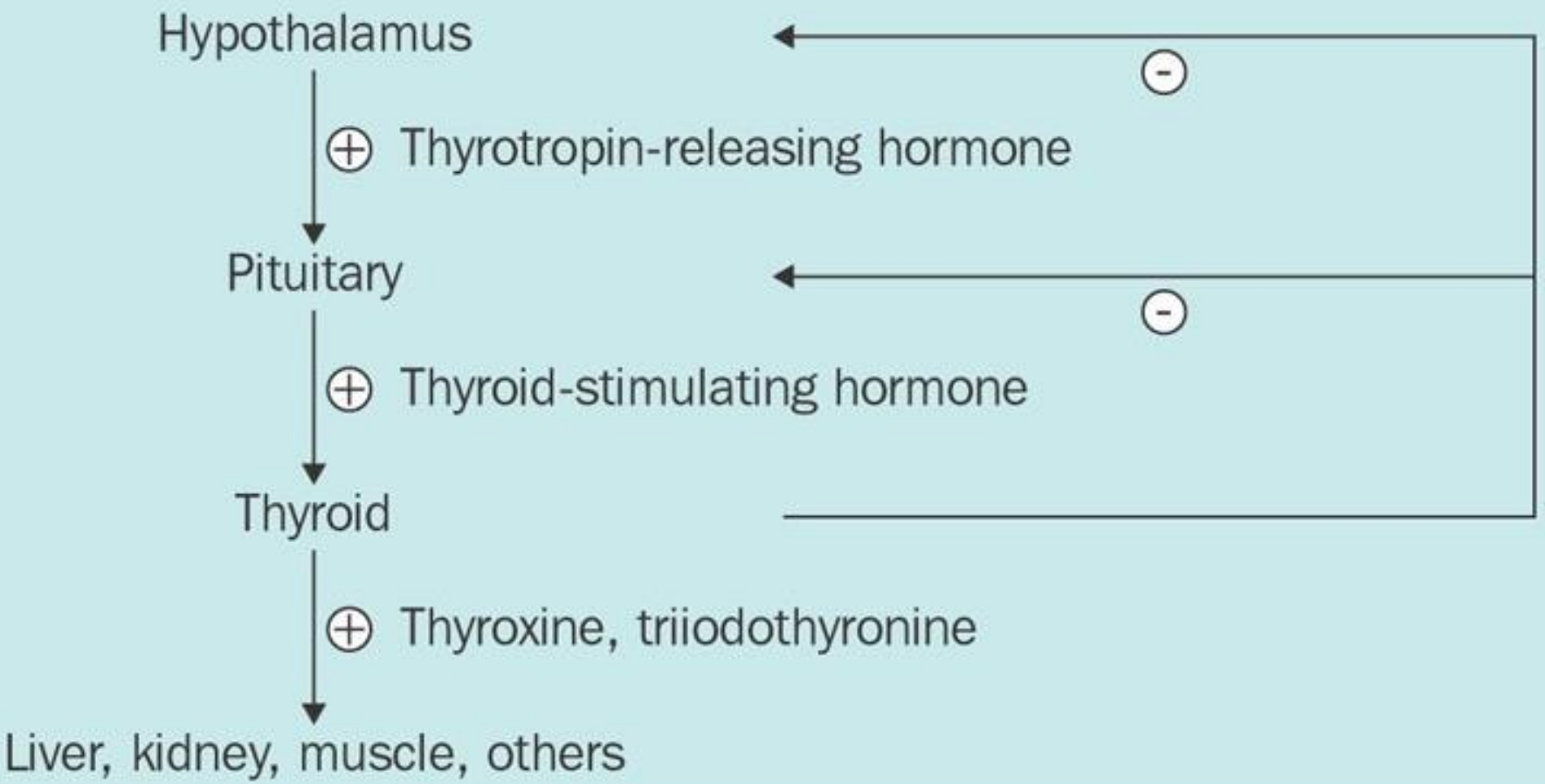
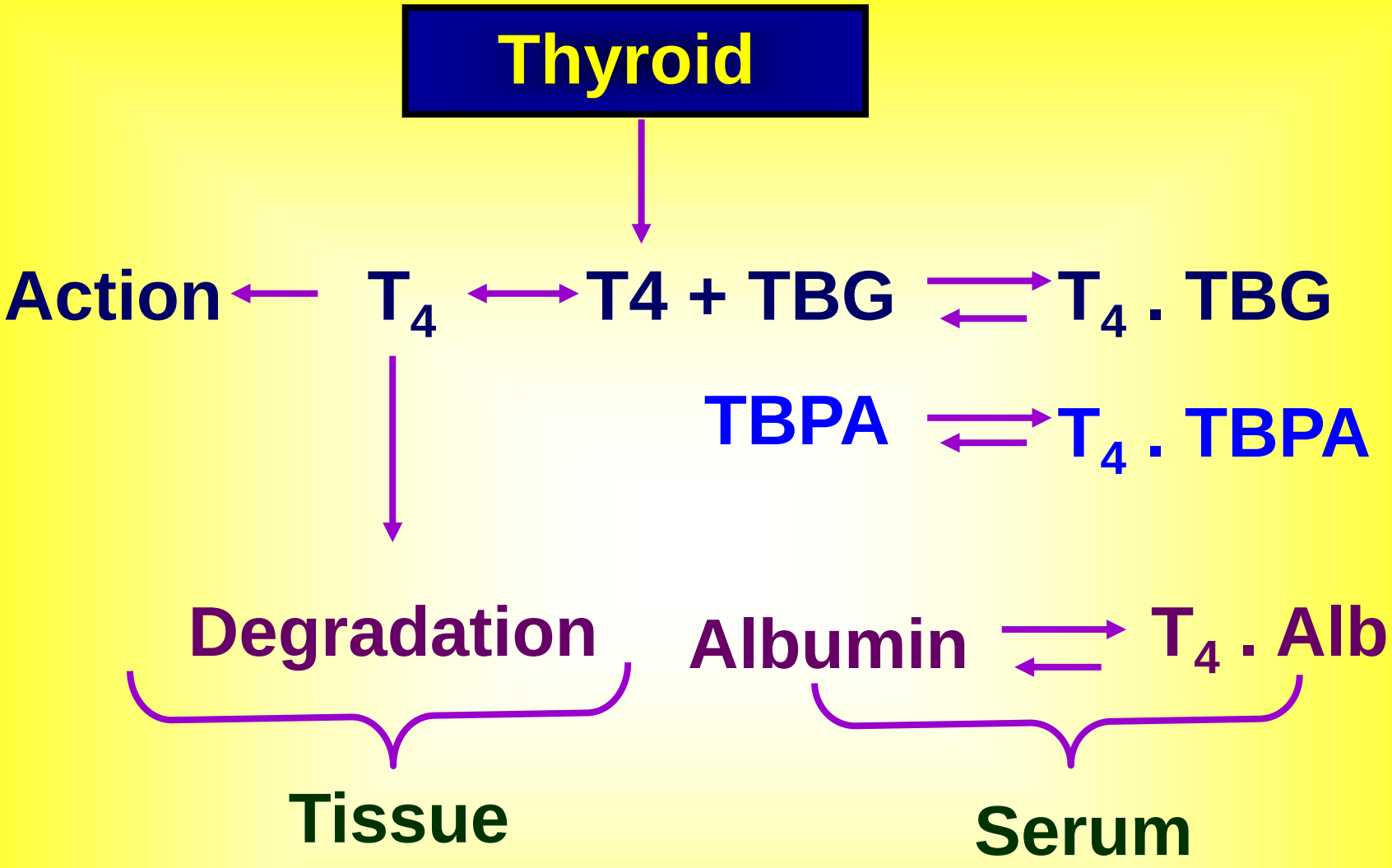
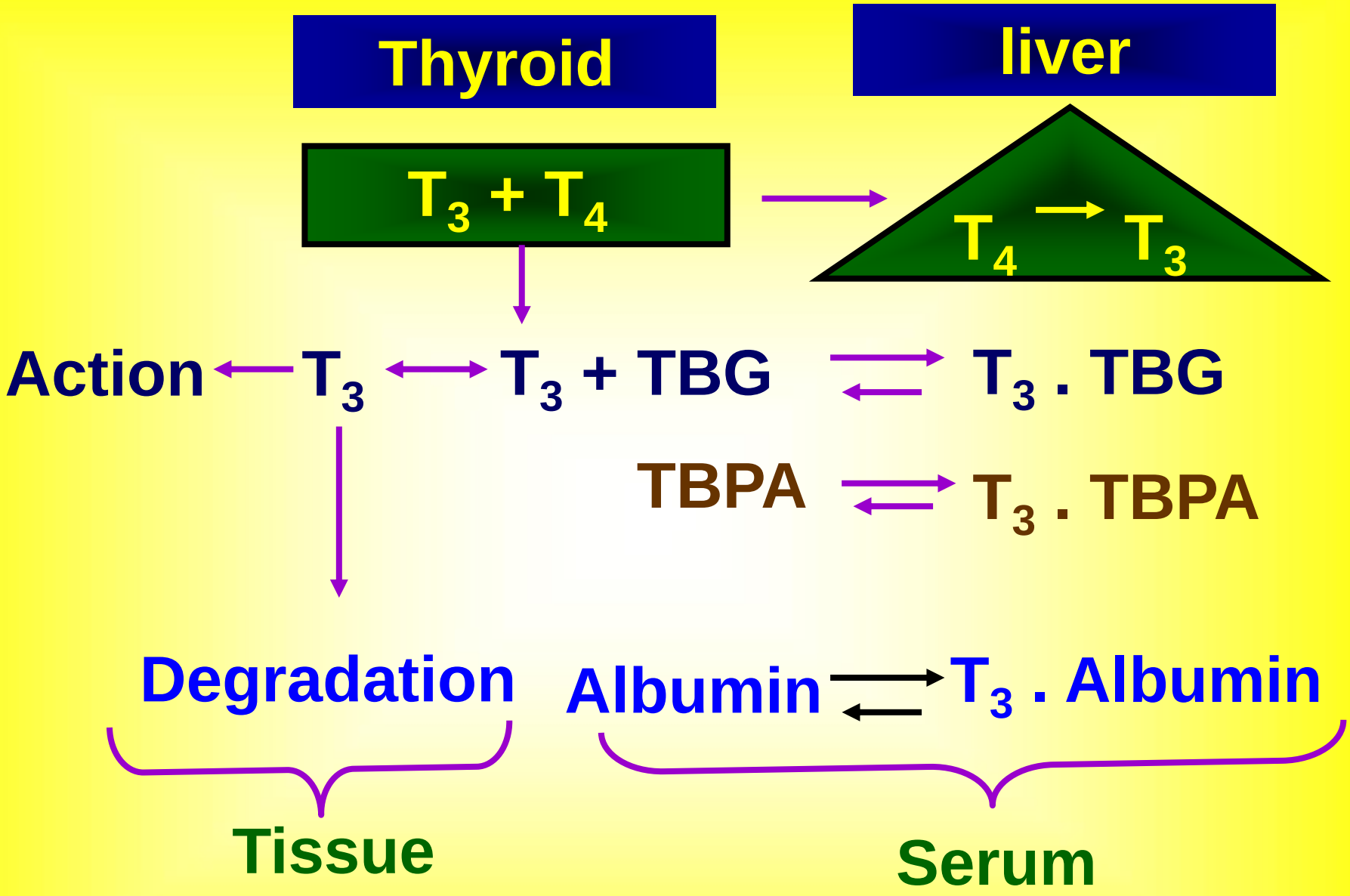

به نام خدا

Thyroid function tests

Regulation of thyroid hormones secretion




Thyroid
Action
T_4
T4 + TBG
T_4 . TBG
TBPA
T_4 . TBPA
Degradation
Albumin
T_4 . Alb
Tissue
Serum


Thyroid
liver
$T_3 + T_4$
$T_4 \rightarrow T_3$
Action
T_3
T_3 + TBG
T_3 . TBG
TBPA
T_3 . TBPA
Degradation
Albumin
T_3 . Albumin
Tissue
Serum

Circumstances Associated with Alterations in Binding of T4 by TBG

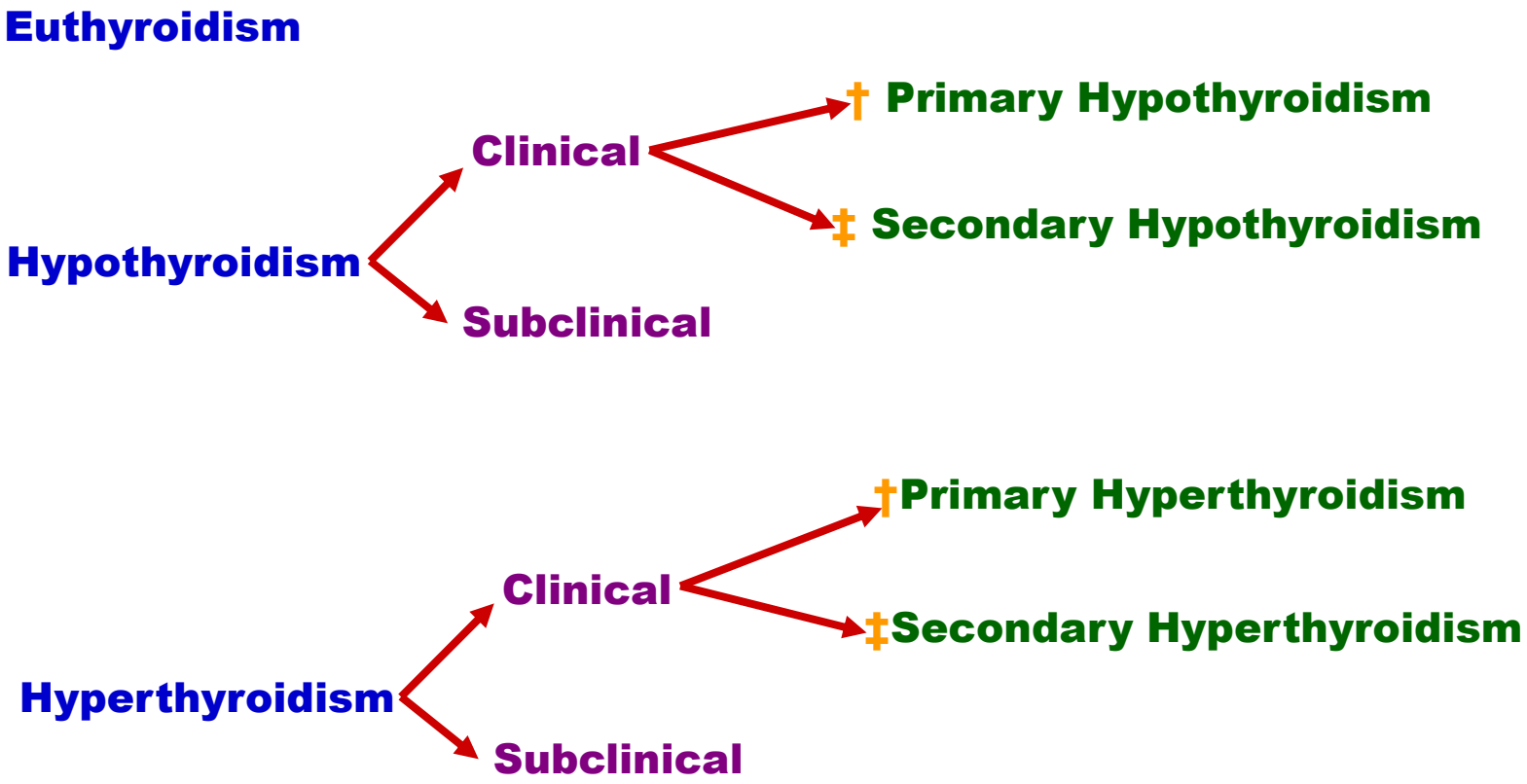
Increased Binding

- Pregnancy
- Neonatal state
- Estrogens and hyperstrogenemic states
- Tamoxifen
- Oral contraceptives
- Acute intermittent porphyria
- Infectious and chronic active hepatitis
- Biliary cirrhosis
- Genetic determination
- Perphenazine
- HIV infection

Decreased Binding

- Androgenic or anabolic steroids
- Large doses of glucocorticoids
- Active acromegaly
- Nephrotic syndrome
- Major systemic illness
- Cenetic determination
- Asparaginase

Patterns of Thyroid Function



† → Normal HP Axis → Thyroid dysfunction

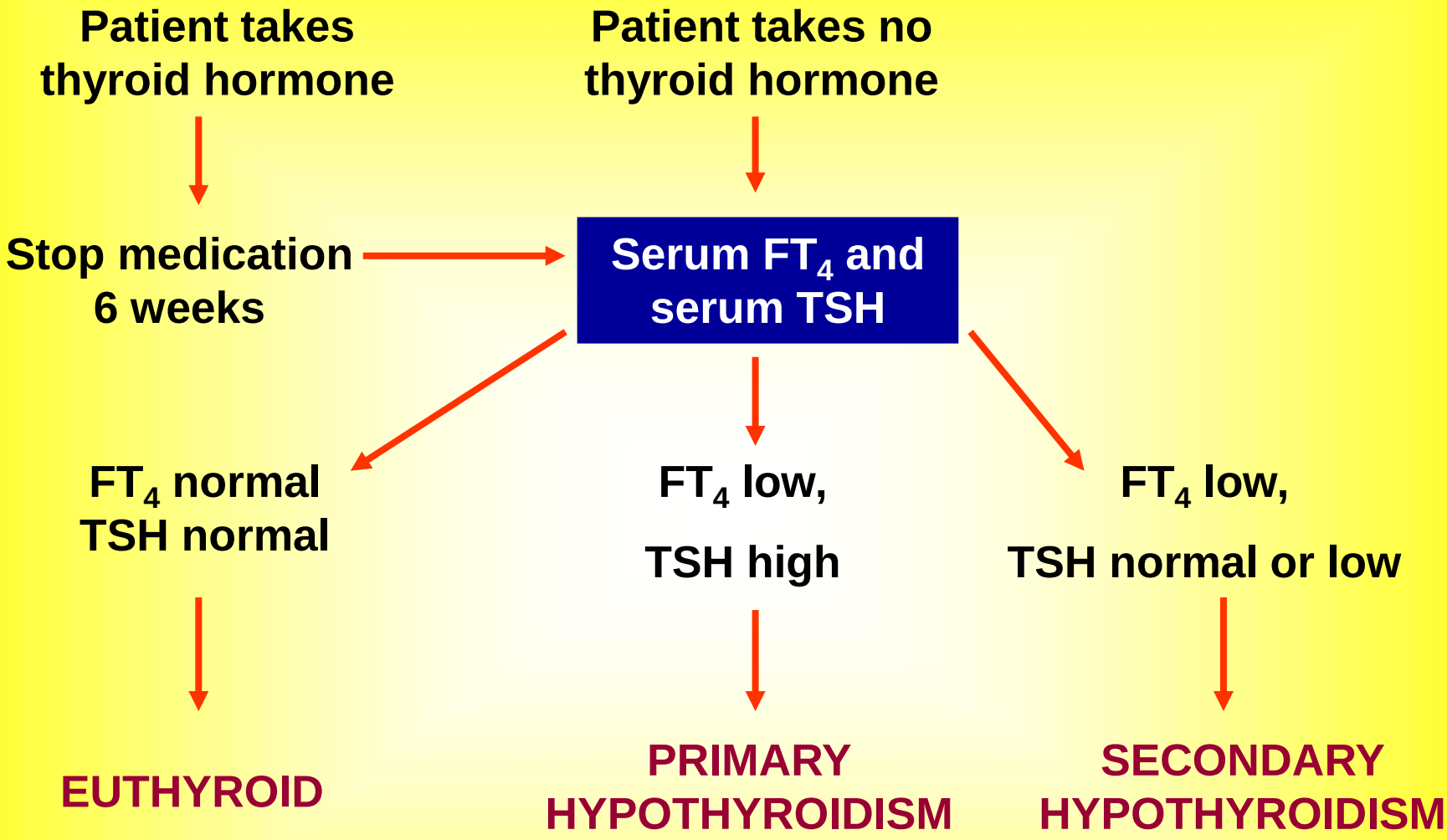
‡ → Abnormal HP Axis → Thyroid dysfunction. Secondary to abnormal TSH Secretion

Clinical Utility of Thyroid-Related Laboratory Tests

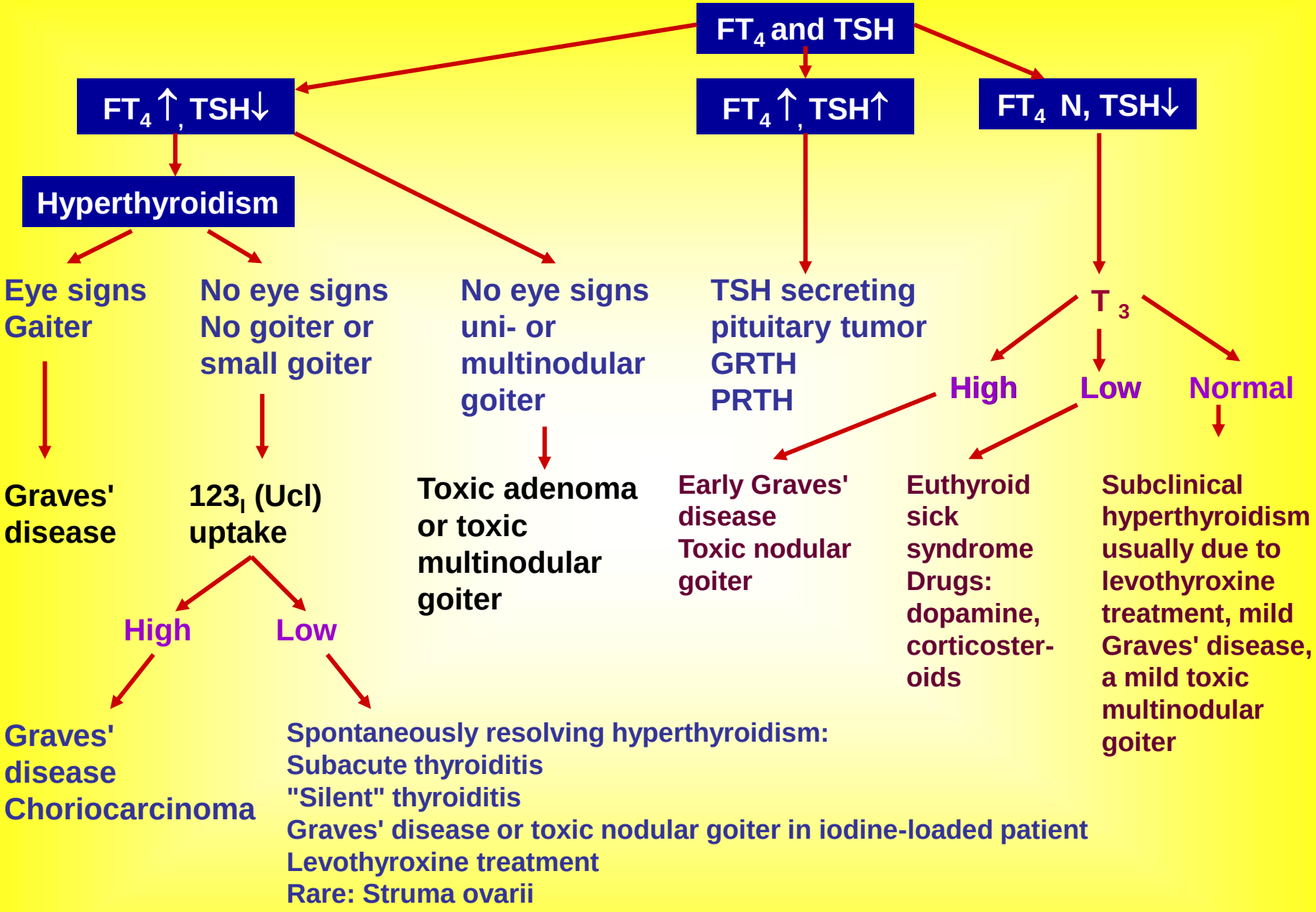
NAME OF TEST	ABBREVIATION	CLINICAL UTILITY
Tests for Evaluation of Thyroid Status		
Thyrotropin (by asensitive IA)	sTSH	Best general test;
(by conventional RIA)	TSH	should be phased out
Free thyroxine (by appropriate method)	FT_4	Second-best general test
Free (3,5,3′) triiodothyronine	FT_3	Adjunct test, diagnosis of T_3 toxicosis, rare forms of hyperthyroidism
Total (3, 5, 3′ -) triiodothyronine	T_3	Used in lieu of FT_3
Total thyroxine	T_4	Inadequate as general test
Thyroglobulin	Tg	Valuable in follow-up of thyroid cancer
TSH response to TRH	TRH	Largely superseded by sTSH
Reverse (3,3′5′ -) triiodothyronine	rT_3	Not used routinely
Free T_4 index:	FT_4I/FTI	
$T_4 \times T_3$-BR		Should be replaced by FT_4
$T_4 \times T_4$-BR		Need further evaluation
T_4/TBG ratio	T_4/TBG	Should be replaced by FT_4
Free T_3 index ($T_3 \times$ THBR)	FT_3I	Obsolete

Diagnostic Utility of the Free Thyroxine Index Values

	Total T_4	T_3U	FT_4 Index
Euthyroid	N	N	N
Hyperthyroid	↑	↑	↑
Hypothyroid	↓	↓	↓
Increased TBG	↑	↓	N
Decreased TBG	↓	↑	N



Diagnosis of hypothyroidism



Laboratory tests useful in the differential diagnosis of hyperthyroidism (see text for details)

Clinical Utility and Limitations of TSH Immunometric Assays *Limitations.*

A subnormal sTSH is not entirely specific for, or diagnostic of, hyperthyroidism. A misleading, subnormal sTSH may be recorded in

(1) hypopituitary or hypothalamic disease,

(2) in the first trimester of pregnancy,

(3) in patients with NTI and/or under treatment with dopamine, glucocorticoids, and certain other drugs, and

(4) in acute psychiatric illness.

Elevated sTSH levels are not always a sign of hypothyroidism.

Causes of a low or undetectable TSH level

Lowered TSH	Free thyroid hormone levels
Overt thyrotoxicosis	↑
Subclinical thyrotoxicosis	N
Recently treated hyperthyroidism	N
Thyroid-associated ophthalmopathy without Graves' disease	N
Excessive thyroxine treatment	N or↑
Nonthyroid illness (sick euthyroid syndrome)	↓ or N
First trimester of pregnancy	N or↑
Pituitary or hypothalamic disease	N or↓
Anorexia nervosa	N or↓
Dopamine, somatostatin (acute effect)	N
Glucocorticoids	N

Thyroid function tests in pregnancy

During pregnancy, subclinical hypothyroidism occurs in 2% of women, but overt hypothyroidism is present in only 1 in 500. Prospective randomized controlled trials have not shown a benefit for universal thyroid disease screening in pregnancy. Targeted TSH testing for hypothyroidism is recommended for women planning a pregnancy if they have a strong family history of autoimmune thyroid disease, other autoimmune disorders (e.g., type 1 diabetes), prior preterm delivery or recurrent miscarriage, or signs or symptoms of thyroid disease.

Maternal hyperthyroidism occurs at a rate of ~2 per 1000 pregnancies and is generally well tolerated by pregnant women. Clinical signs and symptoms should alert the physician to the occurrence of this condition.

Although pregnant women are able to tolerate mild hyperthyroidism without adverse sequelae, more severe hyperthyroidism can cause spontaneous abortion or premature labor, and thyroid storm is associated with a significant risk of maternal death.

Physiologic Changes in Pregnancy that Influence Thyroid

Physiologic change	Thyroid function test change
↑ Thyroid hormone binding globulin (TBG)	↑ Serum total T_4 and T_3 concentration
First trimester hCG elevation	↑ Free T_4 and ↓ TSH
↑ Plasma volume	↑ T_4 and T_3 pool size
↑ Placental type III 5-deiodinase (inner ring deiodination) is increased	↑ T_4 and T_3 degradation resulting in requirement for increased T_4 and T_3 production
Thyroid enlargement (in some women)	↑ Serum thyroglobulin
↑ Iodine clearance	↓ Hormone production in iodine-deficient areas

Causes of Hyperthyroidism in Pregnancy

Immune Thyroid Disease

- Graves' Disease
- Chronic Thyroiditis
- Sporadic Silent Thyroiditis

Non-autoimmune Thyroid Disease

- Multinodular Goiter (MNG)
- Toxic Adenoma
- Subacute Painful Thyroiditis
- Non Autoimmune Transient Hyperthyroidism
- Transient Hyperthyroidism of Hyperemesis Gravidarum (THHG)
- Multiple Gestation
- Nausea and Vomiting
- Familial Gestational Thyrotoxicosis (Thyrotropin Receptor Mutation)
- Hyperplacentosis
- Hyperreactio Luteinalis
- Trophoblastic Tumor
- Hydatidiform Mole
- Choriocarcinoma
- Resistance to Thyroid Hormone

Iatrogenic

- Excessive Levothyroxine intake
- Overtreatment
- Factitious
- Iodine induced
- Amiodarone

در پیش خانم ۲٤ ساله ای با حاملگی ۱۰ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

Total T_4 = 16 µg/dL (5 – 12.5)

Total T_3 = 241 ng/mL (80 – 180)

TSH = 0.2 mIU/L

تشخیص شما چیست؟

در پیش خانم ۳۰ ساله ای با حاملگی ۱۶ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

Total T_4 = 18 µg/dL (5 – 12.5)

Total T_3 = 312 ng/mL (80 – 180)

T_3 R uptake = 22% (25 – 35%)

TSH = 0.1 mIU/L

تشخیص شما چیست؟

در پیش خانم ۱۹ ساله ای با حاملگی ۱۲ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

Total T_4 = 24 µg/dL (5 – 12.5)

Total T_3 = 412 ng/mL (80 – 180)

TSH = 0.1 mIU/L

تشخیص شما چیست؟

در پیش خانم ۳٤ ساله ای با حاملگی ۲۰ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

Total T_4 = 18 µg/dL (5 – 12.5)

Total T_3 = 312 ng/mL (80 – 180)

T_3 R uptake = 32%

TSH = 0.1 mIU/L

تشخیص شما چیست؟

در پیش خانم ۲۸ ساله ای با حاملگی ۱٤ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

FT_4 = 4.1 ng/mL

TSH = 0.09 mIU/L

تشخیص شما چیست؟

در پیش خانم ۳۲ ساله ای با حاملگی ۸ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

FT_4 = 1.6 ng/mL

TSH = 0.09 mIU/L

تشخیص شما چیست؟

در پیش خانم ۲۰ ساله ای با حاملگی ۱۲ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

FT_4 = 0.4 ng/mL

TSH = 6.6 mIU/L

تشخیص شما چیست؟

در پیش خانم ۳۷ ساله ای با حاملگی ۲۸ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

FT_4 = 1.6 ng/mL

TSH = 0.2 mIU/L

تشخیص شما چیست؟

در پیش خانم ۲۴ ساله ای با حاملگی ۱۰ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

FT_4 = 0.8 ng/mL

TSH = 41 mIU/L

تشخیص شما چیست؟

در پیش خانم ۳٤ ساله ای با حاملگی ۲۰ هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است:

FT_4 = 1.4 ng/mL

TSH = 4.6 mIU/L

تشخیص شما چیست؟

KEY POINTS: THYROID DISEASE IN PREGNANCY

- All women at increased risk for thyroid disease should be screened in the first trimester.
- The normal ranges of thyroid-stimulating hormone (TSH), total thyroxine (TT_4) and total triiodothyronine (TT_3) change in pregnancy, and free T_4 and free T_3 assays by analogue methods may be inaccurate. TT_4 and TT_3 increase by $\approx$ 50%, and a TSH reference range of 0.1 to 4.0 mU/L has been recently advocated.
- Gestational transient thyrotoxicosis associated with hyperemesis gravidarum can cause overt hyperthyroidism, but this most often is self-limiting and does not require antithyroid drug (ATD) therapy.
- Graves' disease most commonly manifests in the first trimester with improvement in later pregnancy and treatment can often be tapered, but it usually exacerbates after delivery.
- Women with current Graves' disease or a history of Graves' disease (regardless of history of thyroid ablation or thyroidectomy) should be evaluated for TSH receptor antibodies (TRAbs) and thyroid-stimulating immunoglobulins (TSIs). If levels are $\geq$ 3 times elevated at 18 weeks' gestation or beyond, the fetus should be monitored for the development of fetal and neonatal Graves' disease.
- Subclinical hyperthyroidism (only a suppressed TSH) should *not* be treated in pregnancy.
- Treatment of subclinical hypothyroidism should be offered if TSH is $>$ 4 mU/L; treatment is with low doses of levothyroxine (50 mcg daily) and a goal TSH level of 0.5 to 2.5 mU/L.
- Although thyroperoxidase (TPO) antibodies may be associated with a small increased risk of miscarriage, there is currently insufficient evidence to recommend routine screening for TPO antibodies and treatment of TPO antibody–positive women with a history of recurrent pregnancy loss if they are euthyroid.
- Thyroid hormone requirements usually increase in pregnancy, beginning in the first trimester, and it is reasonable to increase thyroid hormone doses by 25% in athyreotic women as soon as pregnancy is confirmed. Only LT_4 (not T_3) should be used for thyroid hormone replacement and a full replacement dose is estimated at $\approx$ 2 mcg/kg in pregnancy.
- Postpartum thyroiditis occurs in approximately 5% of physiologically normal women and approximately 20% to 25% of women with T1D.

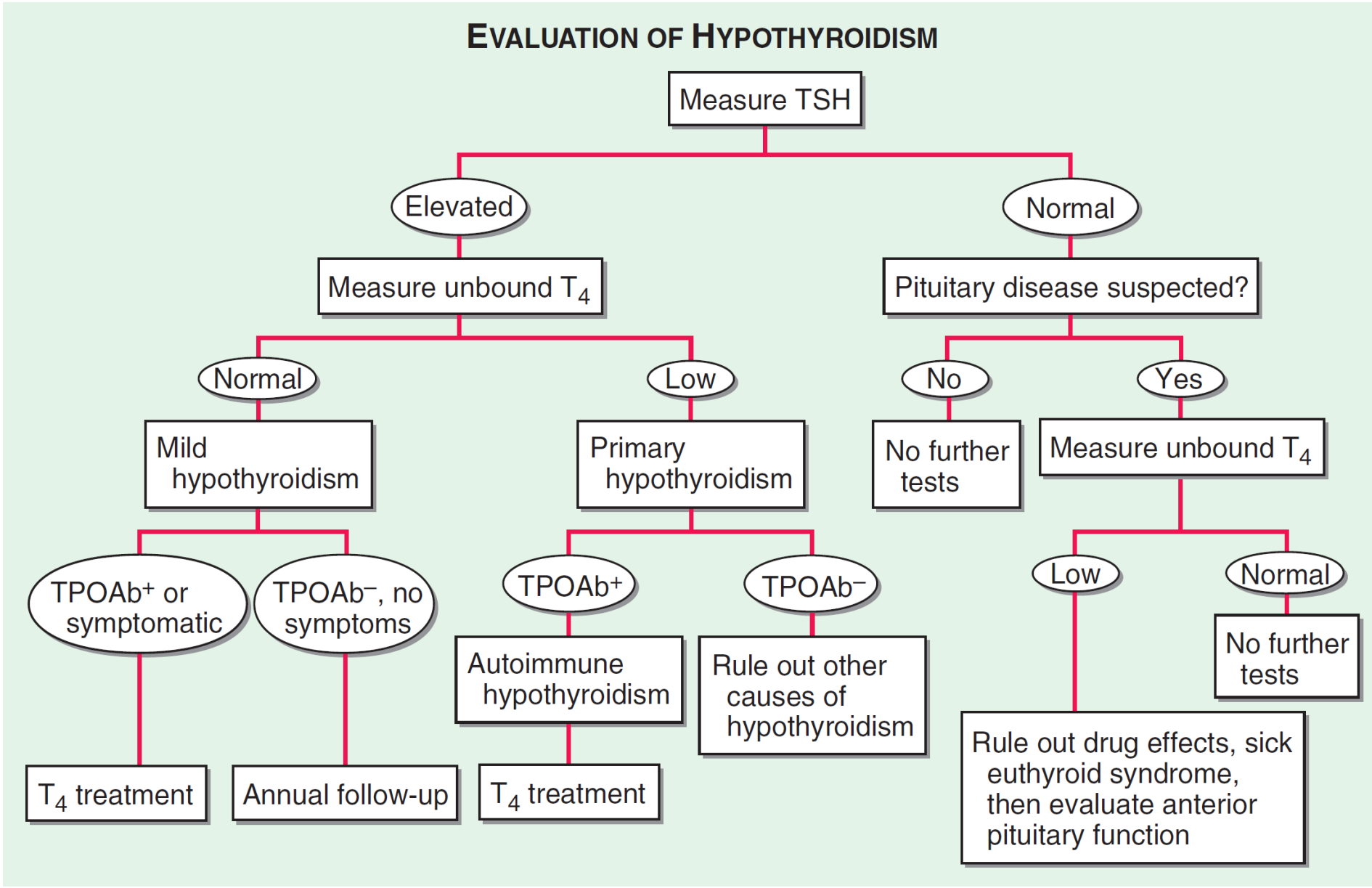


FIGURE 405-7 Evaluation of hypothyroidism. TPOAb+, thyroid peroxidase antibodies present; TPOAb−, thyroid peroxidase antibodies not present; TSH, thyroid-stimulating hormone.

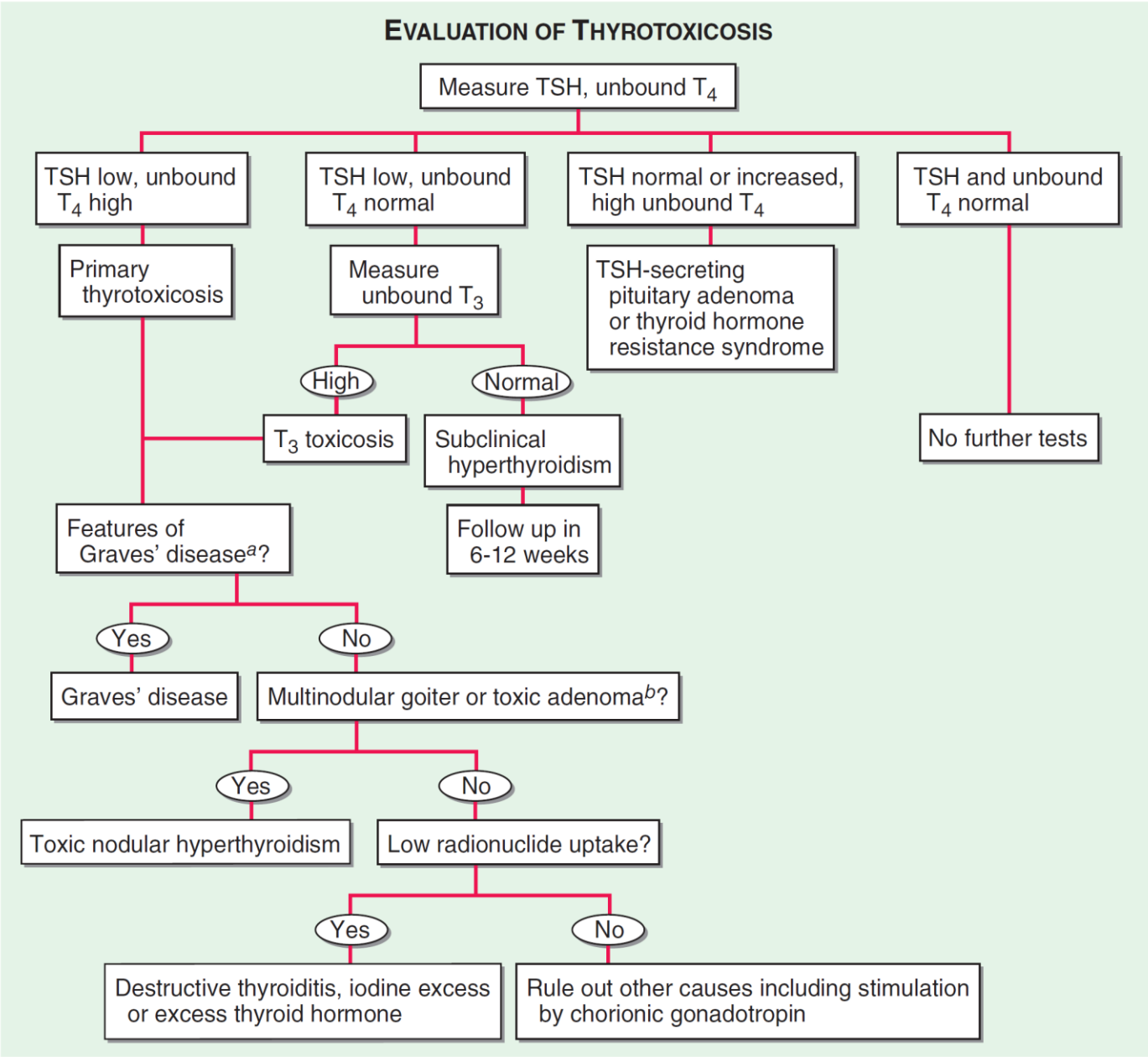


FIGURE 405-9 Evaluation of thyrotoxicosis. [a]Diffuse goiter, positive TPO antibodies or TRAb, ophthalmopathy, dermopathy. [b]Can be confirmed by radionuclide scan. TSH, thyroid-stimulating hormone.