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Editorial

A **goitre** or **goiter** is a swelling in the neck resulting from an enlarged thyroid gland. A goitre is associated with a thyroid that is not functioning properly.

Worldwide, over 90% of goitre cases are caused by iodine deficiency. The term is from the Latin *gutteria*. Most goitres are of a benign nature.

A goitre, associated with hypothyroidism or hyperthyroidism, may be present with symptoms of the underlying disorder. For hyperthyroidism, the most common symptoms are associated with adrenergic stimulation: tachycardia (increased heart rate), palpitations, nervousness, tremor, increased blood pressure and heat intolerance. Clinical manifestations are often related to hypermetabolism, (increased metabolism), excessive thyroid hormone, an increase in oxygen consumption, metabolic changes in protein metabolism, immunologic stimulation of diffuse goitre, and ocular changes (exophthalmos). Hypothyroid individuals may have weight gain despite poor appetite, cold intolerance, constipation and lethargy. However, these symptoms are often non-specific and make diagnosis difficult.



As the main section talks about Goiter so “**INTERPRETATION**” discreetly outlines Thyroid Function Tests for you. Consequently, “**TROUBLE SHOOTING**” highlights ELISA tests that are used for performing THYROID FUNCTION TESTS.

BOUQUET is an integral part of this communiqué and has not been ignored. Happy reading.

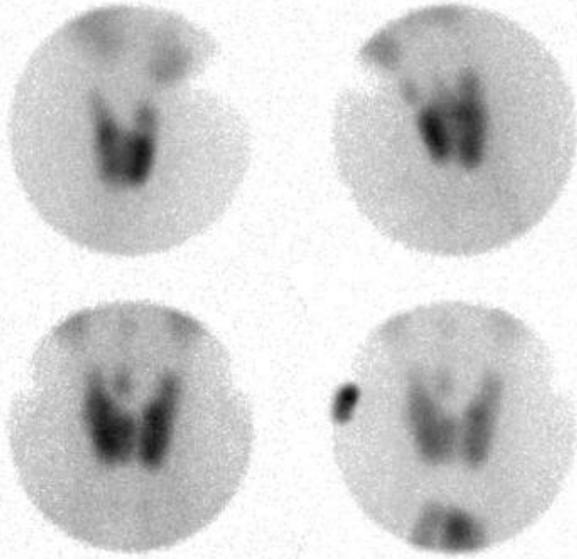


DISEASE DIAGNOSIS

GOITER

Background

In 1656, Thomas Wharton described the distinct nature of what he termed the thyroid gland, distinguishing it from the larynx, as this structure had been considered a laryngeal gland from the time of Andreas Vesalius in the 16th century. It was nearly 200 more years before the function of the thyroid was elucidated. The normal adult thyroid gland weighs 10-25 g and has 2 lobes connected by an isthmus. Nearly 50% of thyroid glands exhibit a pyramidal lobe arising from the center of the isthmus. Longitudinal dimensions of the lobes of the thyroid range up to 5 cm, as shown in the image below.



Thyroid nuclear scan of a patient with a euthyroid goiter showing different projections.

A goiter is an enlarged thyroid gland, and it may be diffuse or nodular. A goiter may extend into the retrosternal space, with or without substantial anterior enlargement. Because of the anatomic relationship of the thyroid gland to the trachea, larynx, superior and inferior laryngeal nerves, and esophagus, abnormal growth may cause a variety of compressive syndromes. Thyroid function may be normal (nontoxic goiter), overactive (toxic goiter), or underactive (hypothyroid goiter).

Pathophysiology

The thyroid gland is controlled by thyroid-stimulating hormone (TSH; also known as thyrotropin), secreted from the pituitary gland, which in turn is influenced by the thyrotropin-releasing hormone (TRH) from the hypothalamus. TSH permits growth, cellular differentiation, and thyroid hormone production and secretion by the thyroid gland. Thyrotropin acts on TSH receptors located on the thyroid gland. Thyroid hormones are synthesized from iodination of tyrosine. The iodine is transported from plasma into the thyroid cell via a sodium-iodide symporter. This is an active process resulting in an intracellular iodine level exceeding 20 times the plasma iodine level. This iodine transport activity is controlled by TSH. Serum thyroid hormones levothyroxine and triiodothyronine feed back to the pituitary, regulating TSH production. Interference with this TRH-TSH thyroid hormone axis causes changes in the function and structure of the thyroid gland. Stimulation of the TSH receptors of the thyroid by TSH, TSH-receptor antibodies, or TSH receptor agonists,

such as chorionic gonadotropin, may result in a diffuse goiter. When a small group of thyroid cells, inflammatory cells, or malignant cells metastatic to the thyroid is involved, a thyroid nodule may develop. A deficiency in thyroid hormone synthesis or intake leads to increased TSH production. Increased TSH causes increased cellularity and hyperplasia of the thyroid gland in an attempt to normalize thyroid hormone levels. If this process is sustained, a goiter is established. Causes of thyroid hormone deficiency include inborn errors of thyroid hormone synthesis, iodine deficiency, and goitrogens. A goiter may result from a number of TSH receptor agonists. TSH receptor stimulators include TSH receptor antibodies, pituitary resistance to thyroid hormone, adenomas of the hypothalamus or pituitary gland, and tumors producing human chorionic gonadotropin.

Epidemiology

Frequency

International

Worldwide, the most common cause of goiter is iodine deficiency. It is estimated that goiters affect as many as 200 million of the 800 million people who have a diet deficient in iodine. In the Wickham study from the United Kingdom, 16% of the population had a goiter. In a German study, 635 people underwent ultrasonographic thyroid screening, as well as basal TSH measurement, during a preventive-health checkup. Thyroid nodules were detected in 432 (68%) of the persons screened; in a previous German study, ultrasonographic screening of more than 90,000 people detected thyroid nodules in 33% of the normal population. The authors of the latter report attributed this difference to the fact that patients in their study were screened using 13 MHz ultrasonographic scanners, which were more sensitive than the 7.5 MHz scanners used in the previous study. According to the investigators, their results indicated that the question of routine iodine supplementation requires renewed attention. The incidence of thyroid cancer has been rising worldwide. The reasons are unclear, but this trend may be related to better detection and diagnostic methods.

Mortality/Morbidity

Most goiters are benign, causing only cosmetic disfigurement. Morbidity or mortality may result from compression of surrounding structures, thyroid cancer, hyperthyroidism, or hypothyroidism.

Race

No racial predilection exists.

Sex

The female-to-male ratio is 4:1.

- In the Wickham study, 26% of women had a goiter, compared to 7% of men.
- Thyroid nodules are less frequent in men than in women, but when found, they are more likely to be malignant.

Age

The frequency of goiters decreases with advancing age. The decrease in frequency differs from the incidence of thyroid nodules, which increases with advancing age.

Prognosis

Benign goiters have a good prognosis. However, all goiters should be monitored by examination and biopsy for possible malignant transformation, which may be signaled by a sudden change in size, pain, or consistency. Fortunately, the risk of this is low. In patients exposed to low levels of radiation the risk rises. Based on the Wickham study, a few of the goiters increased in size. A small percentage of multinodular goiters do cause hyperthyroidism. Lifelong surveillance is necessary.

Patients with chronic lymphocytic thyroiditis generally have glands that become atrophic.

Patient Education

Educate a patient about potential etiologies, eg, adequate dietary iodine intake, avoidance of goitrogens, regular personal neck examination, and physician examination. For patients on medical therapy, reinforce the need to take medications on a regular basis. Review symptoms of hyperthyroidism.

Goiter Clinical Presentation

History

A goiter may present in various ways, including the following:

- Incidentally, as a swelling in the neck discovered by the patient or on routine physical examination
- A finding on imaging studies performed for a related or unrelated medical evaluation
- Local compression causing dysphagia, dyspnea, stridor, plethora or hoarseness
- Pain due to hemorrhage, inflammation, necrosis, or malignant transformation
- Signs and symptoms of hyperthyroidism or hypothyroidism
- Thyroid cancer with or without metastases

Physical

The general examination for hyperthyroidism, hypothyroidism, and autoimmune stigmata is followed by systematic examination of the goiter. A retrosternal goiter may not be evident on physical examination. Examination of the goiter is best performed with the patient upright, sitting or standing. Inspection from the side may better outline the thyroid profile, as shown below. Asking the patient to take a sip of water facilitates inspection. The thyroid should move upon swallowing. See the image below.



Patient with a goiter. Prominent side-view outline.

Palpation of the goiter is performed either facing the patient or from behind the patient, with the neck relaxed and not hyperextended. Palpation of the goiter rules out a pseudogoiter, which is a prominent thyroid seen in individuals who are thin. Each lobe is palpated for size, consistency, nodules, and tenderness. Cervical lymph nodes are then palpated. The oropharynx is visualized for the presence of lingular thyroid tissue.

The size of each lobe is measured in 2 dimensions using a tape measure. Some examiners make tracings on a sheet of paper, which is placed in the patient's chart. Suitable landmarks are used and documented to ensure consistent measurement of the thyroid gland. The pyramidal lobe often is enlarged in Graves disease. A firm rubbery thyroid gland suggests Hashimoto thyroiditis, and a hard thyroid gland

suggests malignancy or Riedel struma. Multiple nodules may suggest a multinodular goiter or Hashimoto thyroiditis. A solitary hard nodule suggests malignancy, whereas a solitary firm nodule may be a thyroid cyst. Diffuse thyroid tenderness suggests subacute thyroiditis, and local thyroid tenderness suggests intranodal hemorrhage or necrosis. Cervical lymph glands are palpated for signs of metastatic thyroid cancer. Auscultation of a soft bruit over the inferior thyroidal artery may be appreciated in a toxic goiter. Palpation of a toxic goiter may reveal a thrill in the profoundly hyperthyroid patient.

Goiters are described in a variety of ways, including the following:

- Toxic goiter: A goiter that is associated with hyperthyroidism is described as a toxic goiter. Examples of toxic goiters include diffuse toxic goiter (Graves disease), toxic multinodular goiter, and toxic adenoma (Plummer disease).
- Nontoxic goiter: A goiter without hyperthyroidism or hypothyroidism is described as a nontoxic goiter. It may be diffuse or multinodular, but a diffuse goiter often evolves into a nodular goiter. Examination of the thyroid may not reveal small or posterior nodules. Examples of nontoxic goiters include chronic lymphocytic thyroiditis (Hashimoto disease), goiter identified in early Graves disease, endemic goiter, sporadic goiter, congenital goiter, and physiologic goiter that occurs during puberty.

Autonomously functioning nodules may present with inability to palpate the contralateral lobe. Unilobar agenesis may also present like a single thyroid nodule with hyperplasia of the remaining lobe. The Pemberton maneuver raises a goiter into the thoracic inlet when the patient elevates the arms. This may cause shortness of breath, stridor, or distention of neck veins.

Causes

The different etiologic mechanisms that can cause a goiter include the following:

- Iodine deficiency
- Autoimmune thyroiditis - Hashimoto or postpartum thyroiditis
- Excess iodine (Wolff-Chaikoff effect) or lithium ingestion, which decrease release of thyroid hormone
- Goitrogens
- Stimulation of TSH receptors by TSH from pituitary tumors, pituitary thyroid hormone resistance, gonadotropins, and/or thyroid-stimulating immunoglobulins
- Inborn errors of metabolism causing defects in biosynthesis of thyroid hormones
- Exposure to radiation
- Deposition diseases/infiltrative disease
- Thyroid hormone resistance (pituitary thyroid hormone resistance with resultant elevated TSH)
- Subacute thyroiditis (de Quervain thyroiditis)
- Silent thyroiditis
- Riedel thyroiditis
- Infectious agents
 - Acute suppurative - Bacterial
 - Chronic - Mycobacteria, fungal, and parasitic
- Granulomatous disease
- Thyroid malignancy
- Low selenium levels: This may be associated with goiter prevalence.

Goiter Differential Diagnoses

Differential Diagnoses

- Anaplastic Thyroid Carcinoma
- Branchial Cleft Cyst

- Carotid Artery Aneurysm
- Lymphatic Malformation (Cystic Hygroma)
- Fibroma
- Granulomatous Disease of the Thyroid
- Infectious Thyroiditis
- Lipomas
- Lymphadenopathy
- Medullary Thyroid Carcinoma
- Papillary Thyroid Carcinoma
- Parathyroid Adenoma
- Parathyroid Cyst
- Pseudogoiter
- Sarcoma
- Subacute Thyroiditis
- Thyroglossal Duct Cyst
- Thyroid Abscess
- Thyroid Lymphoma
- Thyroid Nodule

Workup

Laboratory Studies

Initial screening should include TSH. Given the sensitive third-generation assays in the absence of symptoms of hyper or hypothyroidism further testing is not required. An assessment of free thyroxine index or direct measurement of free thyroxine would be the next step in the evaluation. Further laboratory testing is based on presentation and results of screening studies and may include thyroid antibodies (antithyroid peroxidase formerly the antimicrobial antibodies and antithyroglobulin), thyroglobulin, sedimentation rate and calcitonin in an individual at high risk for medullary carcinoma of the thyroid.

Imaging Studies

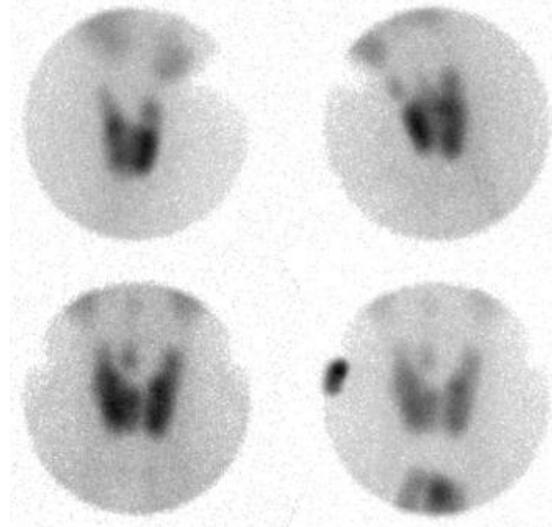
Ultrasonography: Ultrasonography can be used to establish and follow goiter size, consistency, and nodularity. It can also be employed to localize nodules for ultrasonographically guided biopsy. A study by Kelly et al indicated that in some patients with multinodular goiter, the risk of neoplasia can be effectively assessed with ultrasonography rather than with fine-needle aspiration biopsy. The investigators reported that in study patients with no suspicious features on ultrasonography, the average risk of neoplasia in multinodular goiters was 0.0339, although this risk rose significantly when one or more suspicious features were present.

Roentgenography: Roentgenography is used to assess extent of a goiter and presence of calcification. Ultrasonography has replaced this modality. Roentgenography is used to visualize calcifications within a goiter and regional lymph glands.

Computed tomography (CT) scanning: CT scanning is more precise than roentgenography. CT scanning can be used to delineate size and goiter extent. Due to the superficial placement of the thyroid gland, ultrasonography is more useful in following size. CT scanning does a much better job of determining the effect of the thyroid gland on nearby structures. It also may be useful in the follow-up of patients with thyroid cancer that shows evidence of recurrence. CT scanning can be used to guide biopsy of the thyroid.

MRI: Magnetic resonance imaging has the same indications as CT scanning (see above). Radionuclide uptake and radionuclide scanning are used to assess thyroid function and anatomy in hyperthyroidism, as shown below. Additionally, thyroid scanning may be useful in the patient with neck or superior mediastinal masses. Radionuclide scanning allows

determination of the function of a nodule. Function of a thyroid nodule has value both diagnostically and therapeutically. See the image below.



Thyroid nuclear scan of a patient with a euthyroid goiter showing different projections.

Other

Barium swallow is used to assess esophageal obstruction. **Spirometry:** The flow-volume loop is useful in determining the functional significance of compressive goiters. **Perchlorate** discharge test is used in individuals with inborn errors of thyroid hormone synthesis. It is used rarely today to determine the ability to trap and organify iodine.

Procedures

Fine-needle aspiration biopsy is used for cytologic diagnosis. Fine-needle aspiration of the thyroid is used to determine the cause of an enlarged gland. In general, the procedure is not used in the workup of autonomously functioning nodules. The procedure has little morbidity and can be tailored to the situation. **Core biopsy, or large-needle biopsy,** of the thyroid uses a larger gauge needle providing a fragment of tissue. This procedure also carries with it a higher morbidity. Core biopsy has the advantage of more complete sampling. **Partial thyroidectomy** may be used as a first-line procedure for patients with a high probability of cancer. It is reserved mostly if the result of a fine-needle aspiration is suspicious or if the patient/physician prefers it. **Total thyroidectomy** is performed for malignant goiters.

Histologic Findings: Simple nontoxic goiters show hyperplasia, colloid accumulation, and nodularity. Nodular hyperplasia is commonly seen in multinodular goiter. Cytologic findings include benign appearing follicular cells, abundant colloid, macrophages, and, sometimes, Hürthle cells. Inflammatory disorders of the thyroid, such as chronic lymphocytic (Hashimoto) thyroiditis, contain a mixed population of lymphocytes mixed with benign appearing follicular cells. Malignant nodules may be follicular cell in origin, ie, papillary (most common), follicular, Hürthle cell, or anaplastic. They also may be from parafofollicular cells, medullary carcinoma or lymphoma, or other categories.

Goiter Treatment & Management

Medical Care

Small benign euthyroid goiters do not require treatment. The effectiveness of medical treatment using thyroid hormone for benign goiters is controversial. Large and complicated goiters may require medical and surgical treatment. Malignant goiters require medical and surgical treatment.

- The size of a benign euthyroid goiter may be reduced with levothyroxine suppressive therapy. The patient is monitored to keep serum TSH in a low but detectable range to avoid hyperthyroidism, cardiac arrhythmias, and osteoporosis. The patient has to be compliant with monitoring. Some authorities suggest suppressive treatment for a definite time period instead of indefinite therapy. Patients with Hashimoto thyroiditis respond better.
- Treatment of hypothyroidism or hyperthyroidism often reduces the size of a goiter.
- Thyroid hormone replacement is often required following surgical and radiation treatment of a goiter. Use of radioactive iodine for the therapy of nontoxic goiter has been disappointing and is controversial.
- Medical therapy of autonomous nodules with thyroid hormone is not indicated.
- Ethanol infusion into benign thyroid nodules has not been approved in the United States, but it is used elsewhere.

Goiters with primary thyroid malignancy require levothyroxine replacement after surgery and radioactive iodine ablation. Metastatic lesions to the thyroid gland require treatment of the primary malignancy. Granulomatous and infectious etiologies for goiter require specific treatment depending on the underlying cause.

Surgical Care

Surgery is reserved for the following situations:

- Large goiters with compression
- Malignancy
- When other forms of therapy are not practical or ineffective

Preoperatively, establish euthyroid state prior to surgical treatment. Evaluation must include the stability of the airway. This must be secured immediately if ventilatory status appears tenuous. Emergency surgical treatment of a goiter in a patient with hypothyroidism requires intravenous levothyroxine and glucocorticoids at stress doses.

Emergency surgical treatment of a goiter in a thyrotoxic patient requires antithyroid medications, beta blockers, and glucocorticoids at stress doses. Suppressive doses of iodine are helpful. **Intraoperative and postoperative management** includes hemodynamic monitoring, which is important in patients with preoperative hyperthyroidism or hypothyroidism. **Postoperative management also includes** monitoring of serum calcium. **A literature review by Li et al indicated** that total thyroidectomy is a safe procedure for the treatment of bilateral multinodular nontoxic goiter, demonstrating a lower recurrence rate than bilateral subtotal thyroidectomy. However, total thyroidectomy was also found to carry a significantly higher risk of postoperative transient hypoparathyroidism than did the other procedure. **A study by Khan et al indicated** that in patients with retrosternal goiter, a transcervical surgical approach is preferable to a transthoracic procedure. The study, which employed the National Surgical Quality Improvement Program (NSQIP) database, found that various postoperative morbidities, including those involving transfusions and unplanned intubations, were higher with the transthoracic approach. The data suggested that overall mortality might be increased as well with this procedure. **A study by Bove et al indicated** that in patients with retrosternal goiter, recurrence and extension of the goiter beyond the carina are preoperative risk factors for postoperative complications following total thyroidectomy. The study also found evidence that compared with total thyroidectomy for cervical goiter, the risk for transient hypocalcemia and transient recurrent laryngeal nerve palsy is greater following the same procedure for retrosternal goiter.

Consultations

An endocrinologist should assess a patient at least once, and assessment should be even more frequent if the goiter is complicated by

thyroid dysfunction or malignancy or if the patient is being considered for surgical management.

Diet

Nutrition plays a role in the development of endemic goiters. Dietary factors include iodine deficiency, goitrogens, protein malnutrition, and energy malnutrition. Often these factors occur concurrently.

- Iodine: If it is practical, treat endemic goiters in iodine-deficient regions with iodine supplementation in the diet and avoidance of goitrogens. Treatment with iodine supplementation or levothyroxine may reduce goiter size.
- Goitrogens: Cyanoglucosides are naturally occurring goitrogens that are digested to release cyanide, which is converted to thiocyanate. Thiocyanate inhibits iodide transport in the thyroid and, at higher levels, inhibits organification. Foods that contain cyanoglucosides include cassava, lima beans, maize, bamboo shoots, and sweet potatoes. Thioglucosides are natural goitrogens found in the Cruciferae family of vegetables and weeds eaten by animals. When digested, they release thiocyanate and isothiocyanate, which have thionamidelike properties and are passed to humans via milk ingestion.

Complications

Potential complications include the following:

- Large goiters may cause compression of the trachea, with tracheomalacia and asphyxiation.
- Hyperthyroidism occurs in some patients exposed to iodine (ie, Jodbasedow phenomenon).
- A patient with autoimmune goiters may develop lymphoma. Multinodular goiters may undergo malignant transformation.
- Nodular goiters may cause pain, intranodular necrosis, or hemorrhage.
- Thyroid abscess may be associated with pain, fever, bacteremia, or sepsis.

Prevention

Goiter prevention is based on etiology. **Correct iodine deficiency** and avoid dietary or iatrogenic goitrogens if practical. In the United States, it is difficult to find iodine deficiency, given the supplementation of table salt with iodine, iodine in cattle feed, and the use of iodine as a dough conditioner. Judicious use of levothyroxine is helpful in patients with a previous diagnosis of nodular hyperplasia who have had a lobectomy to prevent occurrences in the contralateral lobe. **Goiters due to autoimmune thyroiditis** may be controlled with careful use of levothyroxine and, when indicated, anti-inflammatory medication. **Congenital goiters due to inborn errors** of metabolism may be reduced or prevented by careful use of levothyroxine during the postpartum period. **Newborns are screened** for congenital hypothyroidism.

Long-Term Monitoring

Patients are monitored for hypothyroidism by history, examination, and TSH measurements. Initially, monitoring occurs every 6-8 weeks.

Thyroid hormone replacements

Class Summary

Benign goiters can be treated with thyroid hormone. The most widely used thyroid hormone is levothyroxine sodium, administered once a day. Liothyronine sodium requires more frequent administration. Desiccated thyroid powder, thyroglobulin, and liotrix are less predictable following ingestion. **Levothyroxine sodium** (Synthroid, Levoxyl, Levothroid). **Synthetic thyroxine is converted** to the active form, triiodothyronine by 5'-deiodinase. Within the pituitary, type-II deiodinase helps convert T4 to T3, which in turn regulates TSH production, the main growth factor for the thyroid gland.

INTERPRETATION

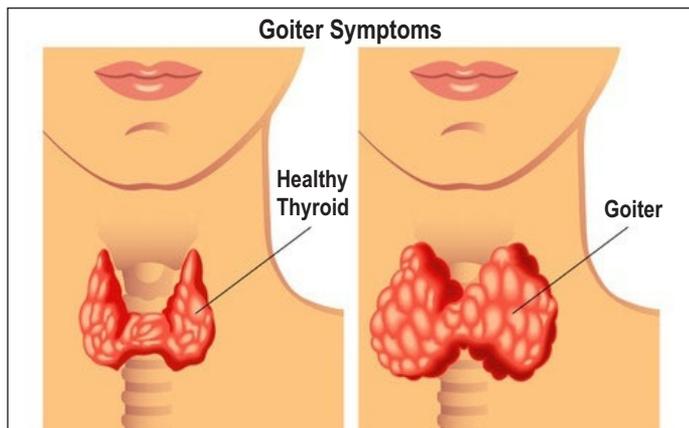
INTERPRETATION OF THYROID FUNCTION TESTS

Reference Ranges

It should be remembered that different testing laboratories may have different reference ranges. These are the reference ranges used by some of the international Labs. They may vary, however, depending on the type of kit and technology used.

TSH	0.2 - 4.0 miu/L
free T4	10 - 20 pmol/L
total T3	0.9 - 2.5 nmol/L

These references ranges are used in all the evaluations shown above.



The Euthyroid Patient

In the Euthyroid patient the free T4 is within the range 10 - 20 pmol/L and the TSH is within the range 0.2 - 4.0 miu/L. **However in sick euthyroidism T4 and or TSH** may be lowered during the non-thyroidal illness. TSH may be transiently elevated during recovery from non-thyroidal illness but almost any combination of thyroid tests can be seen in sick patients.

Hypothyroidism

TSH Low or Normal	TSH Elevated
If T4 is normal then Thyroid status is Normal	<ul style="list-style-type: none"> If T4 is normal, subclinical hypothyroidism exists. Consider T4 replacement if TSH > 12 miu/L. When the TSH is mildly elevated ie 4 - 12 miu/L, positive TPO antibodies indicate an increased risk of future hypothyroidism of 5% per year.
If T4 is low consider secondary hypothyroidism (but more commonly Sick Euthyroid)	<ul style="list-style-type: none"> If T4 is low, primary hypothyroidism.

- A normal or low TSH level usually excludes primary hypothyroidism. However, the rare diagnosis of secondary (pituitary) hypothyroidism should be considered if T4 is also low. The commonest cause of this pattern is sick euthyroid syndrome.

- A TSH level between 10-16 miu/L indicates hypothyroidism, and usually indicates that replacement therapy should be commenced.
- A TSH level between 6-12 miu/L with normal T4 may represent subclinical or compensated hypothyroidism.
- Anti-thyroid peroxidase autoantibodies (TPO Ab) are recommended as their presence predicts the development of hypothyroidism at a rate of approx 5% per year.

Sick Euthyroid Syndrome

During severe illness or starvation, the metabolic drive on the human body by the thyroid is reduced. The term 'sick euthyroid' is used in this condition since it represents a state of thyroid function appropriate for a sick individual; and it returns to normal with the return of good health. **The most active thyroid hormone tri-iodothyronine, T3**, is largely produced by peripheral ie non-thyroidal conversion of thyroxine, T4. In the typical sick euthyroid, circulating T3 is usually low but the total T4 may be normal or even raised since there is reduced conversion to T3. Conversely, T4 may be low since the majority is carried on serum binding proteins and their synthesis may be suppressed by severe illness. The absence of a raised TSH excludes primary hypothyroidism. However, almost any pattern of thyroid hormones may be seen in an unwell patient!! **Suppressed TSH** may be seen in elderly patients who do not have thyrotoxicosis (since the T3 is low or normal). TSH may also be suppressed in depression.

Interference with TFT interpretation due to committant drug therapy

Amiodarone interferes both with the synthesis of TSH, with iodine uptake by the thyroid gland and with conversion of T4 to T3. It may be impossible to interpret TFTs in isolation and decisions may need to be taken on clinical grounds or on the pattern of change in TFTs over a period of time. Overt hypo- or hyperthyroidism probably occurs in 4% (2% each) of patients treated with amiodarone but the exact proportion is strongly affected by iodine intake. Minor abnormalities may be seen in approximately 50% of patients.

Beta-blockers interfere with conversion of T4 to T3 but this does not cause hypothyroidism.

Lithium interferes with thyroid hormone synthesis and inhibits their release from the gland. Long term lithium treatment results in goitre in up to 50% of patients, subclinical hypothyroidism occurs in 20% and overt hypothyroidism in a further 20%. The presence of thyroid peroxidase antibodies may be useful to predict the future development of hypothyroidism in long-term treated patients.

Cortisol (or hydrocortisone or prednisolone) given orally transiently suppresses TSH secretion for a few hours. Patients taking corticosteroids should have blood taken for TFTs before the morning steroid medication is taken.

Antiepileptics, NSAIDS & aspirin all interfere with the binding of thyroxine and its binding proteins resulting in lowish free T4 in the presence of normal thyroid binding globulin. It is most marked with carbamazepine; there appears to be no interference by valproate.

Hyperthyroidism

- TSH is the most useful parameter in screening for thyroid dysfunction in most non critically ill patients since TSH is almost always suppressed in hyperthyroidism.
- A raised T4 and T3 with suppressed TSH and an elevated TSH receptor antibody level confirms the diagnosis of Grave's disease.
- A proportion of cases have normal T4 with suppressed TSH and

represent T3 toxicosis and T3 measurements may be necessary. This is usually performed automatically by the laboratory.

- A raised T4 with normal or raised TSH usually indicates T4 → T3 conversion defect, or analytical artefacts.
- A rare cause is secondary hyperthyroidism (TSH resistance or secreting pituitary tumours).

Thyroxine Replacement Therapy in Primary Hypothyroidism

Replacement Therapy	
TSH Level	This Indicates
< 0.05 mIU/L	Over Replacement
0.05 - 0.2 mIU/L	Indicates Possible Over Replacement
0.2 - 2.0 mIU/L	Sufficient Replacement
> 2.0 mIU/L	Likely under Replacement

- Clinical symptomatology and TSH are the major parameters used in assessing the adequacy of replacement therapy.
- T4 level is an index of recent patient compliance.
- TSH may take up to 4-6 weeks to stabilise. Thus, repeat TFT following alteration of dose should only be performed after this period.
- Patients with Thyroid Cancer should have their TSH suppressed to inhibit regrowth of malignant thyroid cells.

Medications interfering with thyroxine replacement

Treatment with iron and calcium salts, proton pump inhibitors and oestrogens is associated with reduced therapeutic efficacy and rises in TSH. The effect with iron and calcium is due to impaired absorption and these agents should be taken at a different time of day than the thyroxine.

Thyroxine Replacement Therapy for Secondary Hypothyroidism

Replacement Therapy	
freeT4 Level	This Indicates
< 17 pmol/L	Likely under replacement
17-25 pmol/L	Sufficient replacement
>25 nmol/L	Likely over replacement

- Clinical symptoms and T4 are used to monitor the adequacy of therapy in hypopituitarism as TSH is not representative of thyroid function.
- Results should always be interpreted in combination with clinical status.

Thyroid Dysfunction

HYPOTHYROIDISM

- Dry Hair
- Puffy Face
- Slow Heartbeat
- Weight Gain
- Brittle Nails
- Arthritis
- Cold Intolerance
- Depression
- Dry Skin
- Fatigue
- Memory Loss
- Heavy Menstrual Periods
- Muscle Aches

HYPERTHYROIDISM

- Hair Loss
- Bulging Eyes
- Sweating
- Rapid Heartbeat
- Weight Loss
- Regular Gas
- Soft Nails
- Sleeping Difficulties
- Heat Intolerance
- Infertility
- Irritability
- Muscle Weakness
- Nervousness
- Scant Menstrual Periods



Suggested monitoring schemes

Thyroxine Therapy

Newly commenced

- Measure TFT ~ 6-8 weeks post commencement of thyroxine therapy and adjust the dose accordingly in order to bring TSH into the range of 0.2 - 2.0 mIU/L
- Repeat TFT ~ 6 months after normalisation as metabolic clearance of T4 may increase with correction of hypothyroidism.
- Note that TFT should not be repeated until at least 4-6 weeks post alteration of thyroxine dose.

On Thyroxine

- Repeat TFT only if suspected alteration in thyroid function.
- Perform TFT 4-6 weeks after alteration of dose.
- Yearly TFT is recommended unless earlier measurement is indicated clinically.
- Secondary Hypothyroidism
- Repeat T4 4 weeks after changing the dosage is recommended.

Grave's Disease on Antithyroid Drug Therapy

- Both T4 and TSH are used to assess thyroid function (occasionally T3).
- Clinical status of patient should take precedence over TFT in evaluating the adequacy of treatment as TSH may take months to normalise following commencement of therapy.

Repeating TFT measurements

- Repeat TFT is only indicated in appropriate medical conditions, eg recurrent AF.
- TFT performed more than 3 times a year is usually inappropriate providing previous TFTs are normal.

How to request TFTs

Efficient management of patients requires accurate results from investigations. However, in order for the laboratory to correctly interpret TFT results and provide accurate reports, relevant clinical history on the request forms is essential.

The following points serve as a guide as to what should be included with TFT requests:

- Current diagnosis (in particular, indicate if patient is ill).
- Purpose for which TFT was requested.
- Previous TFT findings and when.
- Current or recent drug therapy (in particular, antiepileptics, NSAIDs, aspirin, amiodarone and lithium).
- Any known thyroid abnormalities or pathologies.
- Antithyroid drug therapy (including when commenced or dose altered).
- Any known thyroid abnormalities or pathologies.
- Thyroxine therapy (including when commenced or dose altered). Any other forms of treatment related to the thyroid dysfunction.
- Other endocrinological pathologies.

TROUBLESHOOTING

SELECTION AND TROUBLESHOOTING OF IMMUNOASSAYS

The most common assays used in workplace drug testing regimes include homogenous assays which are used with different automatic analyzers. Therefore, one single instrument would never meet the requirements of all the laboratories and that is why, dealers offer variety of shapes and sizes in the instrument kits. A laboratory should therefore, identify its goals and objectives so that it can accomplish those using appropriate testing systems. This template can then be utilized to evaluate different options while considering instruments and reagents. Even though, the importance of different factors varies according to different laboratories, some important points to consider are as follows:

- The environment of the laboratory including the labor, space and the compatibility of different systems and the LIS – laboratory information system interface
- The present and predicted sample volumes, thereby allowing enough capacity for growth
- The speed of analyzer – i.e. the reportable test quantity per hour along with sample throughput
- The capacity of test analyzer – i.e. the quantity of reagent slows available
- Validated instruments available for selected assay reagents
- The costs, such as capital equipment, service agreements, time, requirements for reagent volume and labor
- Referral to other laboratories for further consultation
- The advantages and disadvantages of utilizing single or many dealers for supplying instruments and reagents

All analytical systems require regular monitoring of assays and their performance so that accurate results are ensured. For assays, monitoring is done by open Quality control specimens, below and above the cutoff ranges. When systems don't meet the acceptable criteria, trouble shooting is done to find out the basic cause of failure. Therefore, at times, it is not appropriate to separate the reagent from the analyzer in order to find out where the fault is, and it can be a combination of both the

reagent and the instrument. So, routine preventive and daily maintenances are done along with operational checks so that the mechanical as well as the performance operations of the instrument can be verified. Enthusiastic performance as well as the documentation of these tasks minimize the time and provide real time instrument conditions to be used in the troubleshooting procedures. Recording of lot numbers for reagents, quality control material and calibrators with their daily calibration can ensure quality control results.

Some considerations while troubleshooting assay's performance are given below:

Quality Control

The most frequent problem associated is the lack of quality control material to fulfill the acceptability criteria. This can occur as an individual occurrence or can be due to a bias developed over some time. Random failures can likely result due to deterioration or insufficient volume of quality material in the sample, which is resolved by replacing the material. An ongoing bias or shift indicates systematic issue. Though, minor change in the quality control can be due to improper preparation, storage or shipping of the reagent. The manufacturer can provide information related to in-house reagent testing and reports from other alternate users for comparison. The development of quality control bias over a lot of time can be due to the deterioration of quality control reagents or materials or may indicate problems with the storage parts that require temperature control or refrigeration. Mechanisms such as reagent dispensing and pipetting of instruments along with technological errors like improper placement of quality control material should be given consideration.

Other Considerations for Reagents

Monoclonal antibodies used for drug abuse testing have enhanced the consistency of reagents. However, even changes occur in these systems over a period of time and the antibodies shift their affinity and reagents alter their formulations which can gravely impact the performance of immunoassays. The monitoring of calibration, quality control and reaction curves can provide insight about the shifts in reagents. Even though, minute changes don't impact the results' accuracy, the change in the affinity of the antibody and its specificity over time can cause poor recovery and assay performance.

BOUQUET

Need a friend?
Text me.



Need a laugh?
Call me.



Need money?
This number is no longer
in service.



In Lighter Vein

SCHOOL LIFE:

Most Irritating Moments

- Morning Alarm

Most Difficult Task

- To find Socks

Most Dreadful Journey

- Way to Class

Most Lovely Time

- Meeting Friends

Most Tragical Moments

- Surprise Test in 1st Period

Most Wonderful News

- TEACHER IS ABSENT

Major Rohan:

Dude EGGS are extra salty today
Too much Salt..why?

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Waiter:

Sir hen is suffering from
high blood Pressure

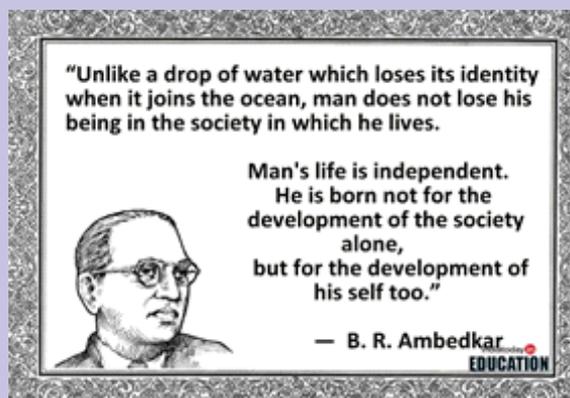
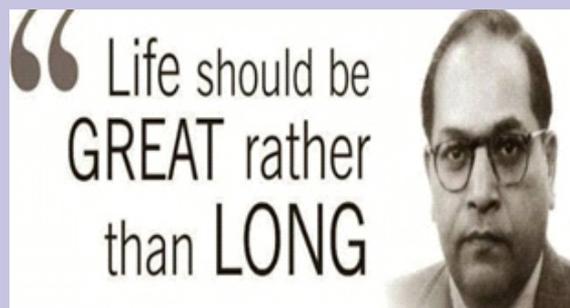
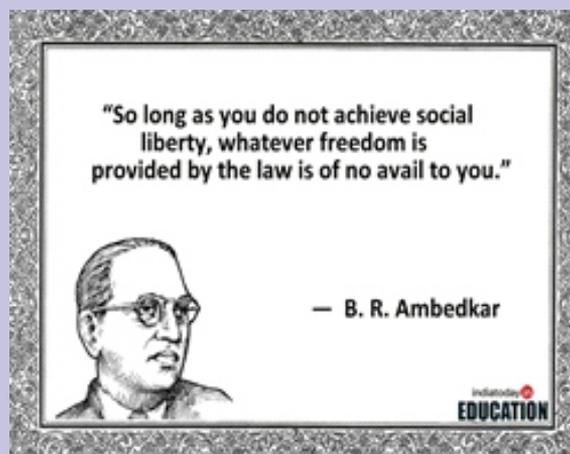
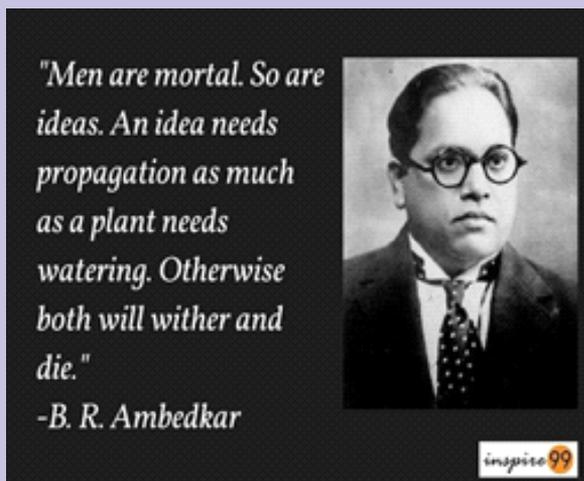
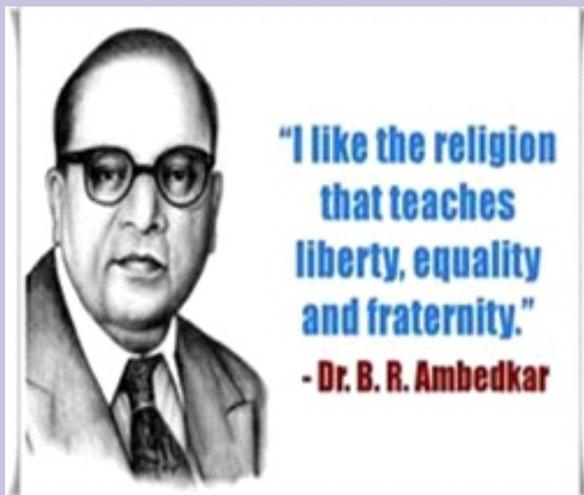
FUNWAQZ
Forget Grammar Miss Future

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BOUQUET

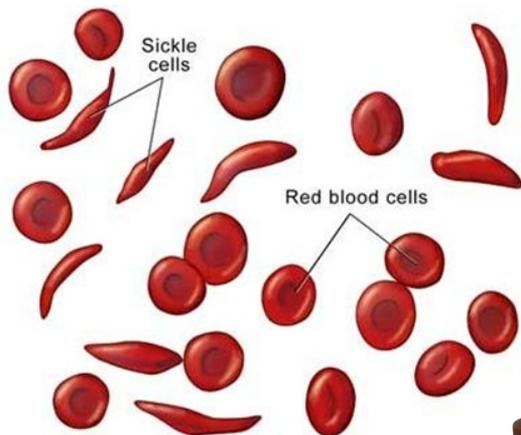
Wisdom Whispers



Brain Teasers

- In which of the following tests for diagnosing syphilis is heat inactivation of the serum required?
 - Conventional VDRL test
 - TRUST antigen
 - Latex agglutination test
 - TPHA.
- In conventional VDRL testing false positive results may be obtained due to:
 - Exposure of reagents to high temperature
 - Cloudy CSF used for testing
 - Slide was rotated for too long, drying takes place
 - All of the above.
- In conventional VDRL testing false negative results may be obtained due to:
 - Excess serum dispensed (prozone)
 - Excess antigen dispensed (postzone)
 - Cold reagents are used for testing
 - Any of the above.
- In which of the following tests for syphilis is heat inactivation of serum not required?
 - RPR
 - TPHA
 - Immunochromatography
 - All of the above.

TULIP NEWS



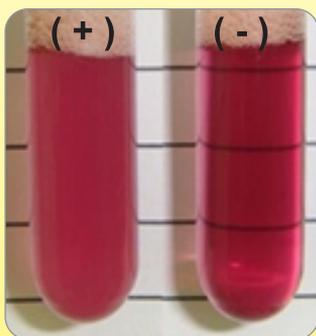
Screen & Differentiate Sickle Cell Hemoglobinopathies with **SICKLEVUE**



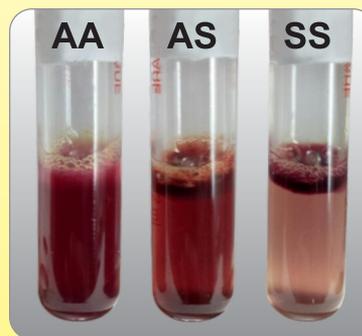
Solubility test kit helps to screen sickle cell patients from normal individual and Differentiate sickle cell trait (Hb AS) & Sickle cell Anemic (Hb SS)

Features & Benefits:

- **Turbidity - solubility test for Hb-S** - Screening test for sickle cell hemoglobin (Hb-S) & Differentiation between Sickle cell Trait (Hb AS) & Sickle cell Anemia (Hb SS).
- **Room temperature storage** - Suitable for on the field testing.
- **Kit with standard accessories** - Ideal for immediate testing & flexible for single/batch testing.
- **Simple & easy test procedure** - Eliminates need of skilled man power & high cost equipment.
- **Convenient pack size of 20 Tests** - Ideal for small and large workload labs.



Screen sickle cell from normal individual (Screening Method)



Differentiate Sickle cell Trait & Sickle cell Anemia patients (Differentiation Method)

*AA - Normal
AS - Sickle cell Trait
SS - Sickle cell Anemia

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