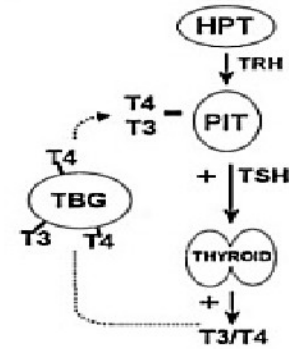




## Interpretation of Thyroid Function Tests During Pregnancy

The thyroid gland is normally regulated by thyroid-stimulating hormone (TSH), also called thyrotropin, which is secreted by the pituitary. TSH stimulates the thyroid gland to produce and release the thyroid hormones thyroxine (T4) and triiodothyronine (T3). T4 and T3 are released from the thyroid into the bloodstream, where they are bound to the serum proteins thyroxine-binding prealbumin, (also called transthyretin), albumin, and thyroxine-binding globulin (TBG). TBG normally accounts for about 75% of the bound hormones. About 0.03% of the total serum T4 and 0.3% of the total serum T3 are free. Only free T4 and T3 are metabolically active.

By a negative feedback mechanism increased levels of free thyroid hormones (T4 and T3) inhibit TSH secretion from the pituitary, whereas decreased levels of T4 and T3 cause an increase in TSH release from the pituitary. TSH secretion is also influenced by thyrotropin-releasing hormone (TRH) synthesized in the hypothalamus. TRH causes release of TSH.



HPT= Hypothalamus, PIT= Pituitary, TBG= Thyroxine-binding globulin.

### Changes in Thyroid Function Test (TFT) Results Due to Pregnancy

Normal changes in thyroid function tests during pregnancy include a transient suppression of thyroid-stimulating hormone [1,2]. Serum total T4 and total T3 steadily increase during pregnancy to approximately 1.5 times the non-pregnant level by mid second trimester [3-6]. Whereas serum free T4 and free T3 gradually decrease during pregnancy [4,7].

While the values for most thyroid function tests generally lie within normal non-pregnant ranges some investigators have found free T4 concentrations [8] and TSH [9] to fall below the lower limit of the normal range using newer assays. These discrepancies highlight the need for each laboratory to develop its own normal ranges in pregnancy [10].

**Serum total T4 and total T3 steadily increase during pregnancy to approximately 1.5 times the non-pregnant level by mid second trimester**

### Total T4

This test measures the concentration of thyroxine in the serum. This includes both bound and free hormone.

Elevated estrogen levels during pregnancy cause thyroid binding globulin (TBG) levels to rise. Because the majority of T4 and T3 circulates bound to TBG the total T4 and total T3 measurements will also rise, but the levels of free T4 and free T3 will not be affected.

Hereditary disorders in TBG production; acute liver disease and medications such as methadone are additional causes of an increased TBG level.

### Total T3

This test measures the concentration of triiodothyronine in the serum. The T3 is increased in almost all cases of hyperthyroidism and will be elevated to a greater degree than T4 in autoimmune hyperthyroidism.

The T3 is decreased during acute illness and starvation, and is affected by several medications including Inderal, steroids and amiodarone.

### %T3 Uptake:

This test is performed by adding radiolabeled T3 to a patient's serum sample. The labeled T3 binds to serum proteins. A resin is then added to bind the remaining free labeled T3. The amount of resin bound free T3 is usually reported as a percent of the total labeled hormone added. A low resin uptake means that most of the labeled T3 has been taken up by serum proteins.

Thus conditions associated with an increase in serum proteins such as pregnancy will cause a low resin uptake, because more labeled T3 binds to proteins and less labeled T3 is available to bind to the resin. The T4 Uptake is a similar test [11]

### FT4

The free T4 (FT4) test measures the concentration of free thyroxine, the only biologically active fraction, in the serum. The free thyroxine is not affected by changes in concentrations of binding proteins.

**A suppressed TSH with normal FT4 and FT3 can usually be observed with repeat laboratories q 4 weeks until it normalizes.**

### TSH

Suppression of TSH with an elevation of free T4 is a common finding during the first trimester of pregnancy [1,11,12]. These findings are believed to be caused by stimulation of the TSH receptor by hCG which results in an increase in FT4 and subsequently suppresses TSH levels [11]. These changes are particularly pronounced in patients with hyperemesis gravidarum where FT4 levels may reach 37.6 and TSH may be suppressed to undetectable levels [13]

A suppressed TSH with normal FT4 and FT3 can usually be observed with repeat laboratories q 4 weeks until it normalizes [11].

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**Considerations in the Interpretation of TFTs [14]:**

- Are the results a possible lab error ?
- Does the patient have a personal or family history of autoimmune disease?
- May the result have been caused by a medication?
- Does the patient have symptoms or signs consistent with the laboratory diagnosis?
- Consider common etiologies first

**Example Thyroid Profiles**

**Normal**

Test	Result	Units	Reference Range
T4 Total	15.8	ug/dl	4.5-12.0
T3 Uptake	18.5	%	24.3-39.0
FT4 Index	2.9	ug/dl	1.2-4.9
TSH	0.923	uIU/ml	0.34-5.6

The TSH, and serum total T4 are within the "normal range for pregnancy" (approximately 9-18 mg/dl or 120-240 nmol/L). The resin T3 uptake value is reduced as expected during pregnancy

**Hyperthyroid**

Test	Result	Units	Reference Range
T4 Total	27	ug/dl	4.5-12.0
T3 Uptake	29.6	%	24.3-39.0
FT4 Index	8.0	ug/dl	1.2-4.9
TSH	< 0.019	uIU/ml	0.34-5.6

The suppressed TSH, and serum total T4 above the "normal range for pregnancy" (approximately 9-18 mg/dl, 120-240 nmol/L) are consistent with hyperthyroidism. The resin T3 uptake value is not reduced as it should be in pregnancy, and confirms that the suppressed TSH and elevated thyroxine level are not due pregnancy.

**Patterns of Thyroid Function Tests**

TSH	FT4	FT3	Possible Etiologies	
Low	L		Central hypothyroidism Euthyroid sick syndrome	
	N	N	Subclinical hyperthyroidism	
	N	H	T3 -toxicosis. Early or relapsing Grave's Iodine deficiency Solitary nodule	
Normal	H		Hashimoto's Grave's Molar pregnancy Choriocarcinoma Hyperemesis Thyrotoxicosis factitia Lithium Multinodular goiter Toxic adenoma Thyroid carcinoma Iodine ingestion	
	L		Hypothyroxinemia Severe nonthyroidal illness(euthyroid sick syndrome) Possible secondary hypothyroidism Medications	
	N		Normal	
	H		Euthyroid hyperthyroxinemia Thyroid hormone resistance Familial dysalbumineic hyperthyroxinemia Meds-amiodarone,beta-blockers, Oral contrast Hyperemesis, Acute psychiatric illness. Rheumatoid factor	
	High	L		Primary hypothyroidism
		N		Subclinical hypothyroidism
		H		TSH mediated hyperthyroidism

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