

Isfahan, Iran



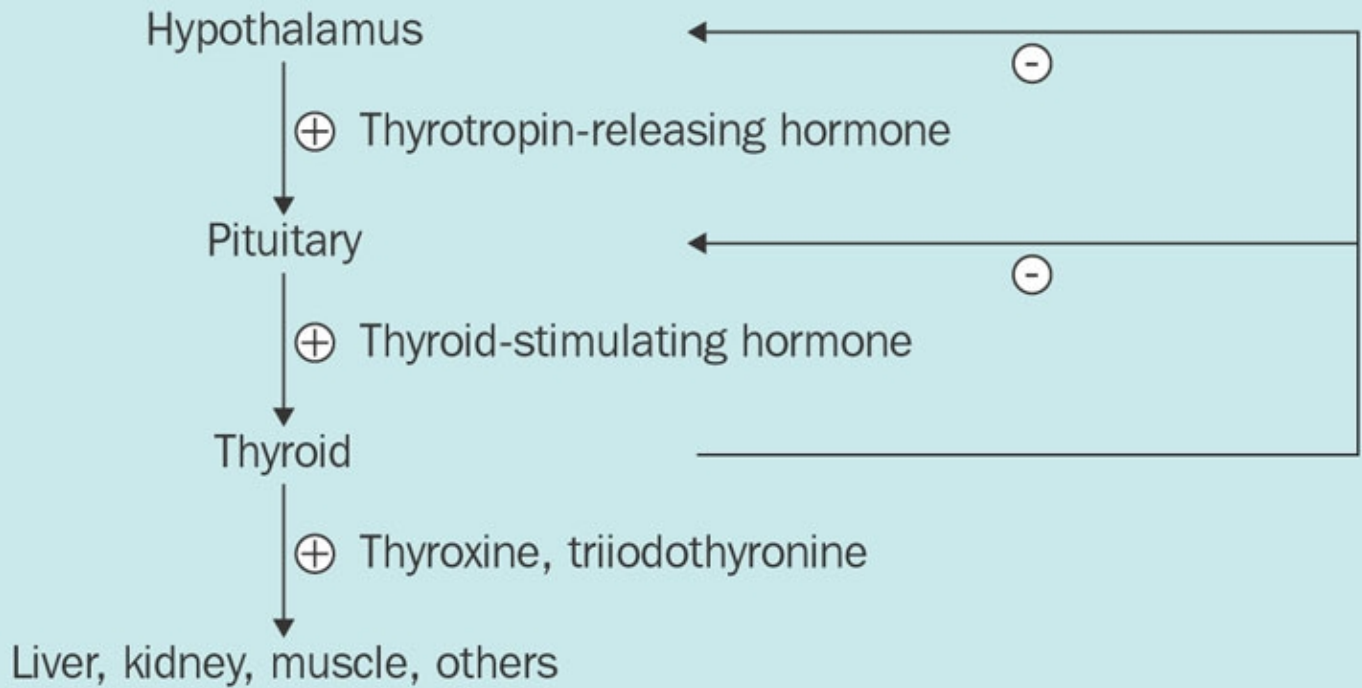
Clinical Utility of Thyroid-Related Laboratory Tests

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)	FT4	Second-best general test
Free (3,5,3') triiodothyronine toxicosis, rare forms of	FT3	Adjunct test, diagnosis of T3 hyperthyroidism
Total (3, 5, 3' -) triiodothyronine	T3	Used in lieu of FT3
Total thyroxine	T4	Inadequate as general test
Thyroglobulin cancer	Tg	Valuable in follow-up of thyroid
TSH response to TRH	TRH	Largely superseded by sTSH
Reverse (3,3'5' -) triiodothyronine	rT3	Not used routinely
Free T4 index:	FT4I/FTI	
T4 □ T3-BR		Should be replaced by FT4
T4 □ T4-BR		Need further evaluation
T4/TBG ratio	T4/TBG	Should be replaced by FT4
	FT3I	

Outline

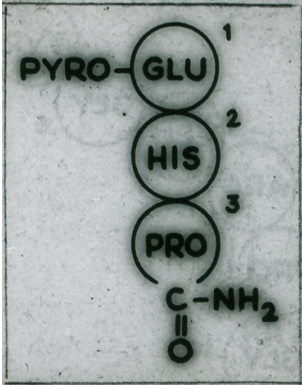
- **Biochemical tests**
- **Imaging studies**
- **Recent diagnostic advances**
- **Anatomy**
- **Cervical map**
- **Iodine metabolism**
- **Thyroid hormone synthesis**
- **Hypothalamic pituitary axis**
- **Thyroid hormone metabolism**
- **Effects of thyroid hormones**

Regulation of thyroid hormones secretion

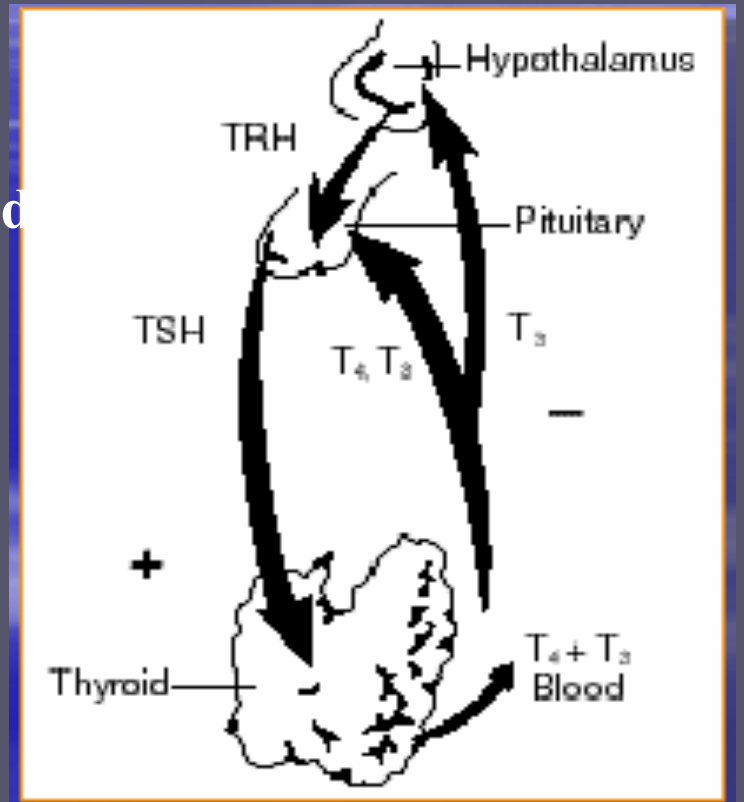


Serum TSH is the most sensitive way to check thyroid function.

The Hypothalamic- Pituitary-Thyroid Axis



Hypothalamic Thyrotropin
Releasing Hormone, (TRH)



Thyroid

liver

T3 + T4

T4

T3

Action

T3

T3 + TBG

T3 . TBG

TBPA

T3 . TBPA

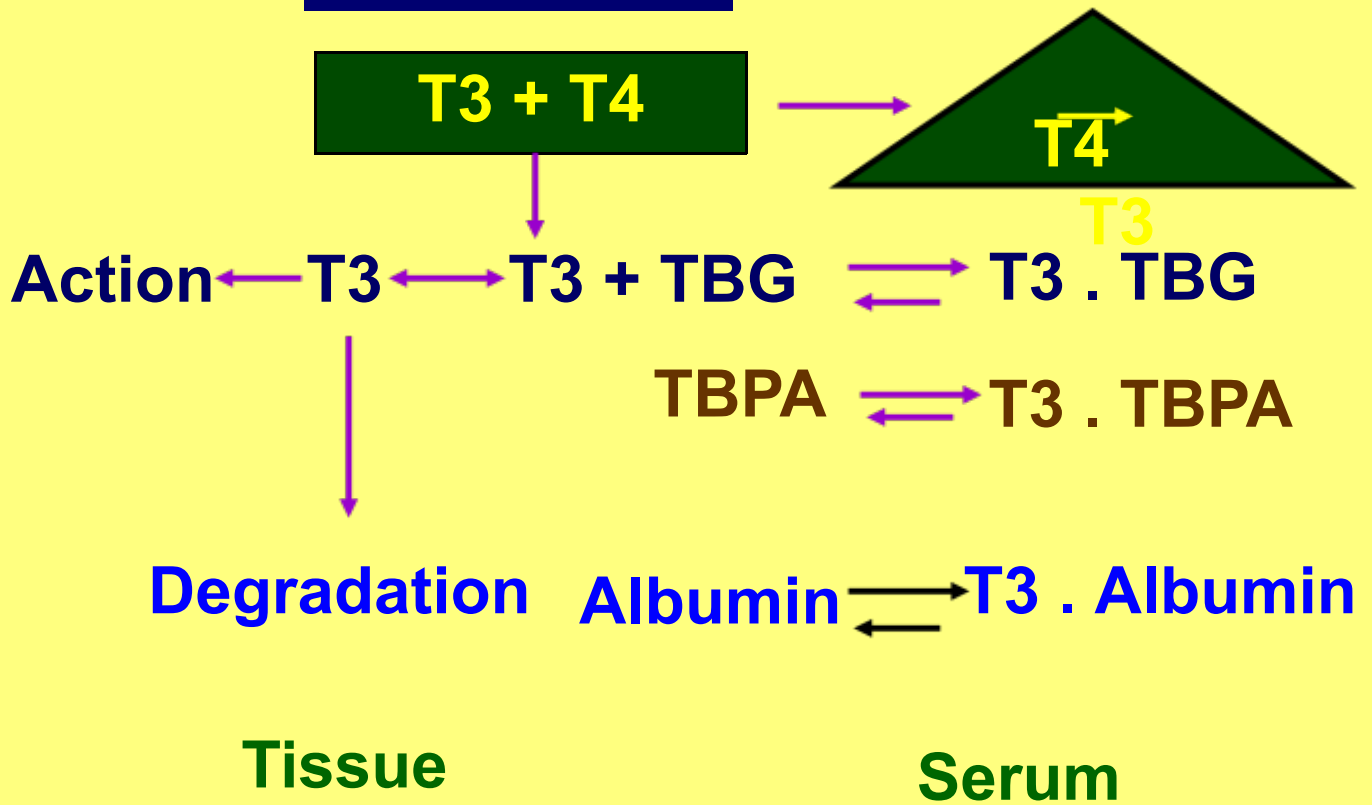
Degradation

Albumin

T3 . Albumin

Tissue

Serum

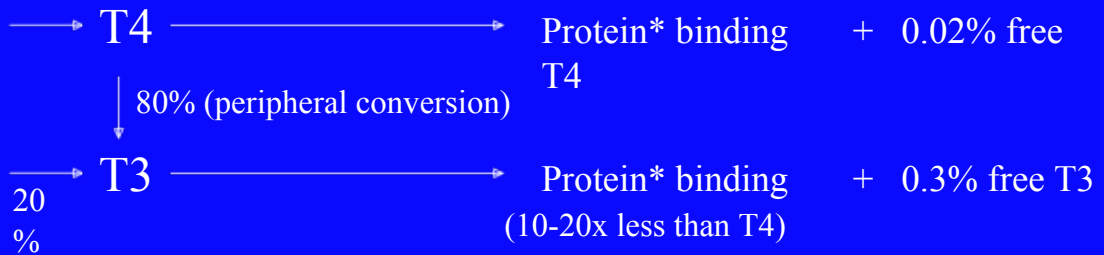


Normal Daily Thyroid Secretion Rate:

T4 = 90-100 ug/day

T3 = 6 ug/day (32 µg/d with peripheral conversion)

(ratio T4:T3 = 14:1)



Total T4 5-12 mcg/dl

Total T3 0.8-2 ng/dl

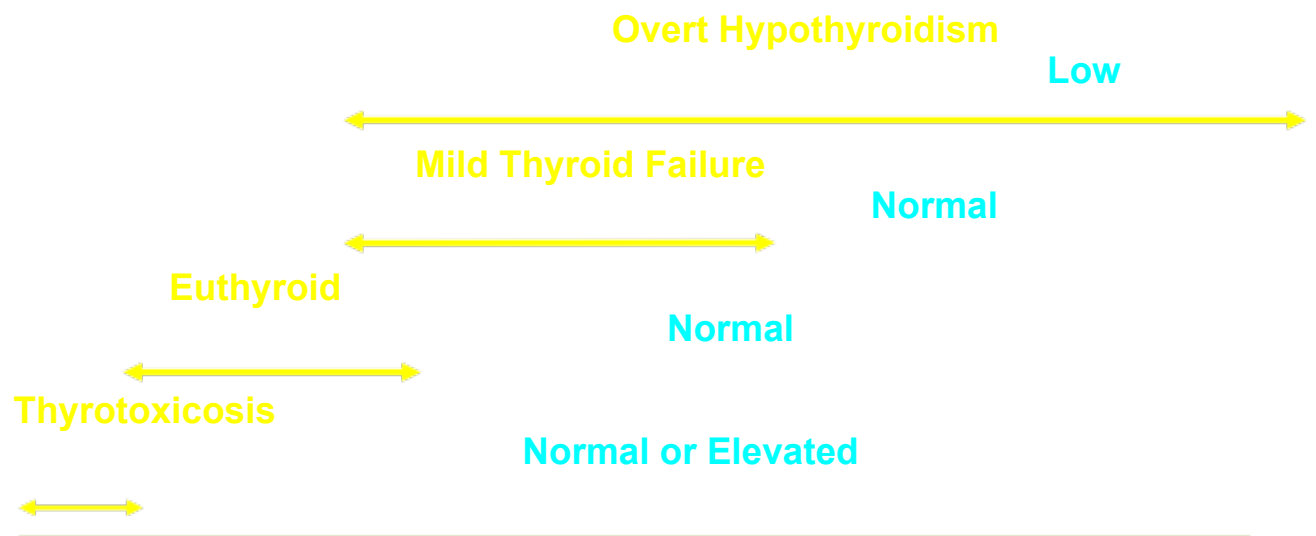
T3RU 25-35 %

TBG : 80% of T4

TBPA : 10% of T4

Albumin: 10% of T4 and
30% of T3

Thyroid Disease Spectrum



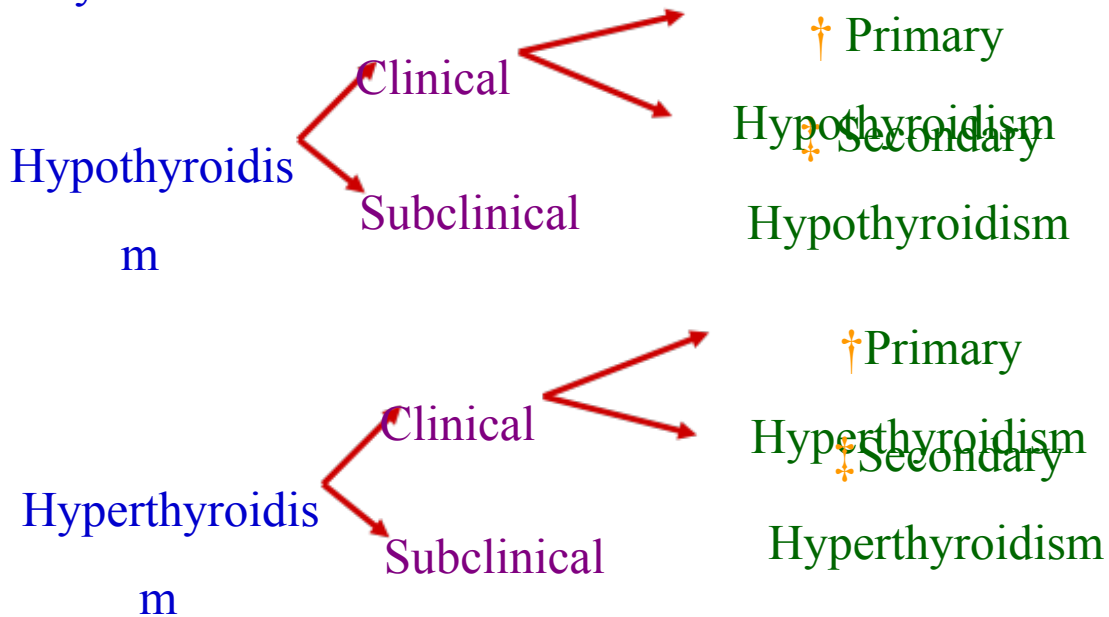
Braverman LE, et al. *Werner & Ingbar's The Thyroid. A Fundamental and Clinical Text*. 8th ed. 2000.

Canaris GJ, et al. *Arch Intern Med*. 2000;160:526-534.

Vanderpump MP, et al. *Clin Endocrinol (Oxf)*. 1995;43:55-68.

Patterns of Thyroid Function

Euthyroidism



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

Secretion

Nine Square Approach

FREE THYROID ROXINE or	LOW	THYROID STIMULATING HORMONE - TSH		
	NORMAL	LOW	NORMAL	HIGH
	HIGH			
		1	2	3
		4	5	6
		7	8	9

Nine Square Approach

FREE THYROID HORMONE or T4	LOW			
	NORMAL	SUB CLINICAL HYPERTHYR OID		
	HIGH			
		LOW	NORMAL	HIGH
		THYROID STIMULATING HORMONE - TSH		

Nine Square Approach

FREE THYROID HORMONE or T4	LOW			
	NORMAL			
	HIGH			
THYROID STIMULATING HORMONE - TSH		LOW	NORMAL	HIGH

Nine Square Approach

FREE THYROIDINE or	LOW		Central Hyperthyroidis m	
	NORMAL			
	HIGH			
		THYROID STIMULATING HORMONE - TSH		
		LOW	NORMAL	HIGH

Nine Square Approach

FREE THYROID HORMONE or T4	LOW			
	NORMAL		Normal	
	HIGH			
		LOW	NORMAL	HIGH
		THYROID STIMULATING HORMONE - TSH		

Nine Square Approach

FREE THYROID HORMONE or T4	LOW	NORMAL	HIGH
		Central Hypothyroidis m	
THYROID STIMULATING HORMONE - TSH			
	LOW	NORMAL	HIGH

Nine Square Approach

FREE THYROID HORMONE or T4	LOW			Central Hyperthyroidis m
	NORMAL			
	HIGH			
		LOW	NORMAL	HIGH
		THYROID STIMULATING HORMONE - TSH		

Nine Square Approach

FREE THYROIDINE or	LOW			
	NORMAL			Subclinical Hypothyroidism
	HIGH			
		LOW	NORMAL	HIGH
		THYROID STIMULATING HORMONE - TSH		

Nine Square Approach

FREE THYROIDINE or T4	LOW			
	NORMAL			
	HIGH			
THYROID STIMULATING HORMONE - TSH		LOW	NORMAL	HIGH

**Primary
Hypothyroidis
m**

Nine Square Approach

FREE THYROID HORMONE or T4	LOW		
	NORMAL		
	HIGH		
TSH	LOW	PRIMARY HYPERTHYROID	Central Hyperthyroidism
	NORMAL	SUB CLINICAL HYPERTHYROID	Normal
	HIGH	Central Hypothyroidism	Primary Hypothyroidism

برای هر یک از موارد زیر تشخیص مطرح
کنید

تشخیص	TSH 0.3-5 (μ U/ml)	Resine T3 uptake 25-35 (%)	T3 80-180 (ng-dl)	T4 4.5-12.5 (μ g/dl) 12.5(μ g/dl)	
	0.1	30	390	20	
	15	26	110	6	
	24	31	50	2	
	48	22	110	3	
	2.7	21	70	4	
	1.2	30	50	10	
	8.1	36	290	16	دو جواب دارد

برای هر یک از موارد زیر تشخیص مطرح

	T4	T3	کنند Resine T3 uptake	TSH	
تشخیص	4.5-12.5 (μg/dl)	80-200 (ng-dl)	25-35 (%)	0.1-5 (μU/ml)	مقادیر طبیعی
	5.5	120	25	18	
	18	200	40	0	
	3	100	22	85	
	4	70	43	1.2	
	4	70	21	0.7	
	17	280	22	1.1	
دو جواب دارد	16	290	30	8.1	
	10.5	170	33	<0.1	

Multinodular Goiter Since Puberty

She is a 29-year old woman with a history of goiter since puberty. She is euthyroid, and feels pressure when she puts her hands over her head. FT4 = 1.4 ng/dl (0.8-2), T3 = 160 ng/dl (80-200), TSH = 0.4 mU/L. What would you recommend?



Which of these individuals has hypothyroidism?



Age
(y)

5

1

2

Symptoms

None

Facial
puffiness
Fatigue

Cold
intolerance
Goiter
Constipation
Leg cramps

Thyroid Failure Can Be Subtle & Progressive



Age (y)	5	16	25
Symptoms	None	Facial puffiness Fatigue	Cold intolerance Goiter Constipation Leg cramps
Normal TSH (0.5- 5.0 mU/L)	TSH 2.9	TSH 7.0	TSH 150
Normal FT4 (0.7- 2.1 ng/dL)	Free T4 0.9	Free T4 0.8	Free T4 0.2

Multinodular Goiter

She is a 48-year-old woman with a long history of slowly growing goiter. FT4 and T3 are within normal range. TSH = 0.1 mU/L. What is your next step?



Normal serum TSH varies between 0.35 uu/ml to 5.50 uu/ml.
 $5.5/0.35 \approx$ a 16 fold difference.

There seems to be a lot of room for going up and down the ladder of TSH & yet stay within the normal limits.



Thyroid Function Tests

TSH

Affected by: Acute illness

Affected by: **Dopamine, Glucocorticoids**
and many other drugs

Thyroid Function Tests

sTSH

Under **negative feedback** by: Free T4 & T3

Under positive feedback by: TRH

Good indicator of treatment with hormone

Indications for the s-STH

- Exclusion of thyroid disease.
- Normal TSH values have the highest sensitivity and specificity for euthyroid patients in an ambulatory setting.

Case Study

- A 44-year-old woman has been referred with a two-year history of fatigue and amenorrhea. Thyroid is barely palpable.
- Thyroid function tests; FT4 0.6 ng/dl (normal 0.8-2), TSH 0.8 mU/L (normal 0.3-5).
- What is your interpretation?

Case Study

- A 44-year-old woman has been referred with a two-year history of fatigue and amenorrhea. Thyroid is enlarged up to 50 grams.
- Thyroid function tests; FT4 0.6 ng/dl (normal 0.8-2), TSH 35 mU/L (normal 0.3-5).
- What is your interpretation?

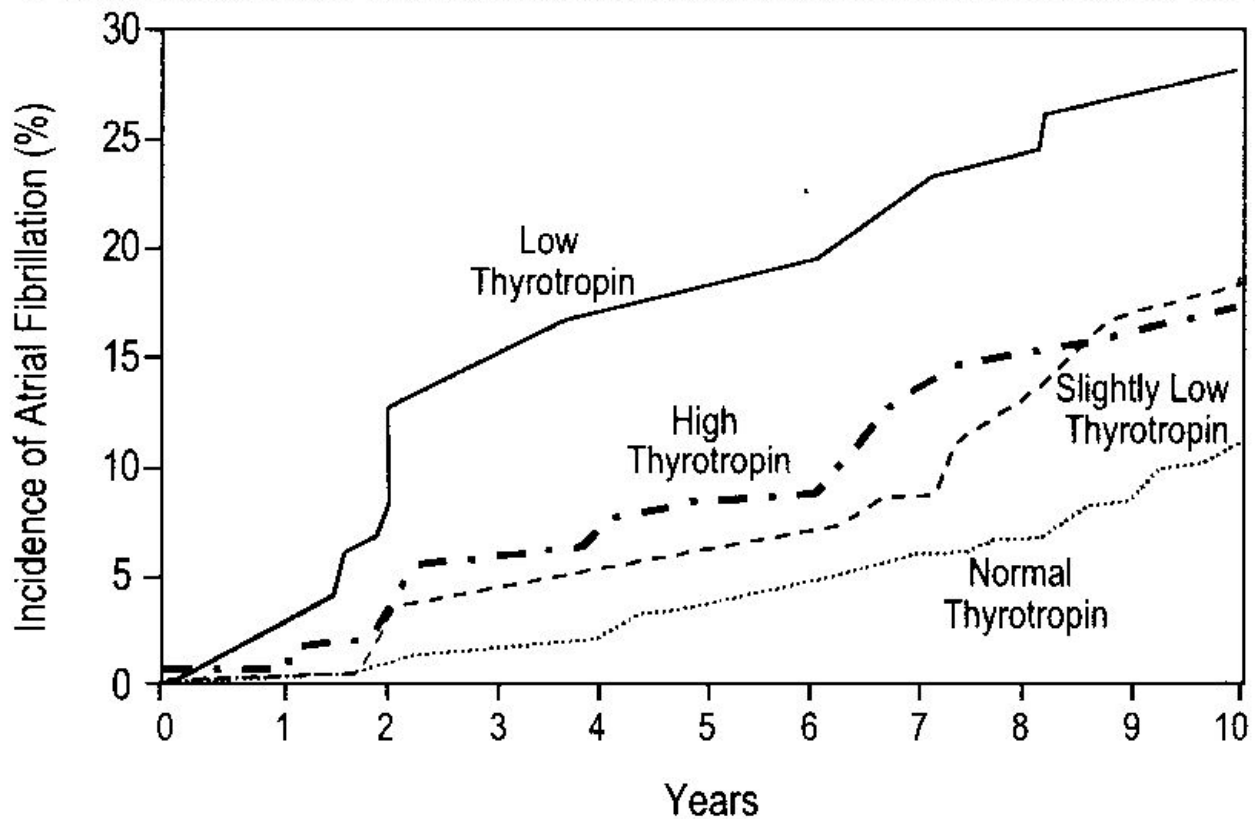
Atrial Fibrillation in SCH

Epidemiologic Study: Low TSH vs. A-fib

- ◆ Framingham database: 2007 patients ≥ 60 y.o.
- ◆ No A-fib at onset of 10 yr follow-up
- ◆ Patients grouped according to initial TSH
 - ▶ Low (< 0.1 mU/L)
 - ▶ Slightly low ($0.1 - 0.4$ mU/L)
 - ▶ Normal (> 0.4 but < 5.0 mU/L)

awin, et al. *N Engl J Med.* 1994;331:1249-1252.

Incidence of Atrial Fibrillation in 10-year Follow-up



Sawin. et al. *N Engl J Med.* 1994;331:1249-1252.

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

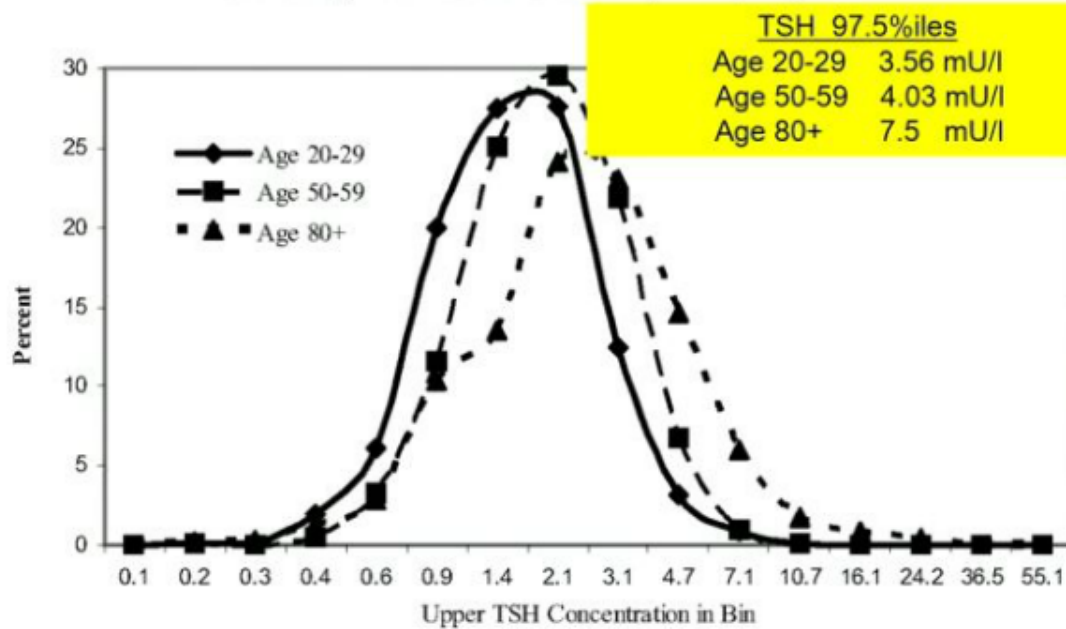
Clinical Situations in Which Measurements of Serum TSH alone May Yield Misleading Results

Condition	Serum TSH	Consequences of clinical action based on serum TSH alone	Serum FT4
Central Hypothyroidism	Normal	Failure to diagnose hypothyroidism	Low
TSH-secreting pituitary adenoma	Normal	Failure to diagnose thyrotoxicosis	High
Thyroid hormone resistance	Normal	Failure to recognize the condition	High
Poor compliance with T4 therapy	High	Inappropriate increase in dose of T4	High

Patient 1

- An 80 year old woman sees her PCP for her annual check up.
- Her TFT's were as follows: **FT4 1.0 ng/dl, TSH 5.6 mU/l**
- She is referred to you for further evaluation 3 months later
- She feels well
- There is no family history of thyroid disease
- Her medications include HCTZ, lisinopril, and metformin
- Her physical exam is normal
- You repeat the TFT's 3 months later and they are unchanged. AntiTPO Ab are negative.
- What is your interpretation?

TSH distribution by age groups in the United States
 excluding individuals with +FH, +AB, or goiter



Surks, M. I. et al. J Clin Endocrinol Metab 2007;92:4575-4582

Sensitive TSH and Free T4

When using the free thyroxine (FT4) and TSH levels to assess thyroid disease, remember that there is a log relationship between the two. If the FT4 level decrease by 50%, TSH increase by 100%.

Thyroid Function Tests

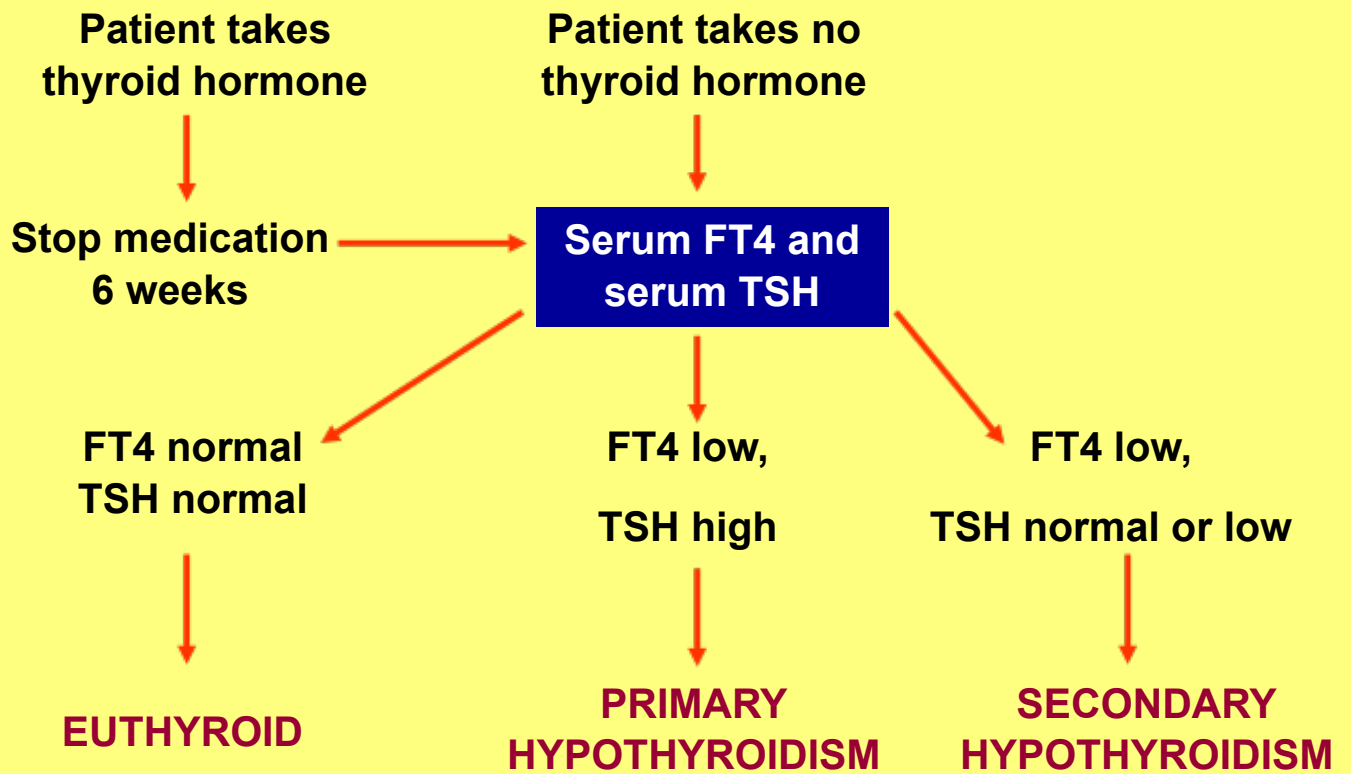
TSH

Affected by: Acute illness

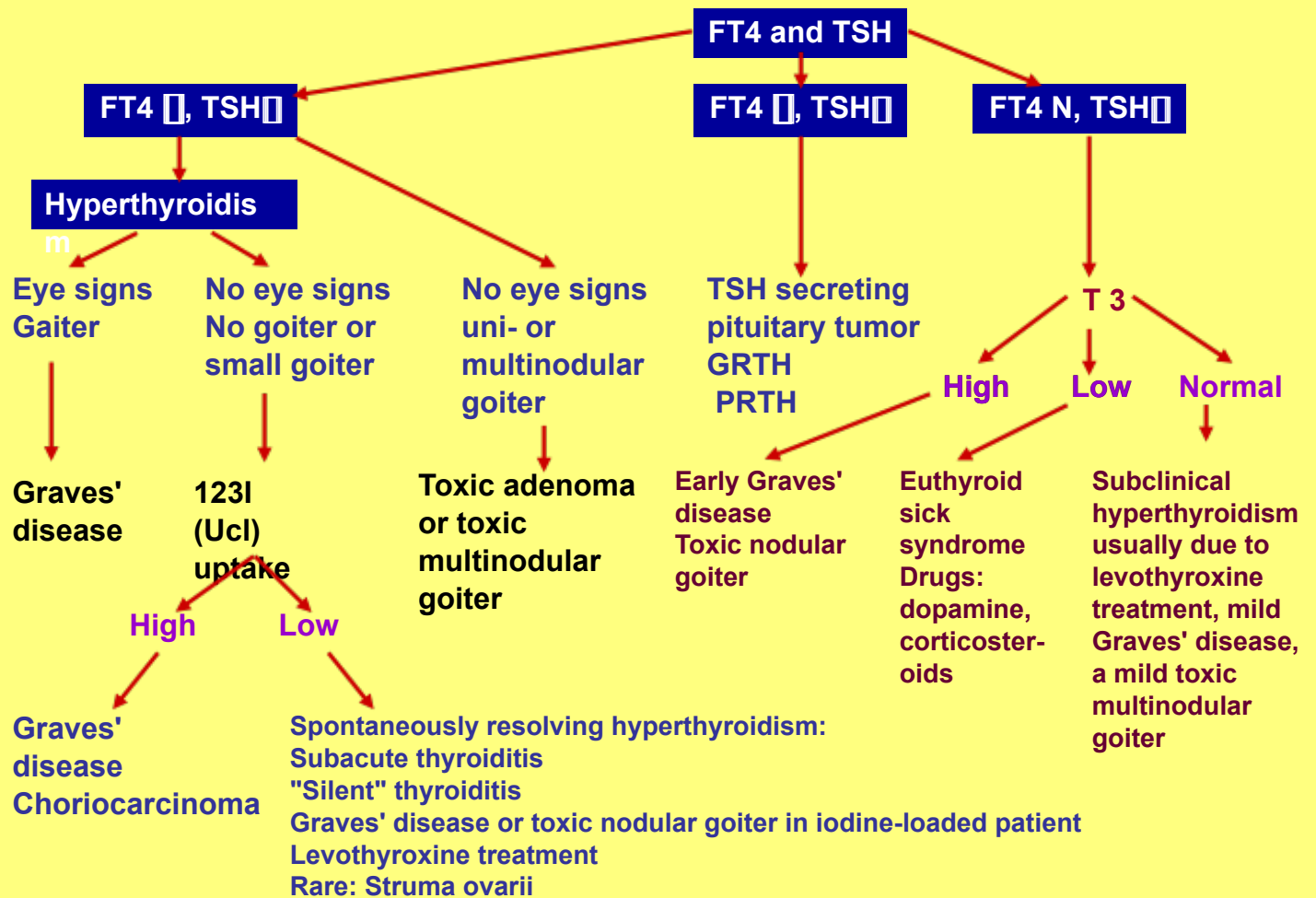
Affected by: **Dopamine, Glucocorticoids**
and many other drugs

Indications for the s-STH

- Exclusion of thyroid disease.
- Normal TSH values have the highest sensitivity and specificity for euthyroid patients in an ambulatory setting.



Diagnosis of hypothyroidism



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

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Causes of a low or undetectable TSH level

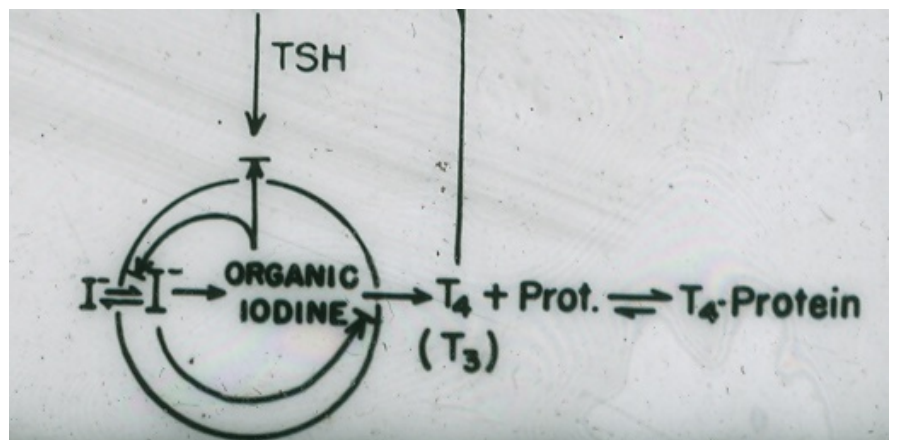
Lowered TSH	Free thyroid hormone levels
Overt thyrotoxicosis	↑
Subclinical thyrotoxicosis	N
Recently treated hyperthyroidism	N
Thyroid-associated ophthalmopathy without Graves' disease	N
Excessive thyroxine treatment	N or ↑
Nonthyroid illness (sick euthyroid syndrome)	□ or N
First trimester of pregnancy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

sensitive-TSH

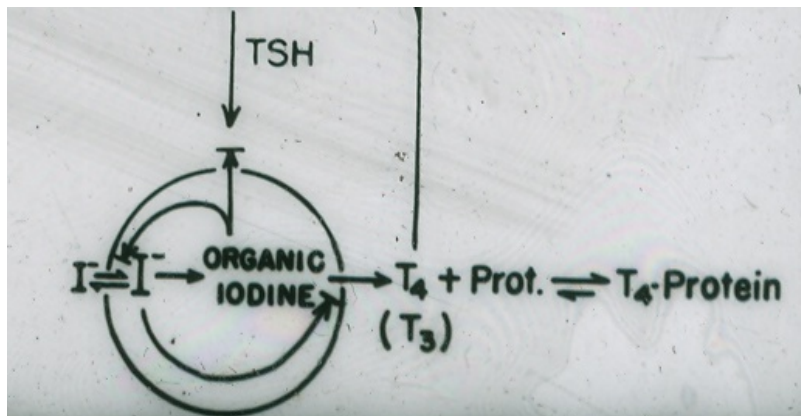
S-TSH assays is not recommended for screening thyroid function in :

- 1) patients with hypothalamic or pituitary diseases
- 2) acute psychiatric disorders in hospitalized patients

T4 & T3



T4 & T3



Circumstances Associated with Altered Binding of Thyroxine by Thyroxine-Binding Globulin

Increased Binding

- Pregnancy
- Neonate state
- Estrogens
- Infectious and chronic active hepatitis
- Genetic
- Perphenazine
- HIV infection

Decreased Binding

- Androgens
- Large doses of glucocorticoids
- Active acromegaly
- Nephrotic syndrome
- Major systemic illness
- Genetic
- Asparaginase

Total Thyroxine

Total T3

Recommendations for T3 measurement

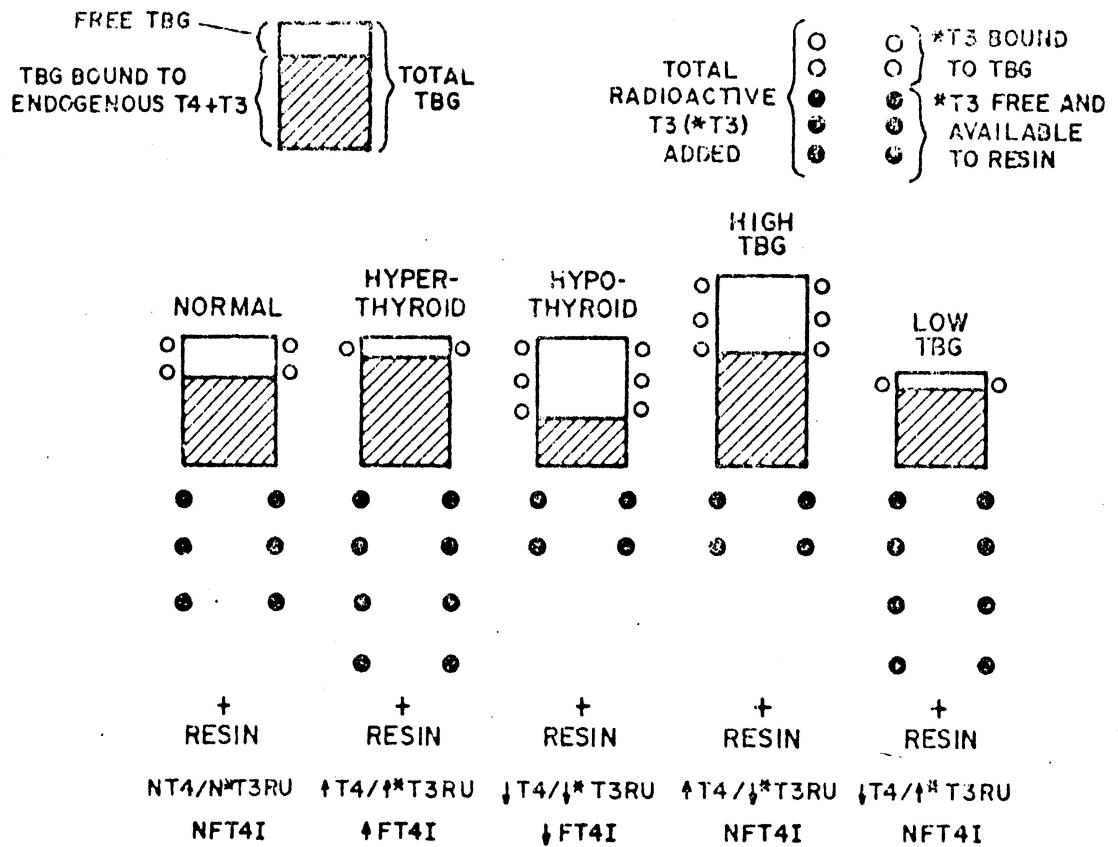
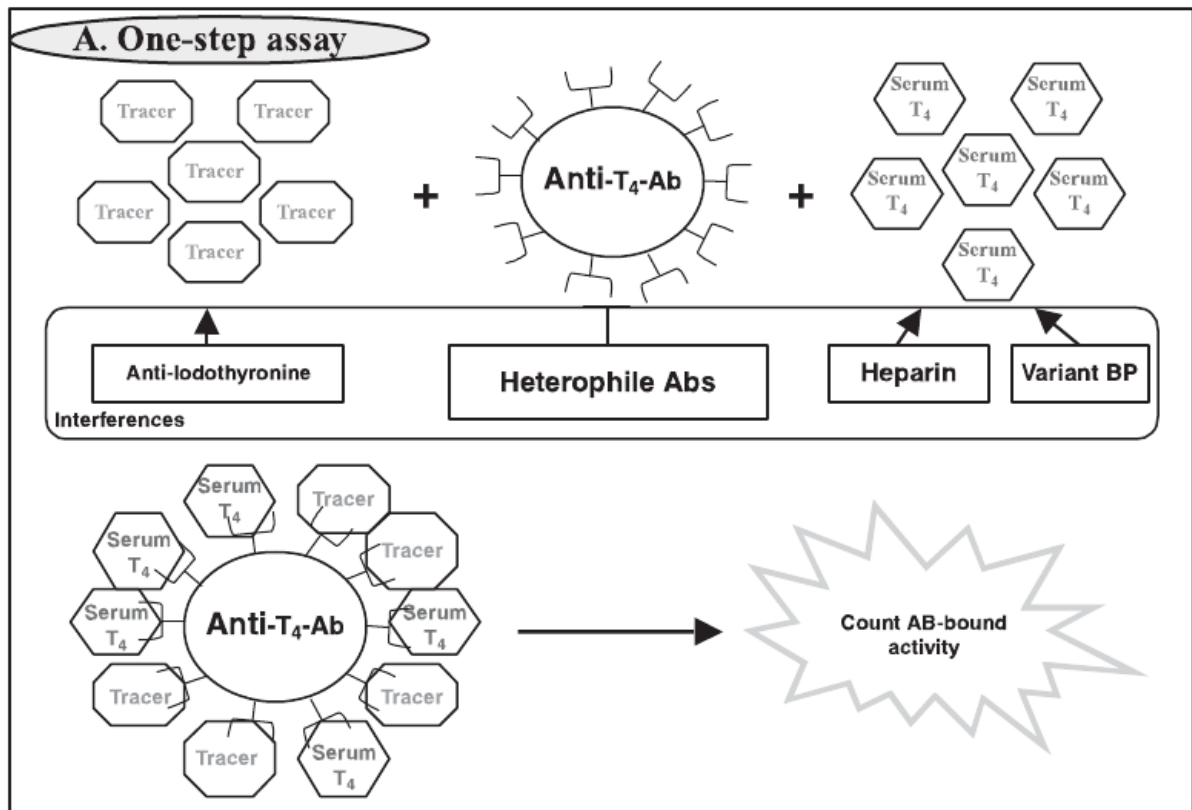


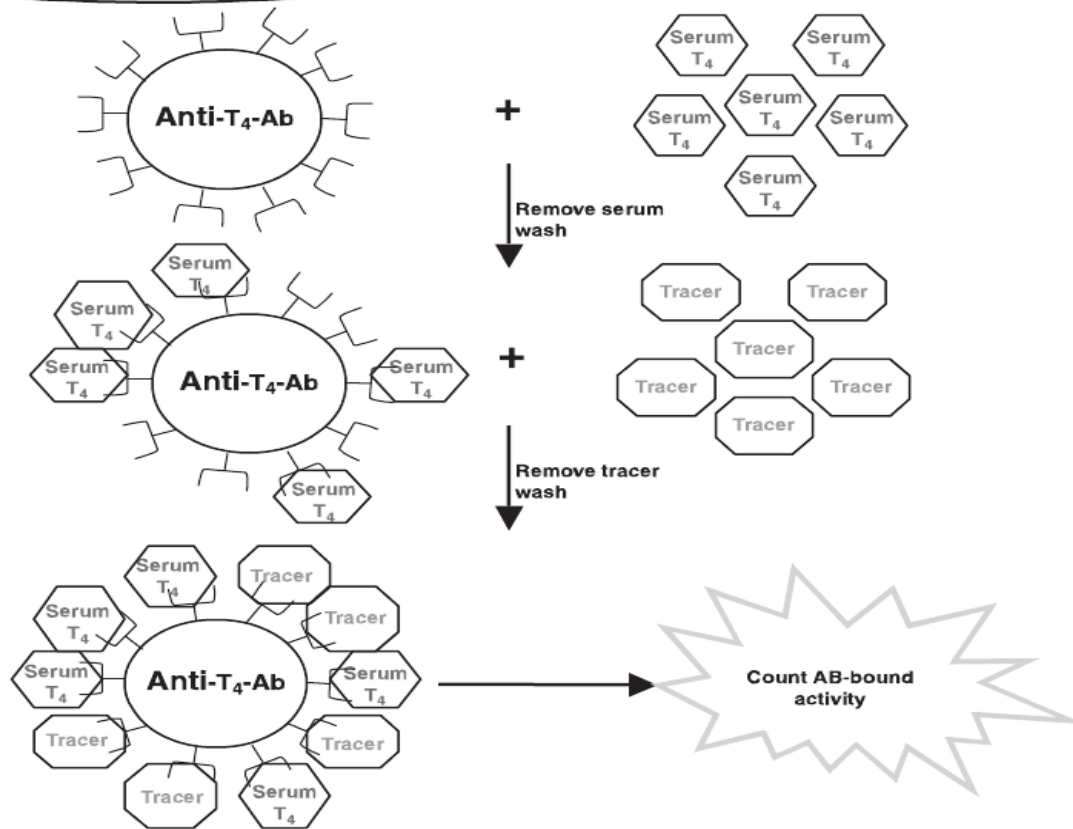
Fig. 5. Schematic representation of T_3 resin uptake test ($*T_3RU$). T_4 , total thyroxine in serum; T_3 , total triiodothyronine in serum; FT_4I , free thyroxine index; N, normal; ↑, supranormal; ↓, subnormal. See text for further explanation.

Serum FT4/FT3 one-step assay methodology



Serum FT4/FT3 two-step assay methodology

B. Two-step assay



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Total thyroxine	T4	Inadequate as general test
Thyroglobulin cancer	Tg	Valuable in follow-up of thyroid
TSH response to TRH	TRH	Largely superseded by sTSH
Reverse (3,3'5' -) triiodothyronine	rT3	Not used routinely
Free T4 index:	FT4I/FTI	
T4 $\square$ T3-BR		Should be replaced by FT4
T4 $\square$ T4-BR		Need further evaluation
T4/TBG ratio	T4/TBG	Should be replaced by FT4

FT3I

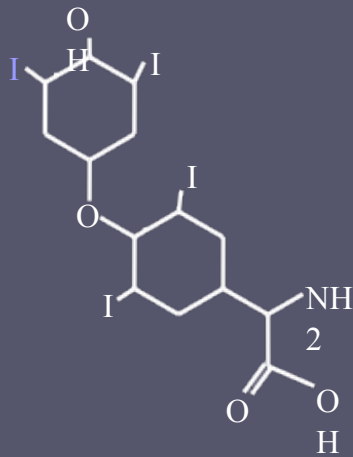
Diagnostic Utility of the Free Thyroxine Index Values

	Total T4	T3U	FT4 Index
Euthyroid	N	N	N
Hyperthyroid	↑	↑	↑
Hypothyroid	↓	↓	↓
Increased TBG	↑	↓	N
Decreased TBG	↓	↑	N

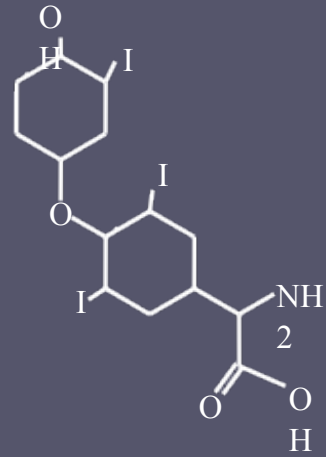
Diagnostic Utility of Free Thyroxine Index Values

	Total T4	T3 Uptake	FT4 Index
Euthyroidism	N	N	N
Hyperthyroidism	↑	↑	↑
Hypothyroidism	↓	↓	↓
Increased TBG	↑	↓	N
Decreased TBG	↓	↑	N

THYROID HORMONES

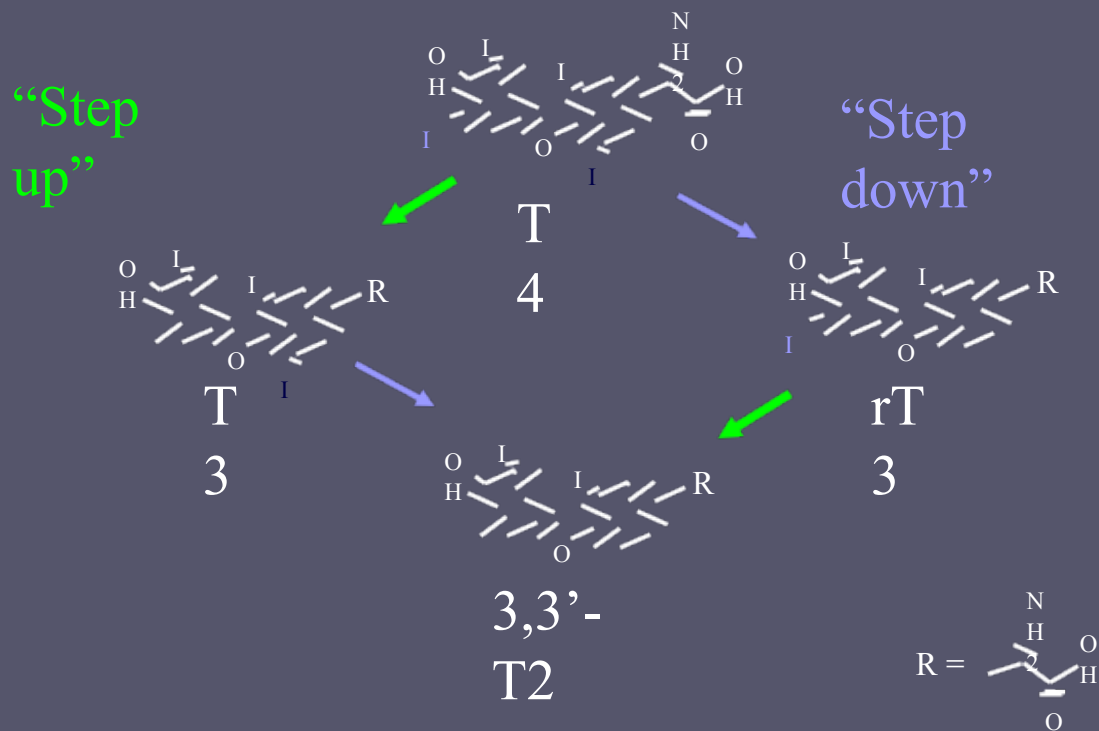


Thyroxine
(T4)



3,5,3'-Triiodothyronine
(T3)

THYROID HORMONE METABOLISM



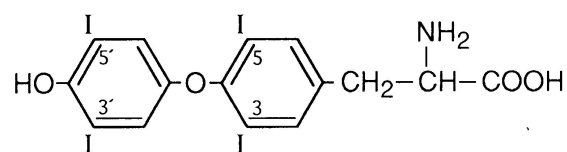
THYROID HORMONE DEIODINASES

- Three deiodinases (D1, D2 & D3) catalyze the generation and/disposal of bioactive thyroid hormone.
- D1 & D2 “bioactivate” thyroid hormone by removing a single “outer-ring” iodine atom.
- D3 “inactivates” thyroid hormone by removing a single “inner-ring” iodine atom.
- All family members contain the novel amino acid selenocysteine (SeC) in their catalytic center.

Thyroid Function Tests

Reverse T3

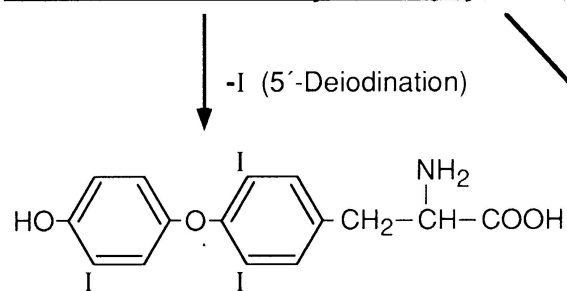
**Deionated T4 at
the 5 position**



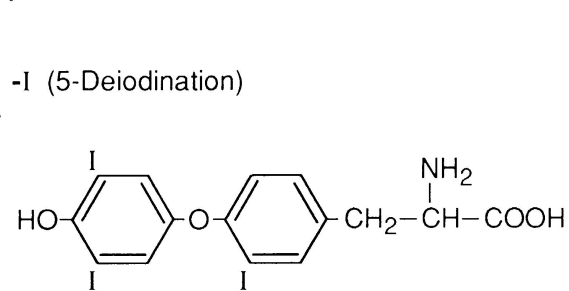
3,5,3',5' - tetraiodo L-thyronine (thyroxine, T4)

ALTERNATE ROUTES

{
 -SO₄ + Gluc. Conjugation
 Deamination + Decarboxylation
 Ether-link Cleavage



3,5,3' - triiodo L-thyronine (T3)



3,3',5' - triiodo L-thyronine (reverse T3)

Three major pathways for peripheral thyroxine metabolism

Primary Care Diagnosis of Thyroid Disease

Biochemical Tests

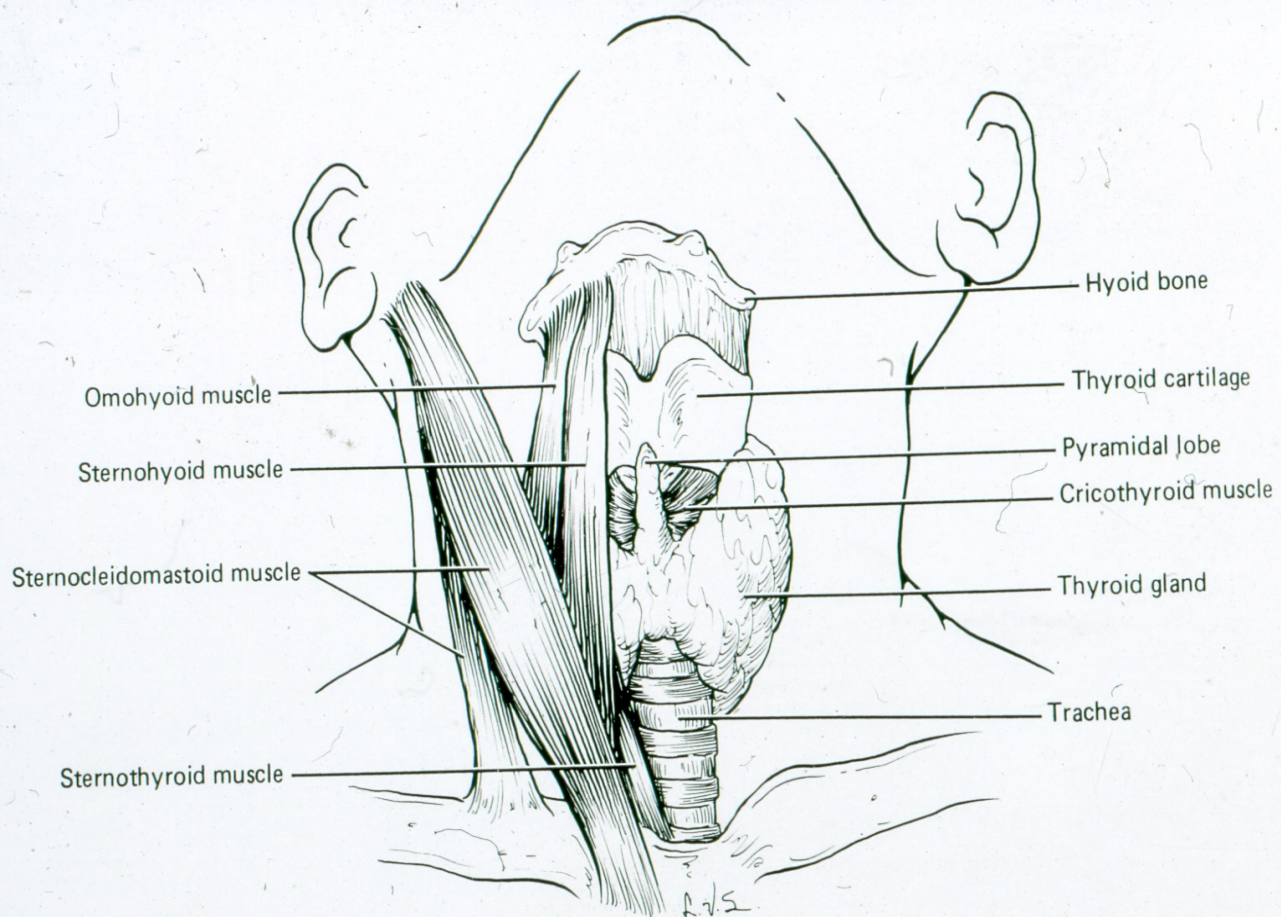
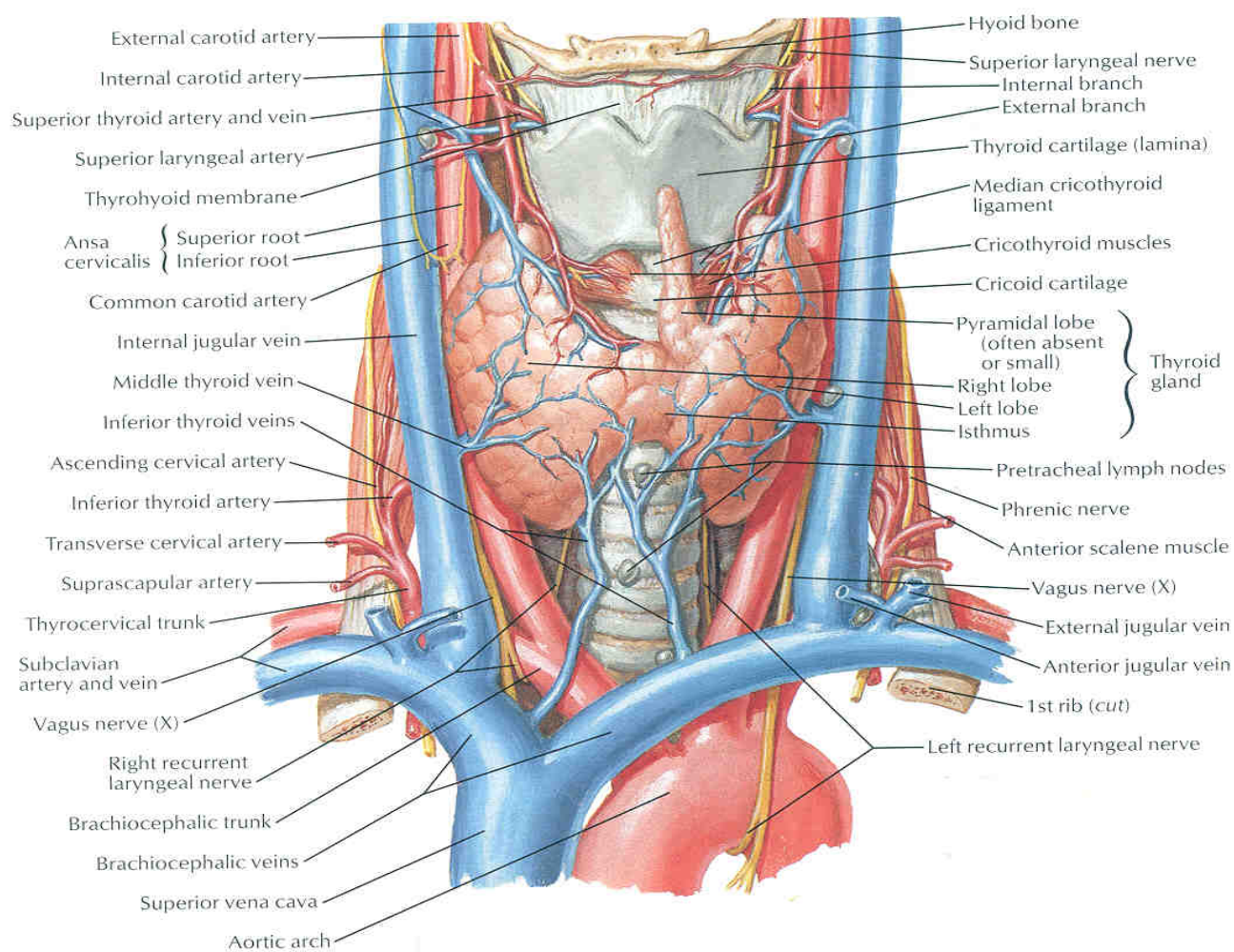
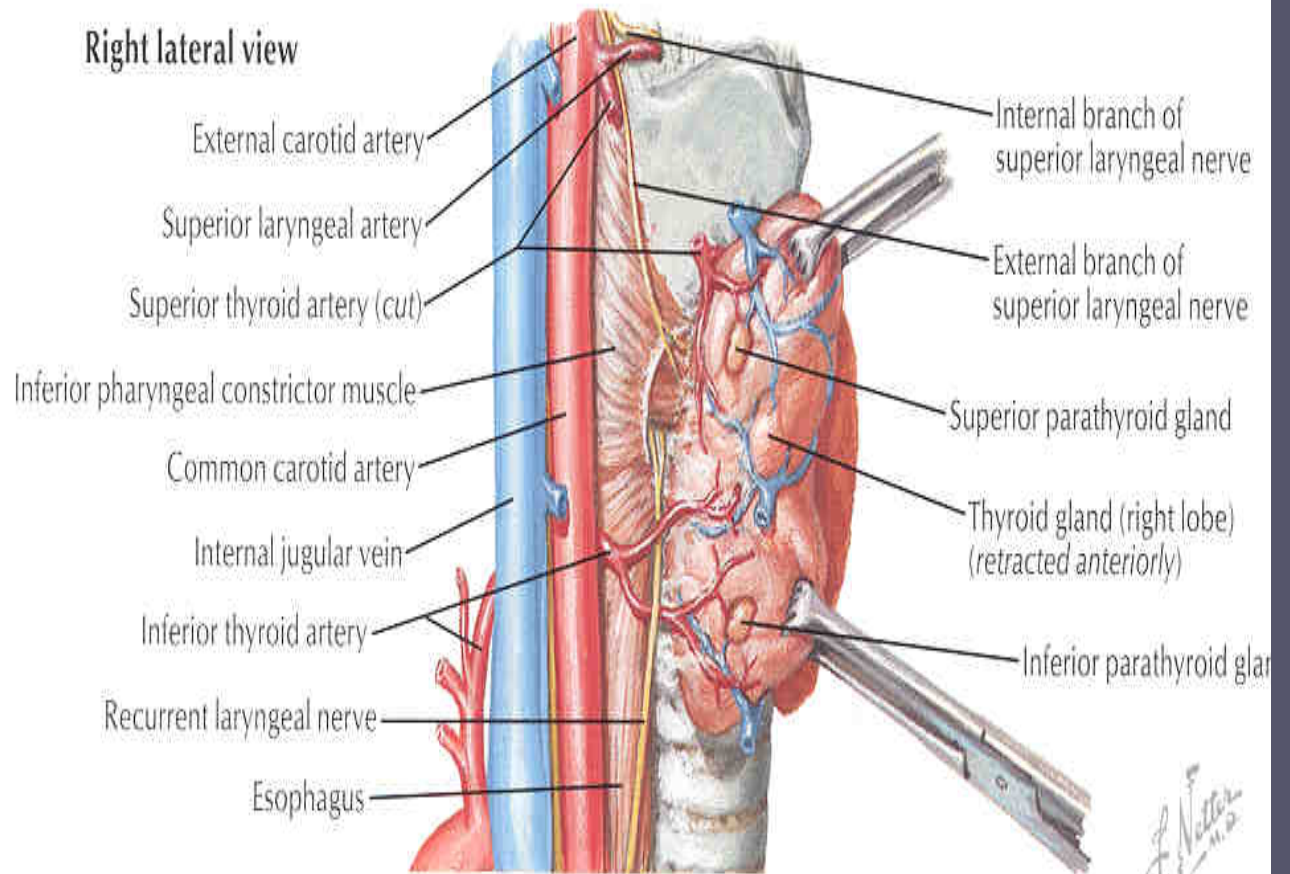


Figure 7-2. Gross anatomy of the human thyroid (anterior view).



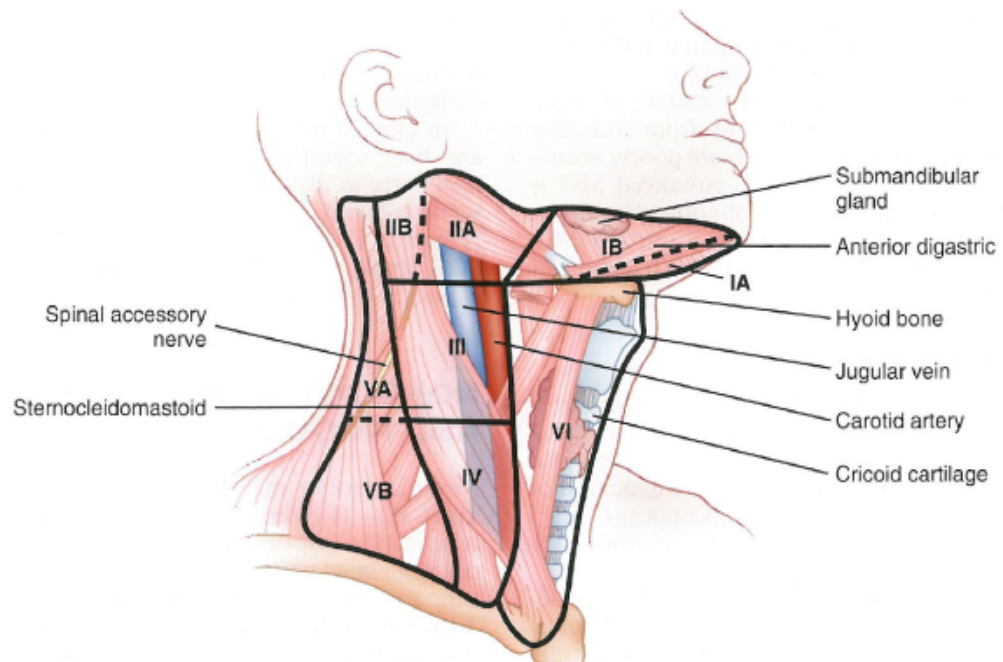
Right lateral view



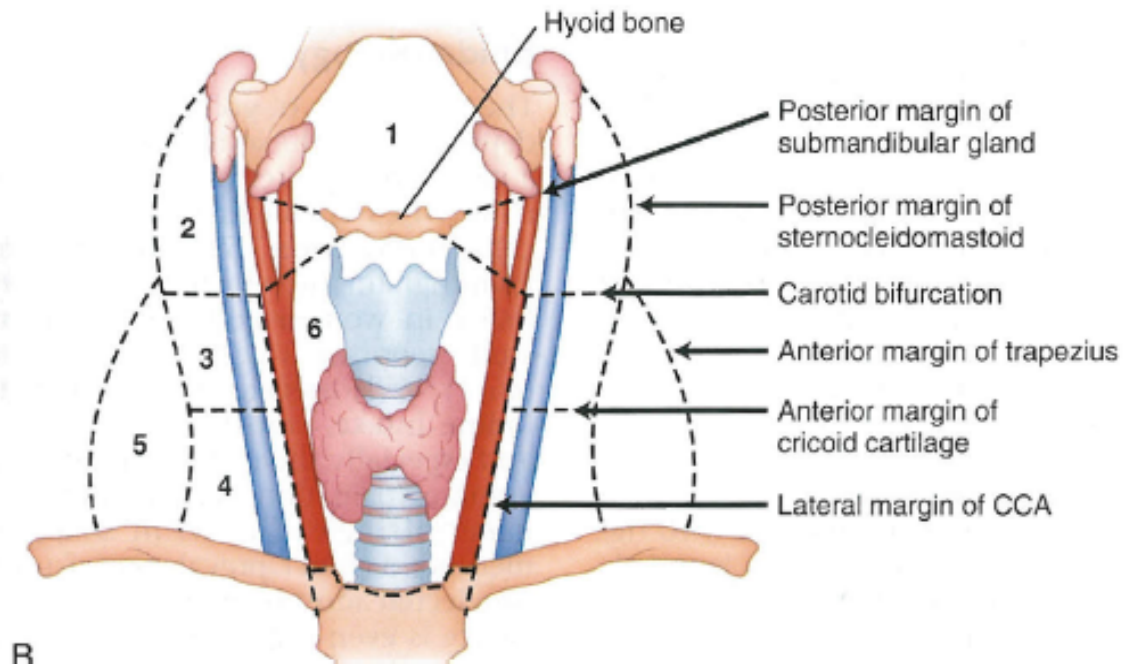
F. Netter
M.D.

© Novartis

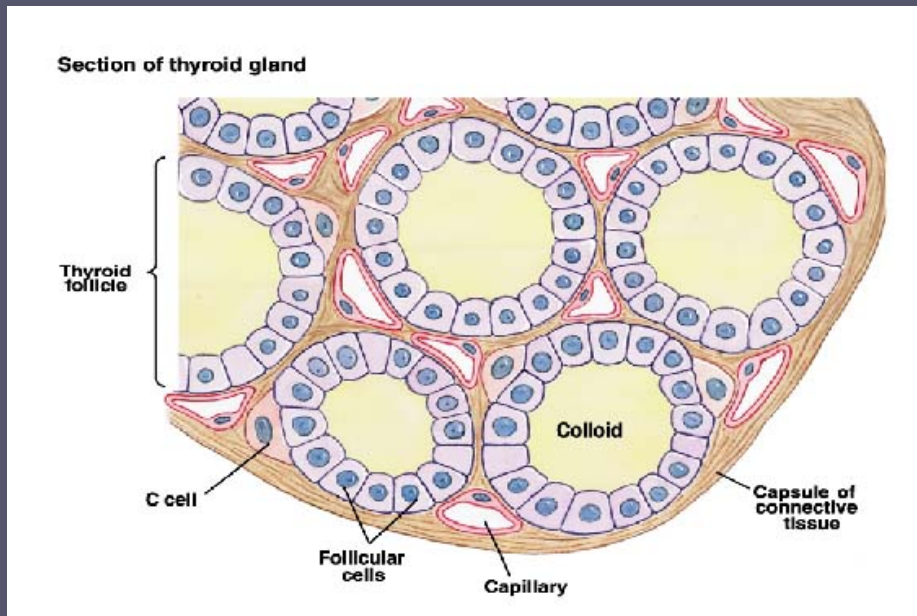
Anatomic Scheme of with Compartments



Cervical Map



Follicles: the Functional Units of the Thyroid Gland



Follicles Are the Sites Where Key Thyroid Elements Function:

- Thyroglobulin (Tg)
- Tyrosine
- Iodine
- Thyroxine (T4)
- Triiodotyrosine (T3)

جدول تناوبی عنصرها

جدول تناوبی عناصر

1 1 H	2 He																
3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba	57 La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
87 Fr	88 Ra	89 Ac	104 Unq	105 Unp	106 Unh	107 Uns	108 Uno	109 Une									

58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr



عدد اتمی

نشانہ

نا فلزات دیگر

گازهای نجیب

شبه فلزات

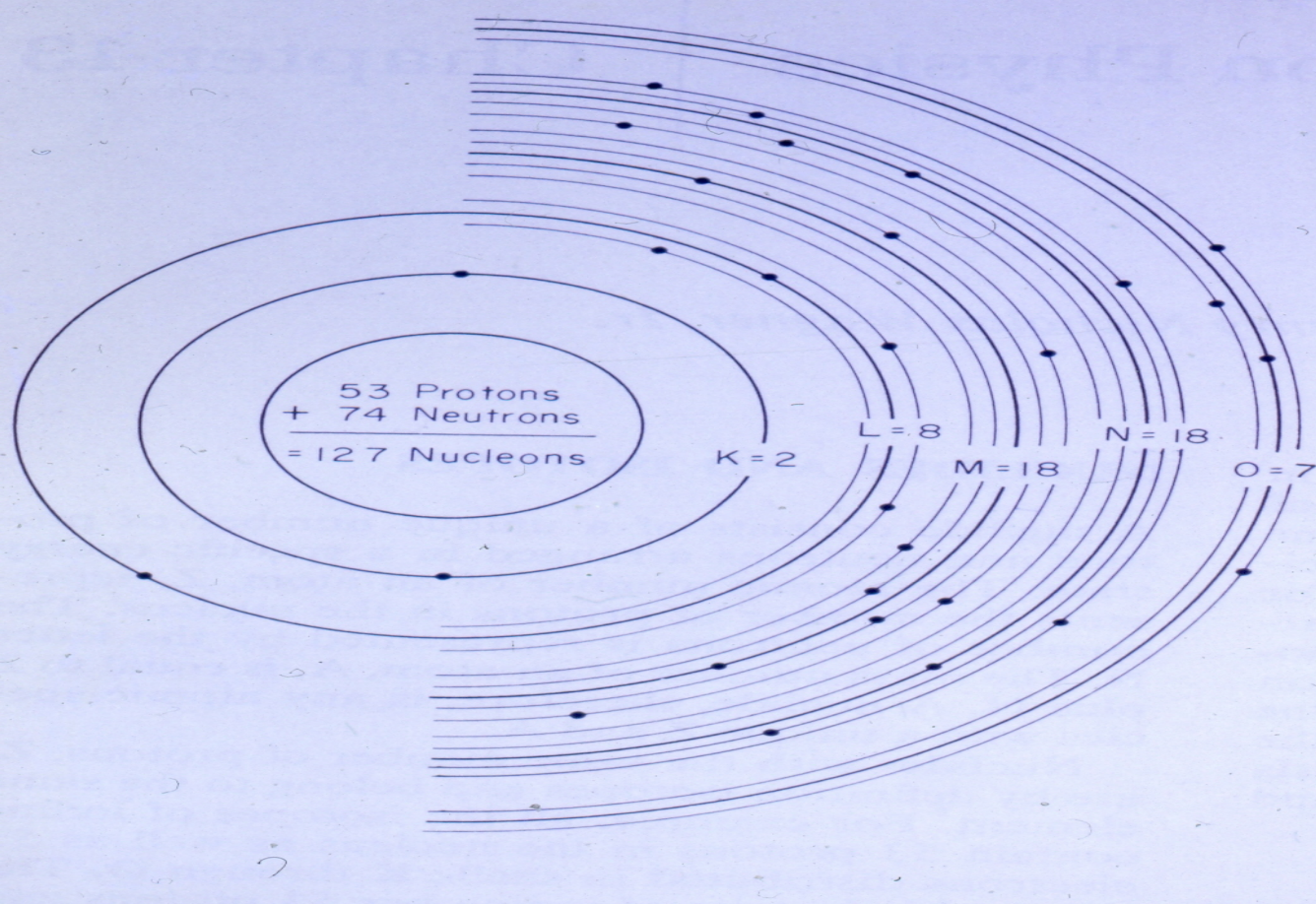
ہالوڑنہا

فلزات نایابدار

فلزات دیگر

فلزات قلیایی

فلزات قلیایی خاکی



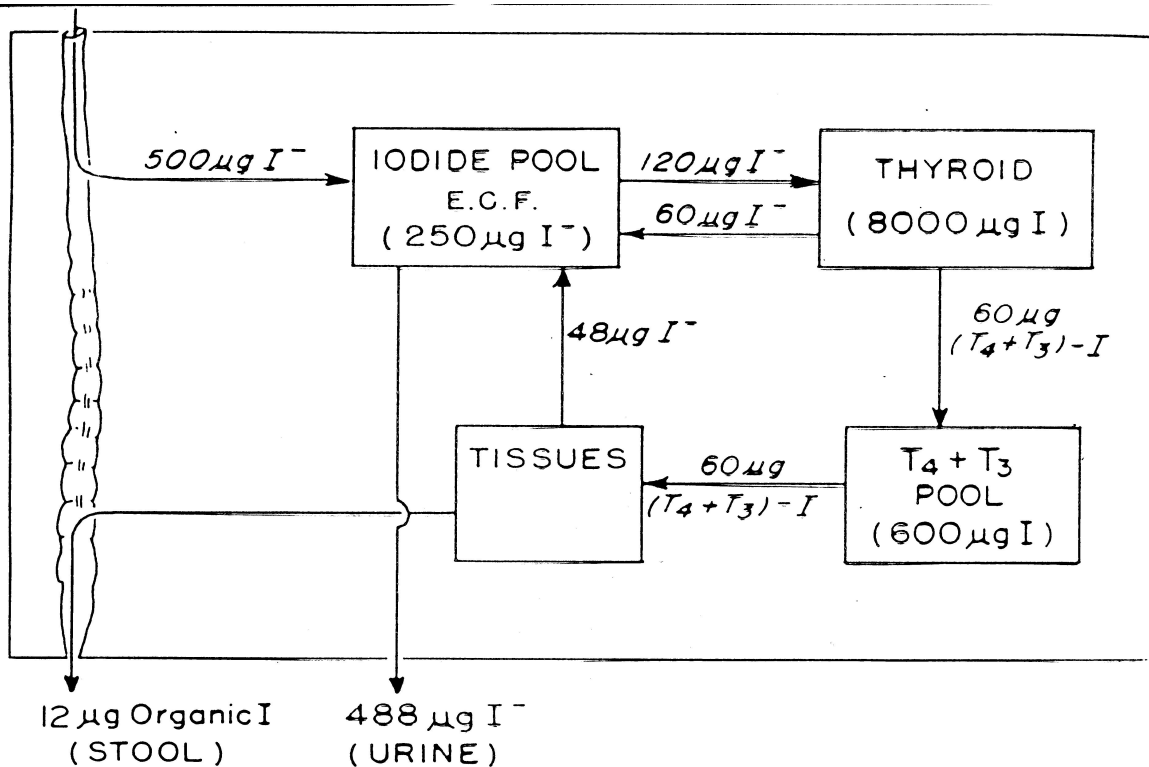


Figure 4-4. Diagram depicting normal pathways of iodine metabolism in a state of iodine balance. Note that most (approximately 90%) of body iodine store is present in the thyroid (chiefly in the organic form). Approximately 10% is present as iodide. Arrows indicate daily flux of iodine from one compartment to another. In this example, one-fifth of the iodide entering the iodide space (120/608) is accumulated by the thyroid. Peak

Iodine Sources



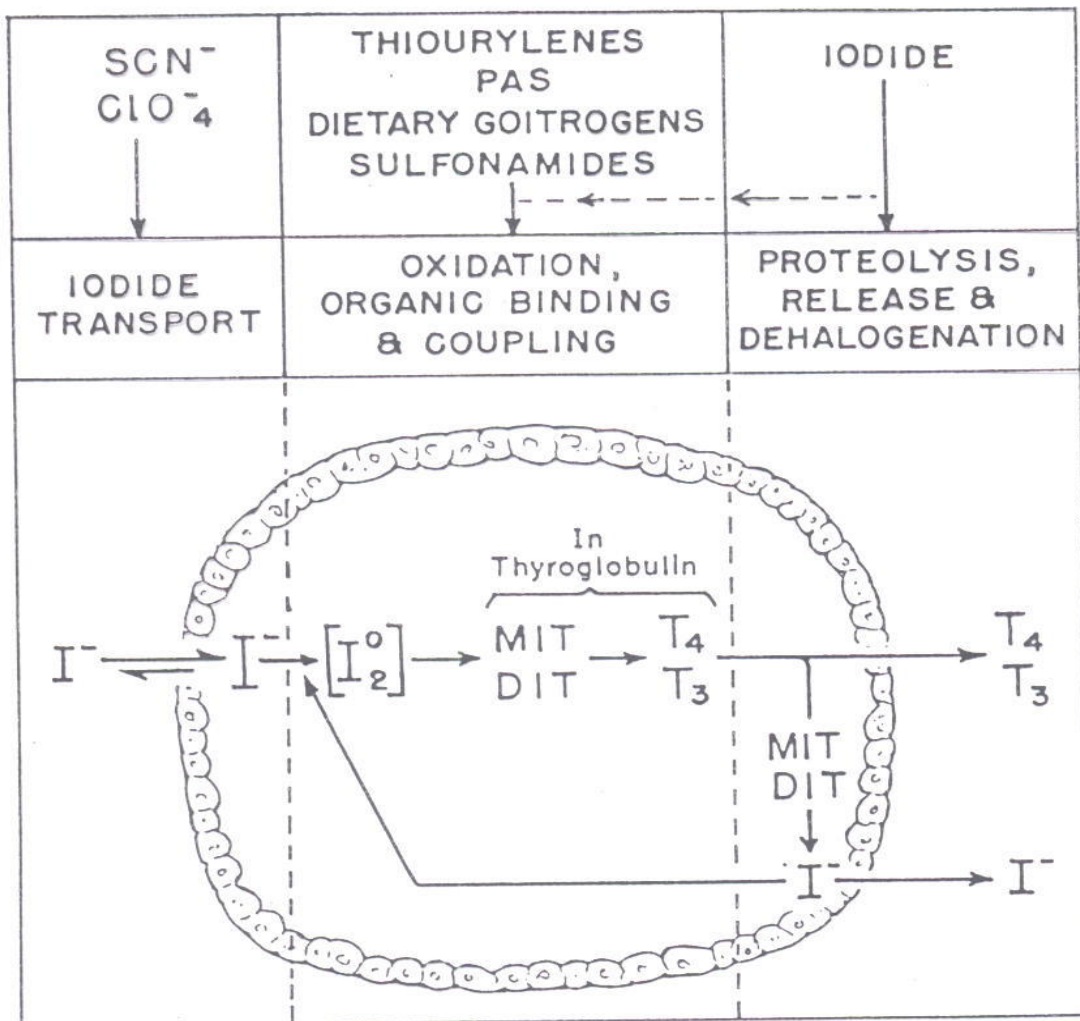
Recommended and Typical Values for Dietary Iodine Intake

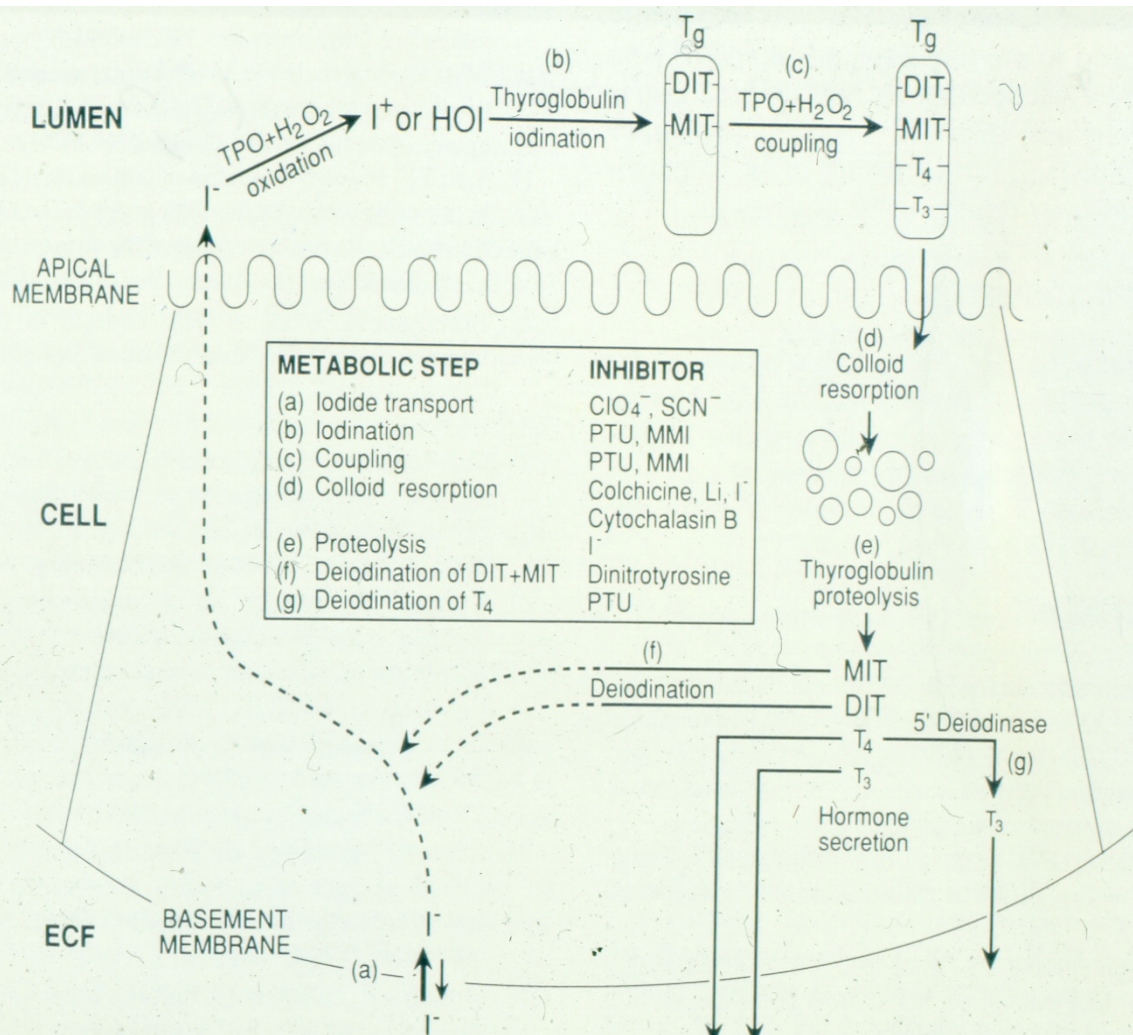
Recommended Daily Intake

Adults	150 µg
During pregnancy	200 µg
Children	90-120 µg

Typical Iodine Daily Intakes

North America (1992)	75-300 µg
Chile (1981)	<50-150 µg
Belgium (1993)	50-60 µg
Germany (1993)	20-70 µg
Switzerland (1993)	130-160 µg





SPECIFIC ACTIONS OF THYROID HORMONE: METABOLIC

- Regulates of Basal Metabolic Rate (BMR).
- Increases oxygen consumption in most target tissues.
- *Permissive actions:* TH increases sensitivity of target tissues to catecholamines, thereby elevating lipolysis, glycogenolysis, and gluconeogenesis.

SPECIFIC ACTIONS OF THYROID HORMONE: DEVELOPMENT

- TH is critical for normal development of the skeletal system and musculature.
- TH is also essential for normal brain development and regulates synaptogenesis, neuronal integration, myelination and cell migration.
- **Cretinism** is the term for the constellation of defects resulting from untreated neonatal hypothyroidism.

Antibodies

- Antimicrosomal or antithyroperoxidase
- Antithyroglobulin
- Anti-TSH receptor
 - Thyroid-stimulating immunoglobulins that mimic TSH action
- Thyroid growth-stimulating immunoglobulin

Prevalence of Thyroid Autoantibodies

Group	TSHRAb	hTgAb	hTPOAB
General population	0	5-20	8-27
Graves' Disease	80-95	50-70	50-80
Autoimmune thyroiditis	10-20	80-90	90-100
Relatives of patients	0	40-50	40-50
Pregnant women	0	14	14

Prevalence of Thyroid Autoantibodies

Group	TSHR-Ab (%)	hTg-Ab (%)	hTPO-Ab (%)
General population	0	5-20	8-27
Patients with Graves disease	80-95	50-70	50-80
Patients with autoimmune thyroiditis	10-20	80-90	90-100
Relatives of patients	0	40-50	40-50
Patients with IDDM	0	40	40
Pregnant women	0	14	14

IDDM, insulin-dependent diabetes mellitus; hTg-Ab, human thyroglobulin antibody; hTPO-Ab, human thyroid peroxidase antibody; TSHR-Ab, thyroid-stimulating hormone receptor antibody.

Primary Care Diagnosis of Thyroid Disease

Biochemical Tests

- Total Thyroxine
- Total Triiodothyronine
- Free T4 and FT3
- Thyroid-stimulating hormone
- Antibodies
- Calcitonin
- Thyroglobulin
- RET Protoncogene

The Serum Levels of Thyroglobulin

- Tg is the protein matrix (Tg) synthesized in the thyroid gland.
- Tg molecule has no peripheral hormonal action
- Tg represent a sensitive, nonspecific, indicator of the activity or stimulation state of the thyroid gland.
- Several studies have indicated that Tg is frequently elevated during pregnancy

Thyroglobulin

- Is a large dimeric glycoprotein that is secreted uniquely by thyroid follicular cells.
- Plays a central role in thyroid pathophysiology.

Tg measurement in DTC

- Detection limit of sensitive IMA method: 0.5 ng/ml.
- $Tg > 10$ ng/ml off T4 therapy, or.
- $Tg > 2.5$ ng/ml after stimulation with rhTSH, indicating residual normal or malignant thyroid tissue.

Tg measurement

May be helpful for diagnosing factitious or some other rare types of thyrotoxicosis , especially when using along with RAIU.

Calcitonin measurement

- The efficacy of surgery for MTC is assessed postoperatively by measurement of plasma calcitonin levels, which may require as long as 6 months to normalized.
- A normal basal & provoked calcitonin level after surgery indicates cure in most patients.

CEA in MTC

A rapid doubling of the CEA, particularly in the setting of a stable calcitonin level, is an ominous indicator.

RET protooncogene in MTC

Genetic screening should be done in all first-degree relatives of any patient who tests positive for a MEN2 or FMTC mutation.

Primary Care Diagnosis of Thyroid Disease

Imaging studies

- Radioisotope scan
- Ultrasonography
- CT-scan, MRI
- Radioactive iodine uptake
- Biopsy
- Antibodies

Ultrasound Exam

Recommended for

Always describe

Nodule Features on US

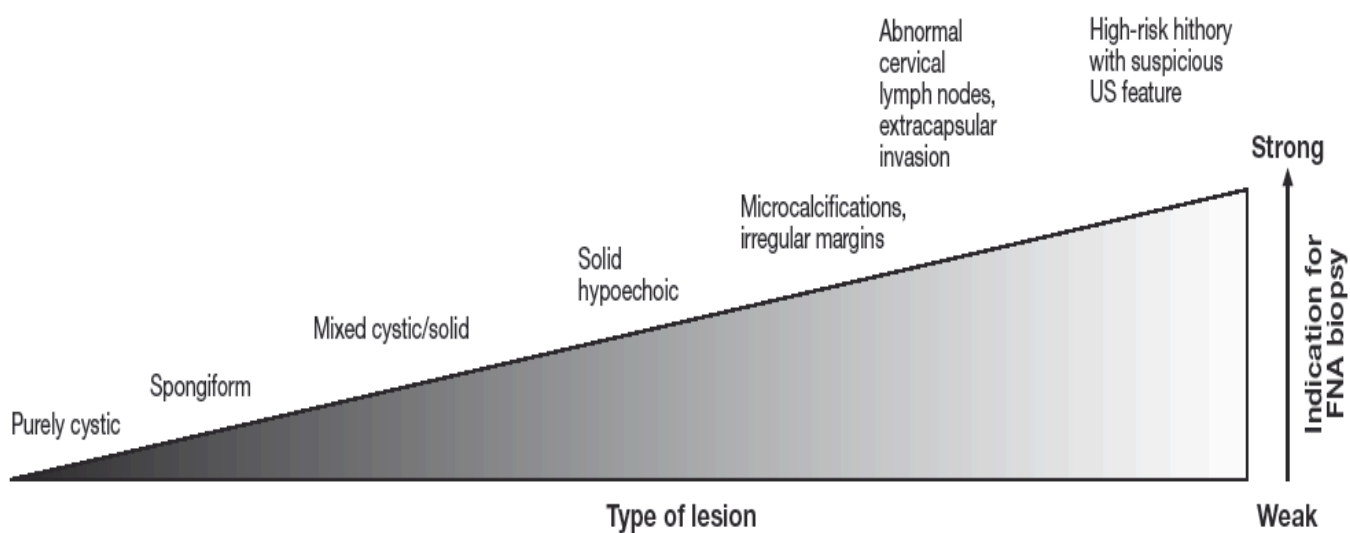
Likely benign

Likely malignant

**American Association of Clinical Endocrinologists,
Associazione Medici Endocrinologi, and European Thyroid
Association medical guidelines for clinical practice for the
diagnosis and management of thyroid nodules**

H. Gharib, E. Papini, R. Paschke, D.S. Duick, R. Valcavi, L. Hegedüs, and P. Vitti;
for the AACE/AME/ETA Task Force on Thyroid Nodules*

Task Force Committee members: S. Tseleni Balafouta, Z. Baloch, A. Crescenzi, H. Dralle, R. Gärtner,
R. Guglielmi, J.I. Mechanick, C. Reiners, I. Szabolcs, M.A. Zeiger, and M. Zini



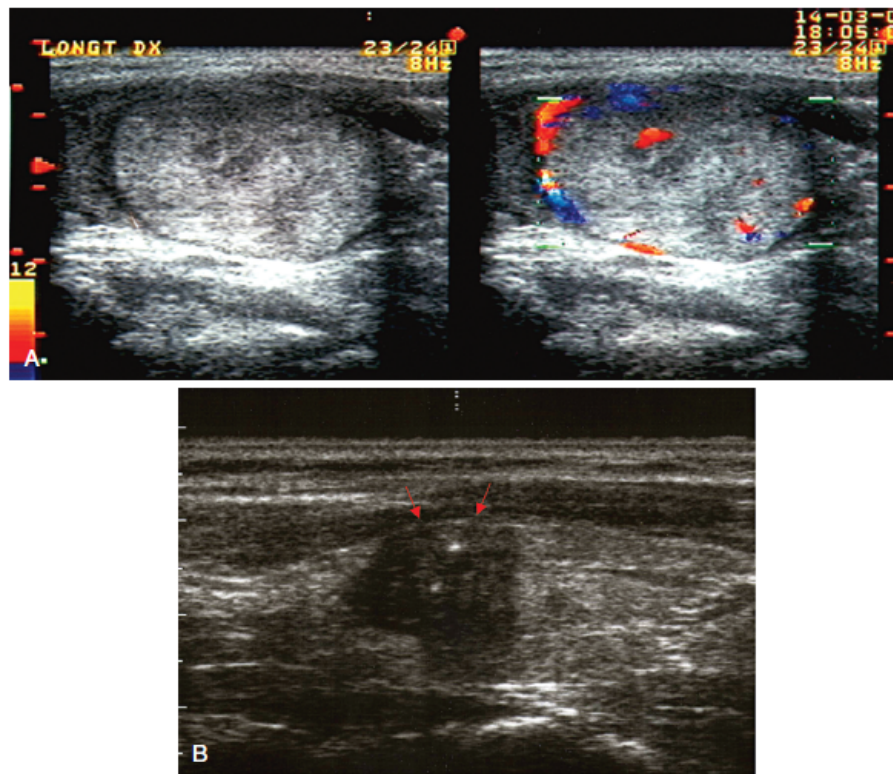
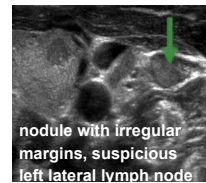
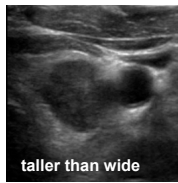
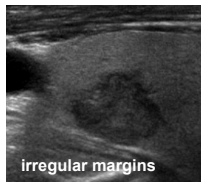
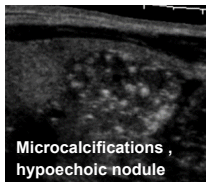


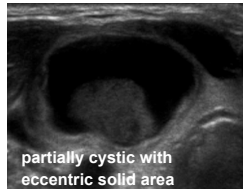
Figure 14-3 Conventional and color flow Doppler sonography. **A**, Benign lesion. Sonogram shows well-defined, oval, hyperechoic nodule with perinodular and slight intranodular blood flow. **B**, Malignant lesion. Sonogram shows a nodule with inhomogeneous hypoechoic aspect, microcalcifications, irregular borders, with invasion of the thyroid capsule (arrows).



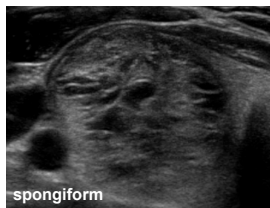
70-
90%



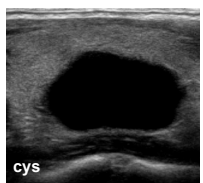
10-
20%



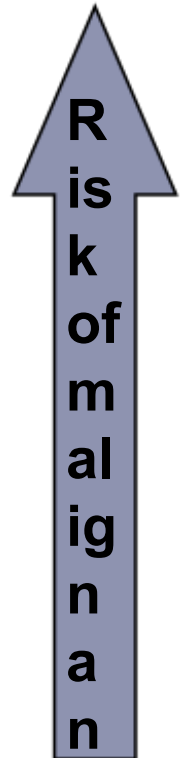
5-
10%



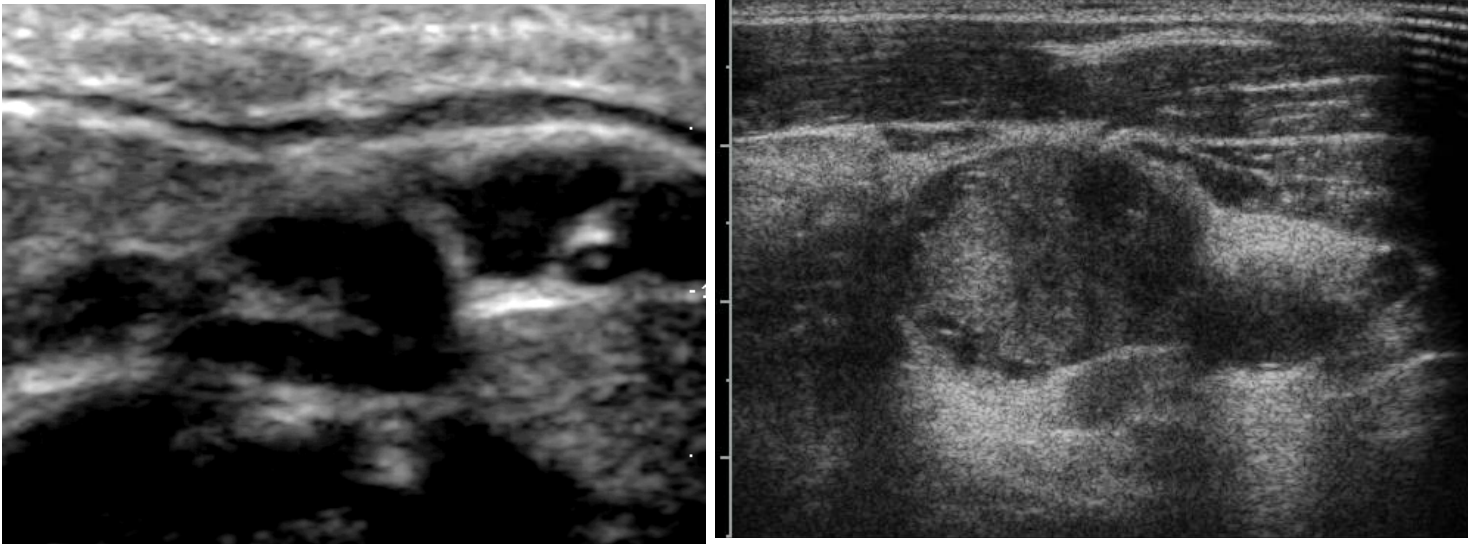
<
3%



<
1%



2. Absence of nodal hilar signal



high sensitivity but low specificity

Primary Care Diagnosis of Thyroid Disease

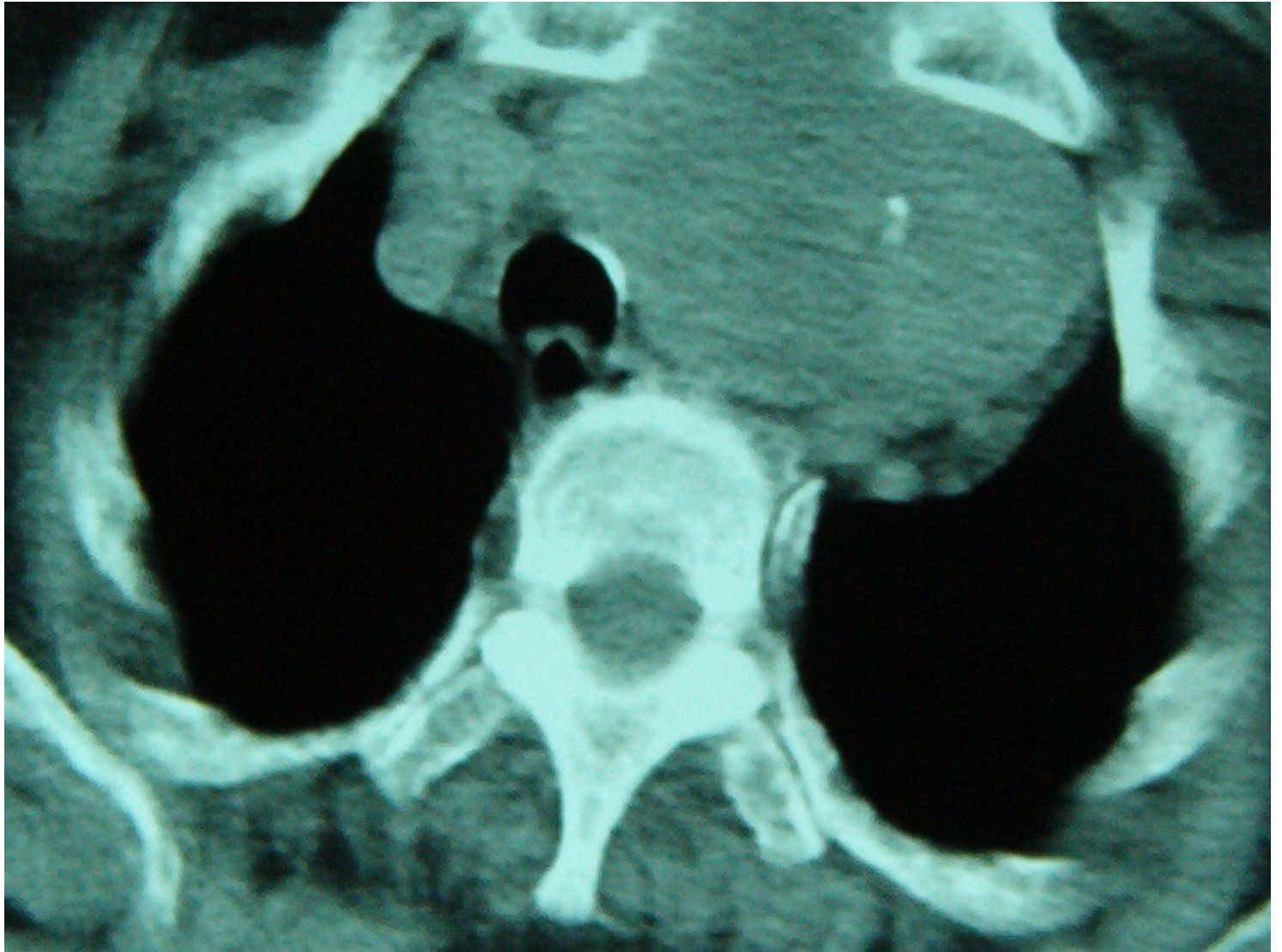
Imaging studies

- Radioisotope scan
- Ultrasonography
- CT-scan, MRI
- Radioactive iodine uptake
- Biopsy
- Antibodies

Primary Care Diagnosis of Thyroid Disease

Imaging studies

- Radioisotope scan
- Ultrasonography
- CT-scan, MRI
- Radioactive iodine uptake
- Biopsy
- Antibodies



FNA Biopsy

- FNA is the most accurate test and cytology is more reliable if FNA done with US
- Clinical management of TN should be guided by both US and FNA
- Guidelines suggest US-guided FNA to increase accuracy of results

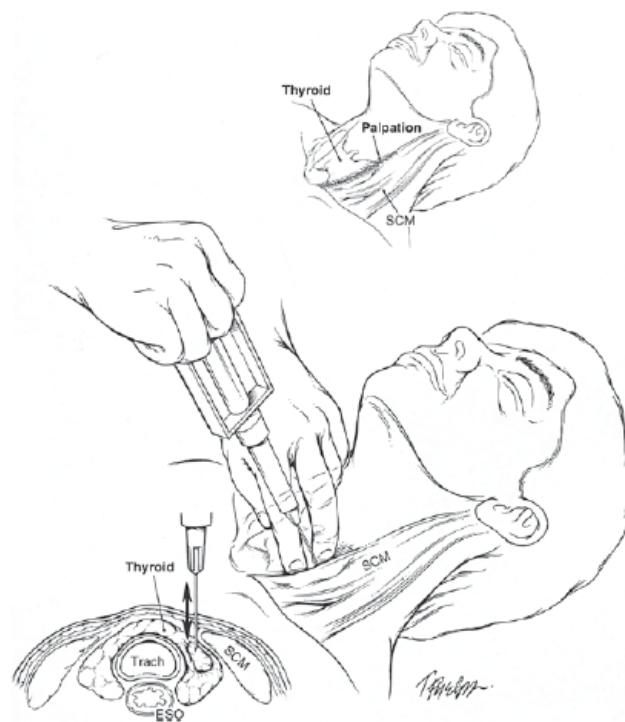
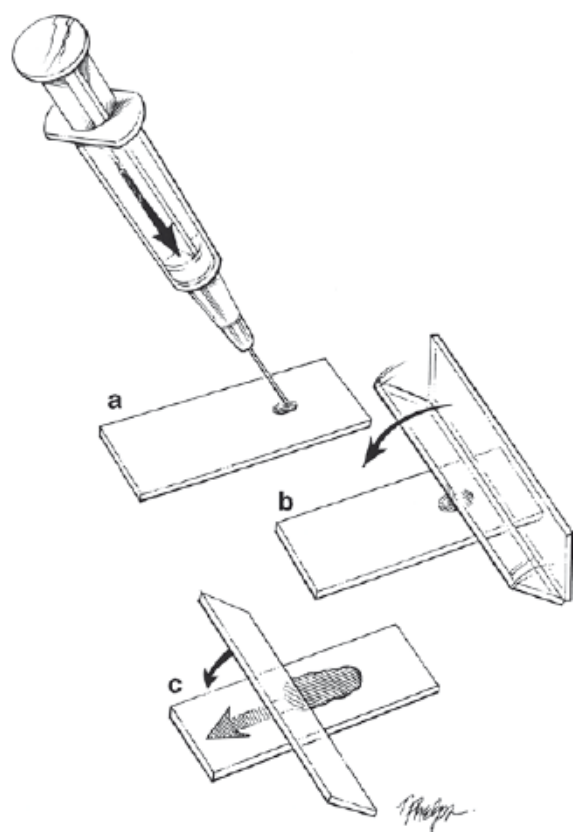


FIGURE 2.2. Performing a thyroid fine needle aspiration (FNA). Immobilization of the nodule and repeated excursions of the needle through the nodule are key steps. *SCM* sternocleidomastoid muscle; *Trach* trachea; *ESO* esophagus.



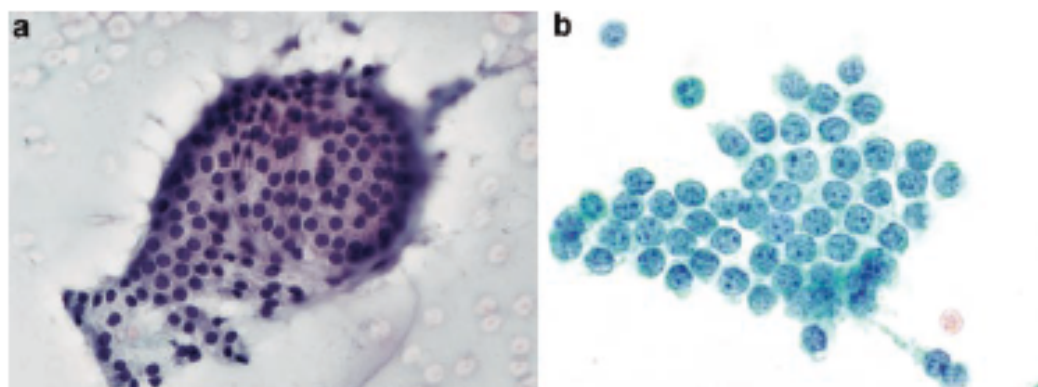


FIGURE 3.8. Benign follicular nodule. Benign follicular cells have round to oval monomorphic nuclei with finely granular chromatin and inconspicuous to absent nucleoli (a: smear, Papanicolaou stain; b: SurePath preparation, Papanicolaou stain). (The case illustrated in Fig. 3.8B is courtesy of Douglas R. Schneider, MD, Excell Clinical Laboratories, Boston, MA, USA).

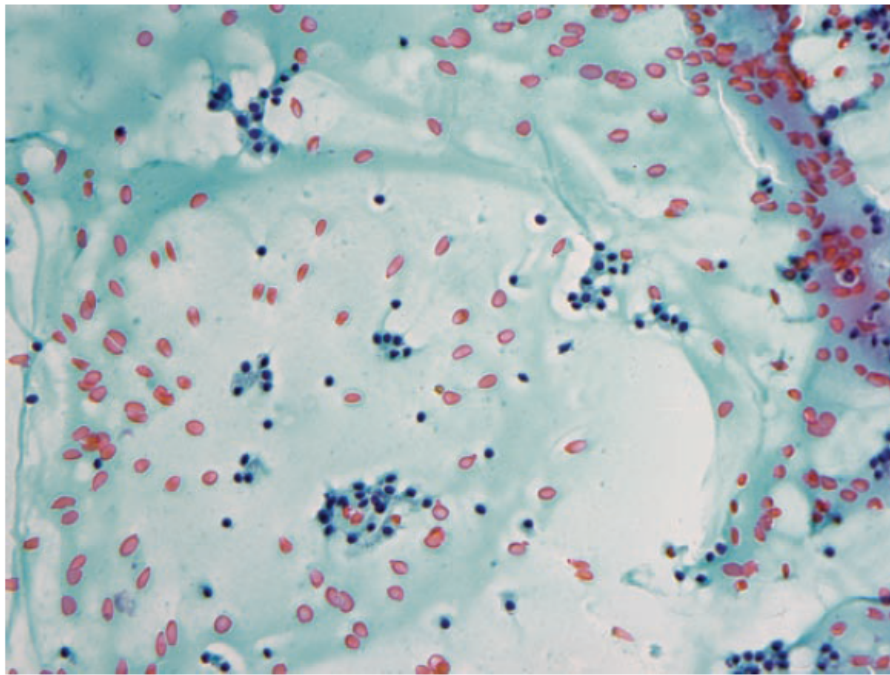


FIGURE 3.10. Benign follicular nodule. Follicular cells may appear shrunken and degenerated when associated with abundant colloid (smear, Papanicolaou stain).

Quik stain).

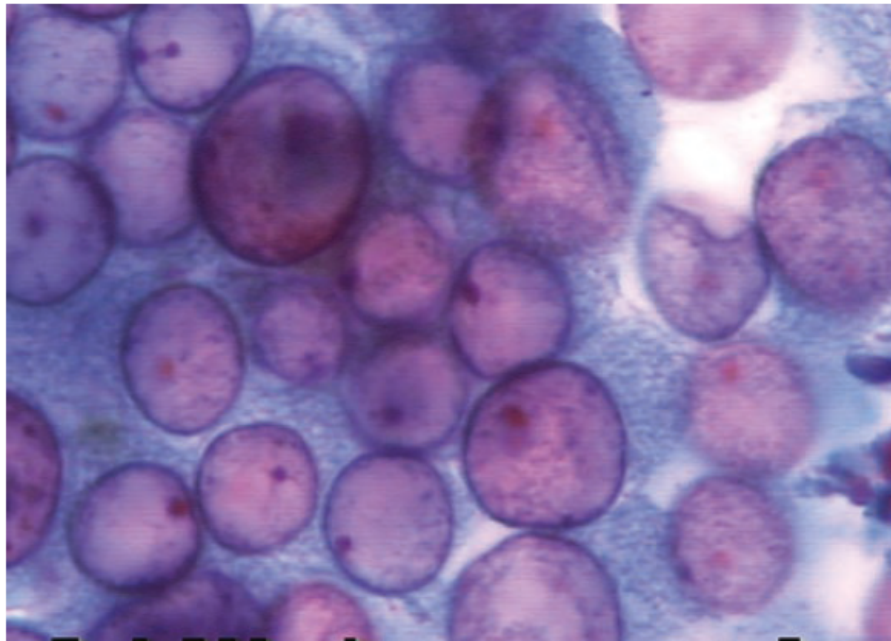


FIGURE 8.9. Papillary thyroid carcinoma. “Orphan Annie eyed” nuclei are very pale, with powdery chromatin and micronucleoli (smear, Papanicolaou stain).

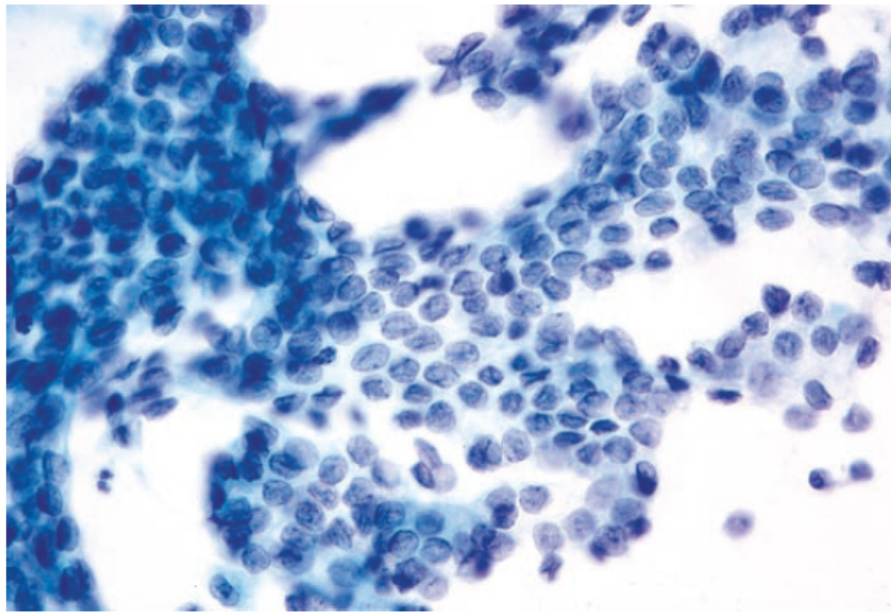


FIGURE 8.5. Papillary thyroid carcinoma. Monolayer sheets with a syncytial-like appearance are characteristic of papillary thyroid carcinoma. These flat sheets resemble those of benign follicular nodules; attention to the nuclear features is essential for this distinction (smear, Papanicolaou stain).

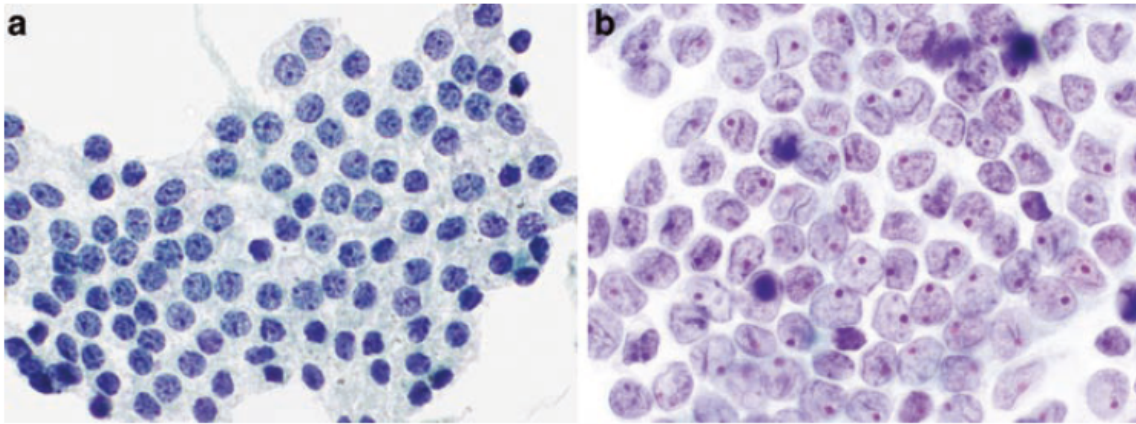
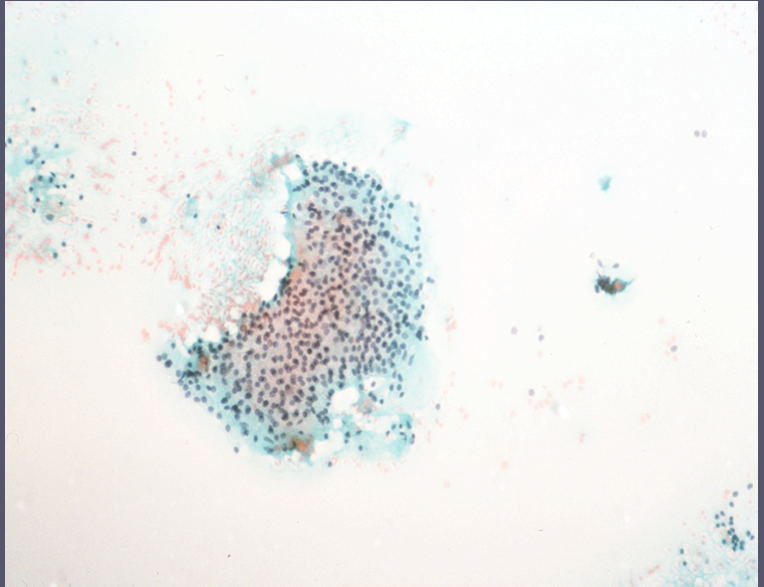


FIGURE 8.11. Comparison of benign follicular cells with the cells of papillary thyroid carcinoma. (**a**) Benign follicular cells (nodular goiter). (**b**) Compared with those of the benign follicular cells, the nuclei of papillary carcinoma are larger, paler, more crowded, and more irregular in contour. (**a** and **b**, ThinPrep, Papanicolaou stain).

29-Year-Old Woman

**FNA: benign,
colloid nodule**

**What is risk of
cancer in this
report?**



New Thyroid FNA Classification

Risk of
Cytologic category malignancy (%)

- Benign <1
- Follicular lesions 10
- Suspicious for malignancy 50-75
- Malignant 100
- Nondiagnostic 3%

Bethesda Thyroid Cytology Classification*



* Cibas & Ali: Thyroid, 2009

* NCI FNA Conf, 2007

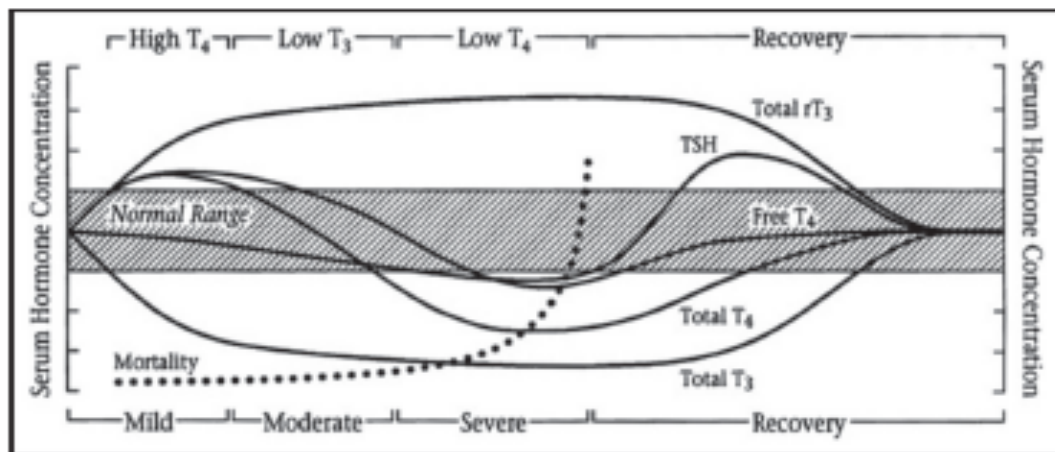
Nonthyroidal Illness

Most hospitalized patients do not have thyroid disease; However, findings on thyroid function tests in such patients can be confused with those of hypothyroidism or hyperthyroidism.

Nonthyroidal Illness

The most common type of change observed in acutely ill patients is a low serum T3 level caused by decreased conversion of T4 to T3.

Changes in serum thyroid hormone concentrations with progressive illness and recovery



Nonthyroidal Illness

- A 54-year-old woman with a past medical history of hypertension was diagnosed with a cancerous mass after a recent colonoscopy. She was admitted to the surgical service for an elective resection of the colonic mass, which was uneventful.

Nonthyroidal Illness

- She was kept NPO postoperatively and because of sluggish return of bowel function, thyroid function tests were obtained on the third postoperative day: FT4, 0.9 ng/dL (normal range, 0.7–1.5 ng/dL); total T3, 70 ng/dL (normal range, 80–180 ng/dL); TSH, 0.36 mIU/L (normal range, 0.35–3.5 mIU/L).

Nonthyroidal Illness

Nonthyroidal Illness

Nonthyroidal Illness

- With progression of the illness, there is a tendency for total T4 to decrease.
- Furthermore, dopamine, corticosteroids, and starvation suppress TSH secretion, causing TSH values to be lower than normal.

Physiologic Changes in Pregnancy that Influence Thyroid

Physiologic change	Thyroid function test change
↑ Thyroid hormone binding globulin (TBG)	↑ Serum total T4 and T3 concentration
First trimester hCG elevation	↑ Free T4 and ↓ TSH
↑ Plasma volume	↑ T4 and T3 pool size
↑ Placental type III 5-deiodinase (inner ring deiodination) is increased	↑ T4 and T3 degradation resulting in requirement for increased T4 and T3 production
Thyroid enlargement (in some women)	↑ Serum thyroglobulin
↑ Iodine clearance	↓ Hormone production in iodine-deficient areas

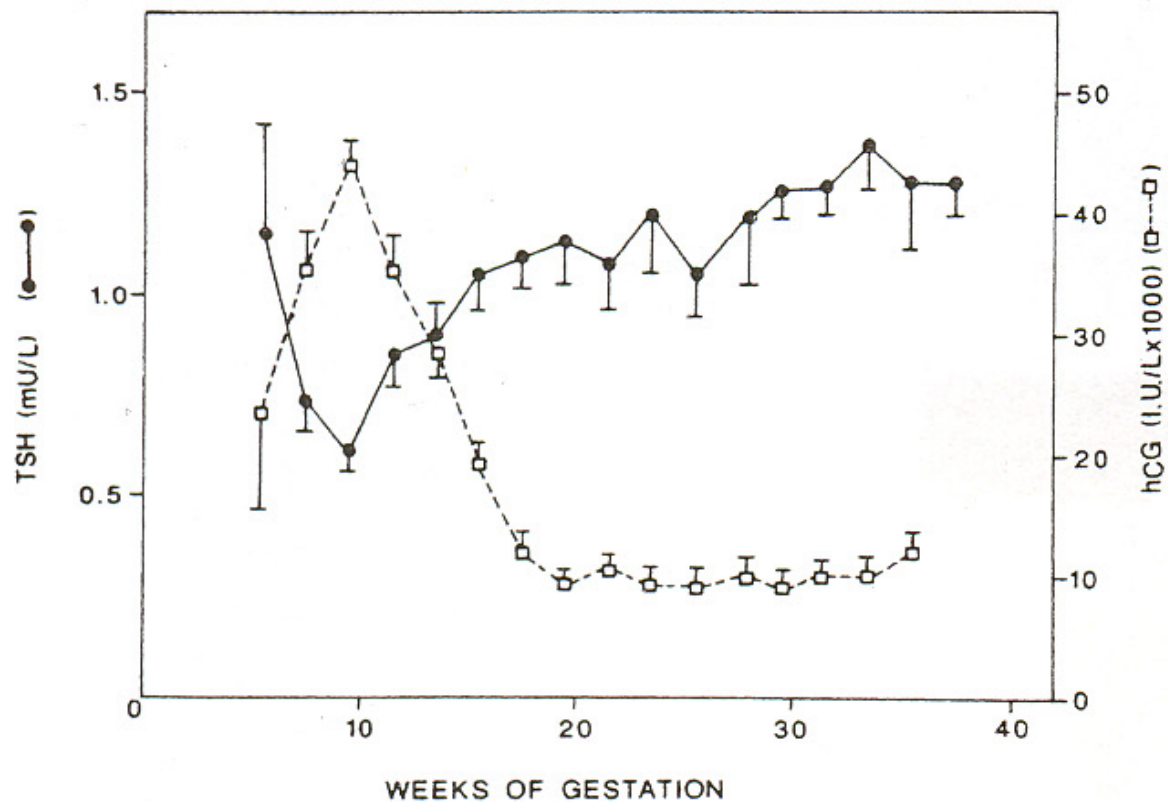


Figure 190-8 Serum thyroid-stimulating hormone (TSH) and human chorionic gonadotropin (hCG) as a function of gestational age in 606 healthy pregnant women. Between 8 and 14 weeks' gestation, the changes in hCG and TSH levels are mirror images of each other, and there is a significant negative correlation between the individual TSH and hCG levels ($P < 0.001$). Each point gives the mean value ($\pm$ SE) of

J Clin Endocrinol Metab 71: 276 – 287, 1990

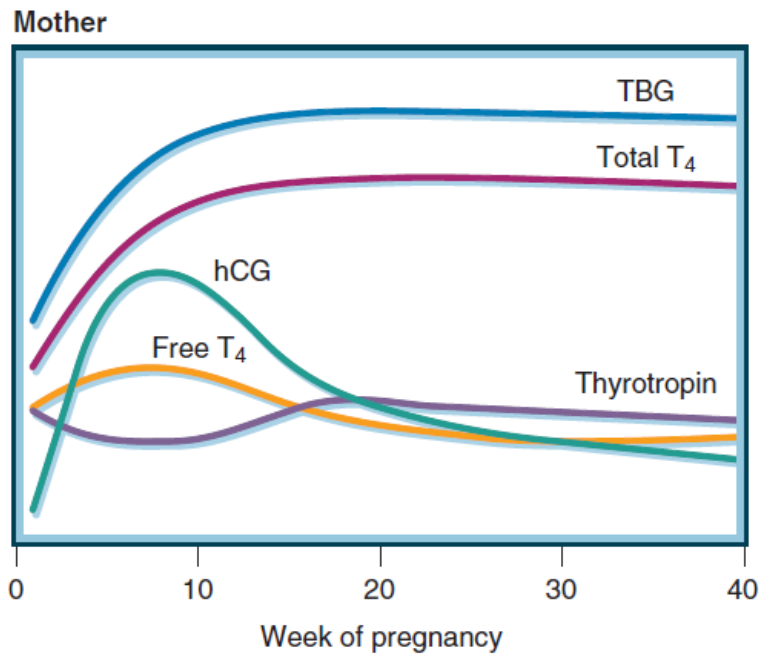


Figure 11-12 Changes in various critical components of the thyroid-pituitary axis during pregnancy. Note the early increase in free thyroxine (T₄), probably due to thyroidal stimulation by human chorionic gonadotropin (hCG), which causes a reciprocal modest suppression of serum thyroid-stimulating hormone (TSH) during the late first trimester. (From Burrow GN, Fisher DA, Larsen PR. Mechanisms of disease: maternal and fetal thyroid function. *N Engl J Med.* 1994;331:1072-1078.)

در خانم 24 ساله ای با حاملگی 10 هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است

Total T4 = 16 μ g/dL (5 – 12.5)

Total T3 = 241 ng/mL (80 – 180)

TSH = 0.2 mIU/L

تشخیص شما چیست؟

در خانم 29 ساله ای با حاملگی 12 هفته ای، تست های عملکرد تیروئید نتایج زیر را بدست داده است

Total T4 = 24 μ g/dL (5 – 12.5)

Total T3 = 412 ng/mL (80 – 180)

TSH = 0.1 mIU/L

تشخیص شما چیست؟