TSH are to be measured.

PROCEDURES

- FINE-NEEDLE ASPIRATION BIOPSY: Thyroid nodules are often found incidentally during physical examination, chest radiograph, CT scan, or MRI, Thyroid nodules can be found in patients who are hypothyroid, euthyroid, or hyperthyroid.
- Fine-needle aspiration (FNA) biopsy is the procedure of choice to evaluate suspicious nodules.
- About 5-6% of solitary nodules are malignant. Suspicious nodules are those that are larger than 1 cm in diameter or those with suspicious features found on a sonogram (eg irregular margins, intranodular vascular spots, microcalci-fications).

Hyperthyroidism

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ABSTRACT: Thyrotoxicosis is the hypermetabolic condition associated with elevated levels of free thyroxine (FT4), free triiodothyronine (FT3), or both. Hyperthyroidism is a subset of thyrotoxicosis (excludes exogenous thyroid hormone intake and sub-acute thyroiditis) that is caused by excess synthesis and secretion of thyroid hormone by the thyroid. The most common forms of hyperthyroidism include diffuse toxic goitre (Graves' [Basedow's] disease), toxic multi-nodular goitre (Plummer's disease), and toxic adenoma. Together with sub-acute thyroiditis, these conditions constitute 85-90% of all causes of thyrotoxicosis.

AETIOLOGY

- GENETICS: Auto-immune thyroid disease and Graves' disease have a higher prevalence in patients with human leucocyte antigen (HLA)-DRw3 and HLA-B89.
- IODINE INTAKE: Clearly, patients in borderline iodine-deficient areas of the world develop nodular goitre, often with areas of autonomy. When this population is moved to areas of sufficient iodine intake, thyrotoxicosis occurs. Evidence that iodine can act as an immune stimulator exists, precipitating auto-immune thyroid disease and acting as a substrate for additional thyroid hormone synthesis.

APPROACH TO THE PATIENT

- HISTORY

Common Symptoms of Thyrotoxicosis

- Nervousness
- Anxiety
- Increased perspiration
- Heat intolerance
- Tremor
- Hyperactivity
- Palpitations
- Weight loss
- Oligomenorrhoea.

COMMON SIGNS OF THYROTOXICOSIS INCLUDE THE FOLLOWING

- Hyperactivity
- Tachycardia or atrial arrhythmia
- Systolic hypertension
- Warm, moist, and smooth skin
- Stare
- Tremor
- Muscle weakness.

It is important to carefully record a family history of auto-immune disease, thyroid disease, and whether the patient has migrated from an iodine-deficient area.

Review a complete list of medications the patient

is taking. Several medications contain large amounts of iodine, including expectorants, amiodarone, health food supplements containing seaweed, and iodinated contrast dyes, that can induce thyrotoxicosis in a patient with thyroid autonomy.

Rarely, iodine exposure can cause thyrotoxicosis in a patient with an apparently healthy thyroid.

On Examination

- Thyroid Examination: Thyrotoxicosis due to Grave's disease is associated with a diffusely enlarged and slightly firm thyroid gland. Sometimes, a thyroid bruit is audible using the bell of the stethoscope.

Toxic multinodular goitres occur in goitres that are generally enlarged to at least 2- 3 times normal size. The gland is often soft, but individual nodules occasionally can be palpated.

If the thyroid is enlarged and painful, the diagnosis is likely sub-acute painful or granulomatous thyroiditis, but consider degeneration or haemorrhage into a nodule or suppurative thyroiditis.

- Thyroid-Specific Physical Examination: Grave's thyrotoxicosis may be associated with mild thyroid ophthalmopathy in 50% of patients.

Often, it is manifested only by periorbital oedema, but it also can include conjunctival oedema (chemosis), injection, poor lid closure, extra-ocular muscle dysfunction (diplopia), and proptosis. Evidence of thyroid eye disease and high thyroid hormone levels confirms the diagnosis of auto-immune Graves' disease. Graves' disease rarely can affect the skin by deposition of glycosaminoglycans in the dermis of the lower leg. This causes non-pitting oedema, usually associated with erythema and thickening of the skin.

- Signs Of Thyrotoxicosis: Usually, signs upon physical examination include sinus tachycardia, atrial fibrillation, systolic hypertension, soft smooth skin, excessive perspiration, palmar erythema and sweating, lid lag, extension tremor, hyperkinesis, and large-muscle weakness.

Investigations: Laboratory evaluation of thyrotoxicosis

- The most reliable screening measure of thyroid function is a TSH level.
- TSH levels usually are suppressed to unmeasurable levels (0.05 mIU/mL) in thyrotoxicosis.
- Third-generation TSH assays are recommended for screening purposes.
- The degree of thyrotoxicosis cannot be estimated easily from the TSH level and must be measured using an assay of thyroid hormone levels in the plasma.
- Measuring free T4 (and T3 if T4 levels are normal) is recommended in patients with suspected thyrotoxicosis when TSH is low.
- Thyroid Auto-Antibodies: The most specific auto-antibody for auto-immune thyroiditis is an enzyme-linked immunosorbent assay (ELISA) for anti-TPO antibody (thyroper-oxidase). The titres usually are significantly elevated in the most common type of hyperthyroidism (Graves' thyrotoxicosis) and usually are low or absent in toxic multi-nodular goitre and toxic adenoma.
- Nuclear Thyroid Scintigraphy Iodine 123 (I-123) Uptake And Scan: If the aetiology is not clear after physical examination and other laboratory tests, the aetiology of thyrotoxicosis can be confirmed by an I-123 uptake.
- Values are elevated in patients with Graves' disease and toxic multi-nodular goitre. Both I-123 and technetium-99m can be used for thyroid scanning, which provides anatomic information on the type of goitre (eg diffuse vs nodular). Scans essentially are pictures of the thyroid and do not necessarily confirm or refute the presence of hyperthyroidism per se; only I-123 uptake provides information in this area.
- Hyperthyroidism in older patients often presents with atrial arrhythmias or CHF. ECG is recommended, if an irregular heart rate or CHF is noted upon examination.

Management

➢ **Treatment**

o With the exception of low I-123 uptake hyperthyroidism (eg subacute thyroiditis), the treatment of hyperthyroidism includes symptom relief and therapy with anti-thyroid medications, therapy with radioactive iodine-131 (I-131), or thyroidectomy.

➢ **Symptom Relief**

o Many of the neurological and cardiovascular symptoms of thyrotoxicosis are relieved by beta blocker therapy.

o Prior to therapy, examine the patient for signs and symptoms of dehydration that often occur with hyperthyroidism. After oral rehydration, beta blocker therapy can be started.

o Do not administer beta blocker therapy to a patient with a significant history of asthma. Calcium channel blockers can be used for the same purposes when beta blockers are contraindicated or poorly tolerated.

➢ **Anti-Thyroid Drugs**

o Anti-thyroid drugs (eg methimazole, propylthiouracil) have been used for hyperthyroidism since they were introduced in the 1940s.

o These drugs inhibit multiple steps in the synthesis of T4 and T3, leading to a gradual reduction in thyroid hormone levels over 2-8 weeks or longer. Titrate the antithyroid drug dose every 4 weeks until thyroid functions normalize.

o Some patients with Grave's disease go into a remission after treatment for 12-18 months, and the drug can be discontinued. Notably, half the patients who go into remission have another recurrence of hyperthyroidism within the following year.

o The antithyroid medications are used for the long-term control of hyperthyroidism in children, adolescents, and pregnant women (propylthiouracil only for pregnancy).

o In women who are not pregnant, the medications are used to control hyperthyroidism prior to definitive therapy with radioactive iodine.

o Methimazole is a more potent and longer-acting drug. Often, patient compliance is better with methimazole taken once or twice daily than with propylthiouracil given 3 or 4 times daily.

o Propylthiouracil often is the drug of choice in severe thyrotoxicosis because of the additional benefit of inhibition of T4 to T3 conversion. Administer propylthiouracil every 6-8 hours. The reduction in T3, which is 20-100 times more potent than T4, theoretically helps reduce the thyrotoxic symptoms more quickly than methimazole.

Adverse Effects Of Antithyroid Medications

➢ The Most Common Effects Are: Allergic reactions of fever, rash, urticaria, and arthralgia, which occur in 1-5% of patients usually within the first few weeks of treatment.

➢ Serious Adverse Effects Include: Agranulocytosis, aplastic anaemia, hepatitis, polyarthritis, and a lupus-like vasculitis. All of these adverse effects, except agranulocytosis, occur more frequently with propylthiouracil. Agranulocytosis occurs in 0.2-0.5% of patients, with an equal frequency for both drugs.

➢ Other Drugs: In severe thyrotoxicosis from Graves' (Basedow's) disease or sub-acute thyroiditis, iodine or iodinated contrast agents have been administered to block T4 conversion to T3 and the release of thyroid hormone from the gland.

Radioactive Iodine Therapy

➢ This is the most common treatment for hyperthyroidism in adults.

➢ Although the effect is less rapid than anti-thyroid medication or thyroidectomy, it is effective, safe, and does not require hospitalization. It is administered orally as a single dose, in capsule or liquid form. The radioactive iodine is quickly absorbed and taken up by the thyroid. No other tissue or organ in the body is capable of retaining the radioactive iodine and, therefore, very few adverse effects are associ-

ated with this therapy.

- The treatment results in a thyroid-specific inflammatory response, causing fibrosis and destruction of the thyroid over weeks to many months.
- Generally, the dose of I-131 administered is 75-150 mCi per gram of estimated thyroid tissue divided by the percent of I-123 uptake in 24 h.
- This dose is intended to render the patient euthyroid. Higher doses of I-131 sometimes are used to intentionally induce hypothyroidism, allowing the patient to be managed for hypothyroidism alone.
- Hypothyroidism is considered by many experts to be the expected goal of radioactive iodine therapy. In several large epidemiological studies of radioactive iodine therapy in patients with Graves' disease, no evidence indicated that radioactive iodine therapy caused the development of thyroid carcinoma. No evidence of increased mortality exists for any other form of cancer, including leukaemia, with radioactive iodine therapy of hyperthyroidism.
- Radioactive iodine is never administered to pregnant or lactating women.
- Radioactive iodine can cross the placenta and be excreted into milk, which can ablate the infant's thyroid and result in hypothyroidism. Checking for pregnancy prior to radioactive iodine therapy and suggesting that the patient not become pregnant for at least 3-6 months after the treatment and until thyroid functions are normal are standard practice.
- Radioactive iodine usually is not administered to patients with severe ophthalmopathy because clinical evidence suggests that usually mild, but occasionally severe worsening of thyroid eye disease occurs after radioactive iodine therapy.

Surgical Care

- Subtotal thyroidectomy is the oldest form of treatment for hyperthyroidism.
- Total thyroidectomy and combinations of hemithyroidectomies and contralateral subtotal thyroidectomies also have been used.

Thyroidectomy is Reserved For Special Circumstances, including The Following

- Severe hyperthyroidism in children.
- Pregnant women who are non-compliant or intolerant of antithyroid medication.
- Patients with very large goitres or severe ophthalmopathy.
- Patients who refuse radioactive iodine therapy.
- Refractory amiodarone-induced hyperthyroidism.
- Patients who require normalization of thyroid functions quickly, such as pregnant women, women who desire to become pregnant within the next 6 months, or patients with unstable cardiac conditions.
- Preoperative preparation includes anti-thyroid medication, stable (cold) iodine treatment (to decrease gland vascularity), and beta blocker therapy.
- Adverse effects of therapy include recurrent laryngeal nerve damage and hypoparathyroidism due to damage of local structures during surgery.

Have a look.....things you may not know....

- The most common name in the world is MOHAMMED.
- Coca-Cola was originally green.
- The name of the entire continents end with the same letter that they start with.
- The strongest muscle in the body is the tongue.
- There are two credit cards for every person in the United States.