

EVALUATION AND MANAGEMENT OF THYROID DISORDERS

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COMMON THYROID CONCERNS

- **Anatomical/histological**
 - Goiter
 - Nodules
- **Function**
 - Hyperthyroidism
 - Hypothyroidism
- **Thyroid test abnormalities due to nonthyroid problems**

GOITER



THYROID NODULES

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Christoph Reiners, MD,
PhD

**Diagnosis of Thyroid Cancer
in Children: Value of Gray-
Scale and Power Doppler US1**

Radiology May 2005

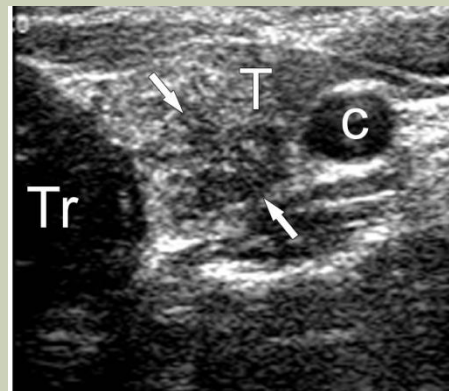
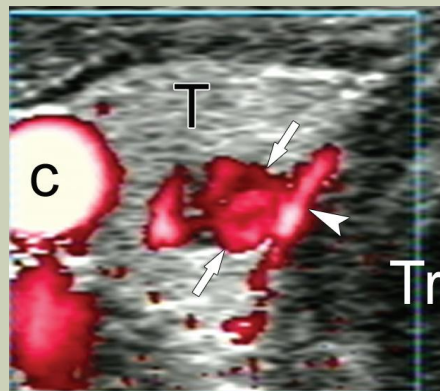
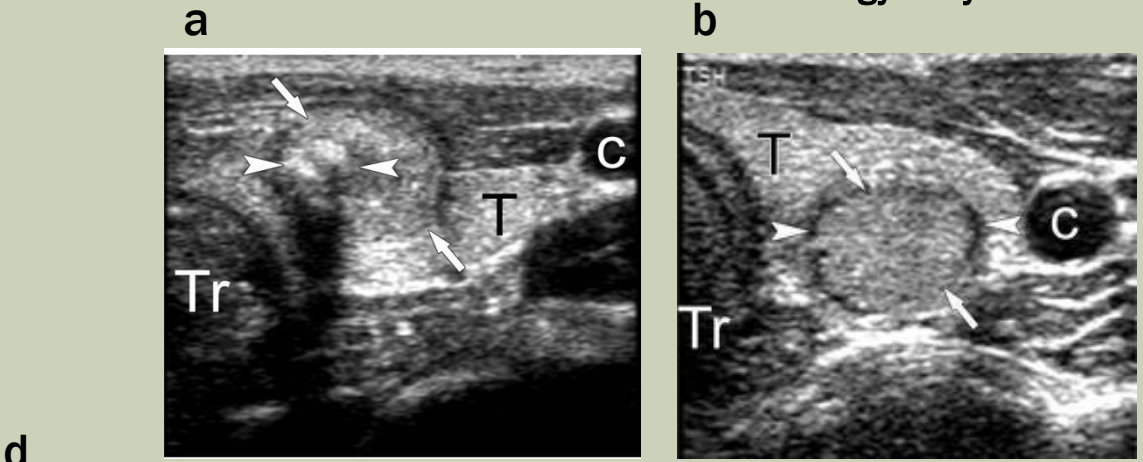
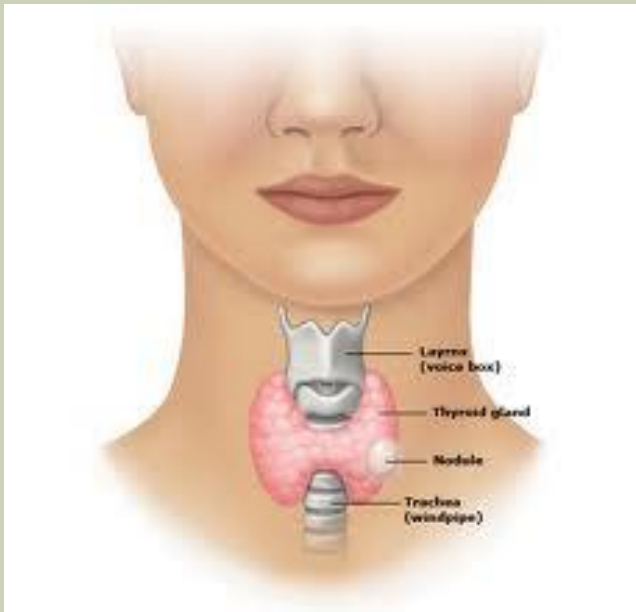


Figure 2. Transverse gray-scale US images. **(a)** Papillary thyroid carcinoma. Image in a 15-year-old girl depicts 11-mm isoechoic heterogeneous subcapsular nodule (arrows) with a halo and microcalcifications (arrowheads). **(b)** Nodular goiter. Image in a 12-year-old boy depicts 13-mm isoechoic homogeneous subcapsular nodule (arrows) with regular margin surrounded by thin hypoechoic halo (arrowheads). **(c)** Papillary thyroid carcinoma. Image in an 11-year-old boy depicts 10-mm hypoechoic homogeneous subcapsular nodule (arrows) with regular margin. **(d)** Papillary thyroid carcinoma. Image in a 13-year-old girl depicts 13-mm heterogeneous nodule (arrows) with mixed echogenicity and irregular margin. *C* carotid artery, *T* thyroid gland, *Tr* trachea.

WORKUP OF A THYROID NODULE

American Thyroid Association Guidelines

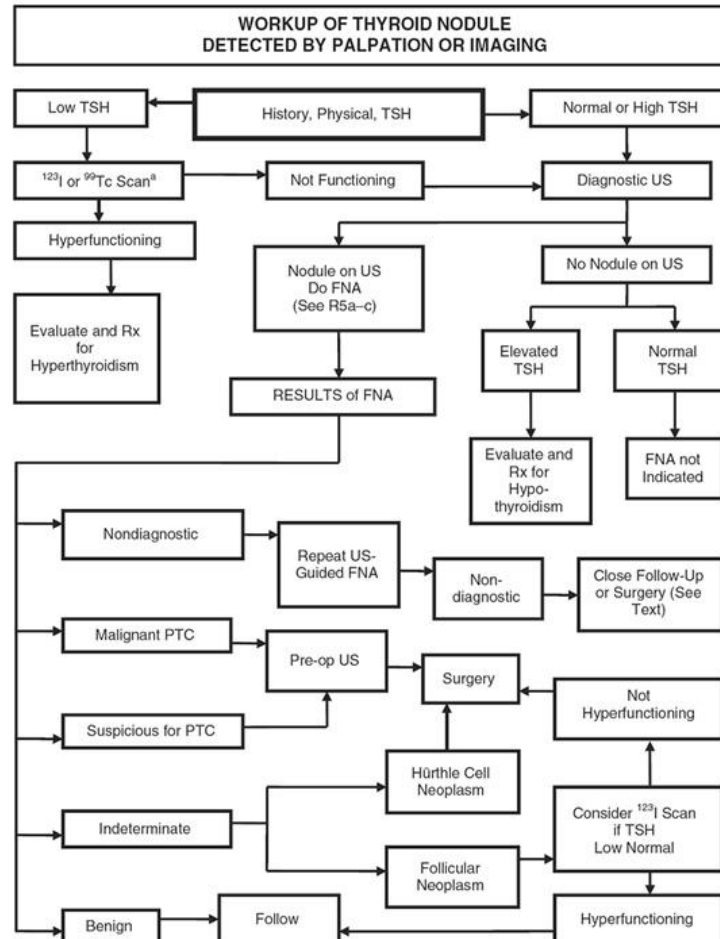


FIG. 1. Algorithm for the evaluation of patients with one or more thyroid nodules.

^aIf the scan does not show uniform distribution of tracer activity, ultrasound may be considered to assess for the presence of a cystic component.

WELL-DIFFERENTIATED THYROID CANCER STAGING

Risk of death

TNM staging of thyroid cancer		
T	Primary tumour	
Tx	Primary tumour can not be assessed	
T0	No evidence of primary tumour	
T1	Tumour 1 cm or less in greatest dimension and limited to the Thyroid	
T2	Tumour between 1 - 4 cm in greatest dimension and limited to the Thyroid	
T3	Tumour more than 4 cm in dimension but limited to the Thyroid	
T4	Tumour of any size extending beyond the Thyroid capsule	
N	Regional lymph nodes (cervical and upper mediastinal lymph nodes)	
Nx	Regional lymph nodes can not be assessed	
N0	No regional lymph node metastasis	
N1	Regional lymph node metastasis	
N1a	Metastasis in ipsilateral cervical lymph node(s)	
N1b	Metastasis in bilateral, midline or contralateral cervical lymph nodes	
M	Distant metastasis	
Mx	Distant metastasis can not be assessed	
M0	No distant metastasis	
M1	Distant metastasis present	
	Age < 45	Age > 45
Stage 1	Any T, any N, M0	T1, N0, M0
Stage 2	Any T, any N, M1	T2 or T3, N0, M0
Stage 3		T4, N0, M0 or any T, N1, M0
Stage 4		Any T, any N, M1

Risk of recurrence

Low Risk: no local or distant metastases, all macroscopic tumor resected, no tumor invasion of locoregional tissues or structures, tumor does not have aggressive histology (tall cell, insular, columnar cell carcinoma) or vascular invasion, and if ^{131}I is given, no ^{131}I uptake outside the thyroid bed on first post treatment whole body radioiodine scan is present

Intermediate Risk: microscopic invasion of tumor into the perithyroidal soft tissues at initial surgery or tumor with aggressive histology of vascular invasion

High Risk: macroscopic tumor invasion, incomplete tumor resection, distant metastases, or ^{131}I uptake outside the thyroid bed on the post-treatment scan done after thyroid remnant ablation

CATEGORIES AND TREATMENT OF THYROID CANCER

- That's a story for another time . . .

QUIZ

- A 29 yo woman has a CT of the chest for chronic cough.
- The lungs are normal, but the Radiologist notes what appears to be a nodule in the thyroid.
- How do you proceed with the workup?

THYROID FUNCTION

ACTIONS OF THYROID HORMONE

- In children, it is a growth and development hormone. It regulates:
 - Bone development and growth
 - CNS/Brain development
- In adults, it regulates:
 - Protein turnover
 - Muscle myosin type
 - Sensitivity to catecholamine action

THE IMPORTANCE OF THYROID HORMONE IN UTERO: CRETINISM



PERTURBATION OF THYROID HORMONE IN ADULTS



Hypothyroidism/myxedema



Hyperthyroidism and/or thyrotoxicosis

SYMPTOMS OF HYPERTHYROIDISM

- Tachycardia or palpitations (sometimes atrial fibrillation)
- Muscle weakness (including cardiac muscle)
- Tremor
- Heat intolerance
- Hyperdefecation
- Fine hair, soft nails, onycholysis
- Oligomenorrhea
- Weight loss
- hyperphagia
- Irritability and impatience
- Beware of unusual symptoms over age 65. “Apathetic Hyperthyroidism” produces a quiet, withdrawn person but loss of muscle and induction of cardiac dysrhythmia.

SYMPTOMS OF HYPOTHYROIDISM

- Puffiness from protein and fluid retention
- Cold intolerance
- Fatigue
- Constipation
- Dry hair, brittle nails
- Irregular menstrual cycles (skipped period, heavy periods)
- Cognitive slowing

SIGNS

■ Hyperthyroidism

- Lid lag/stare
- Goiter
- Skin hot to touch
- Soft nails and/or onycholysis
- Tremor
- Tachycardia or atrial fibrillation
- Brisk DTR relaxation

■ Hypothyroidism

- Goiter
- Dry skin
- Puffiness
- bradycardia
- Myotonic/delayed DTR relaxation

EXTREMES OF THYROID DYSFUNCTION

■ Thyroid storm

- Cardiovascular decompensation from high metabolic needs and weak cardiac muscle (CHF)
- Fever
- Nausea & vomiting

■ Myxedema coma

- Coma
- Weak pulse pressure
- hypothermia

CAUSES OF THYROID DYSFUNCTION

■ Hypothyroidism

- Almost always autoimmune thyroid disease (synonyms: chronic lymphocytic thyroiditis, Hashimoto's thyroiditis)
- Sometimes late stage of subacute thyroiditis (granulomatous thyroiditis)
- Sometimes medication (e.g. lithium, amiodarone, cold iodide, anticonvulsants)
- Sometimes iodine organification defect (usually goiter without hypothyroidism)

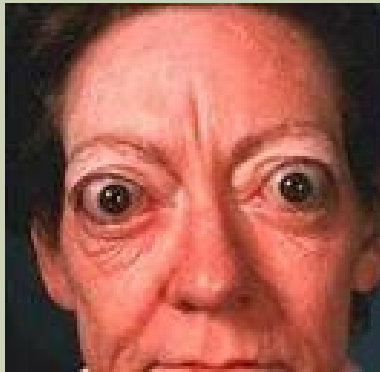
■ Hyperthyroidism

- Autoimmune thyroid disease (Graves' Disease)
- Toxic nodular goiter (augmented by Jod-Basedow phenomenon)
- Sometimes medication (e.g. amiodarone)

■ Thyrotoxicosis

- Excess exogenous thyroid hormone
- Sometimes early phase of subacute thyroiditis
- Sometimes early phase of Hashimoto's ("Hashitoxicosis")

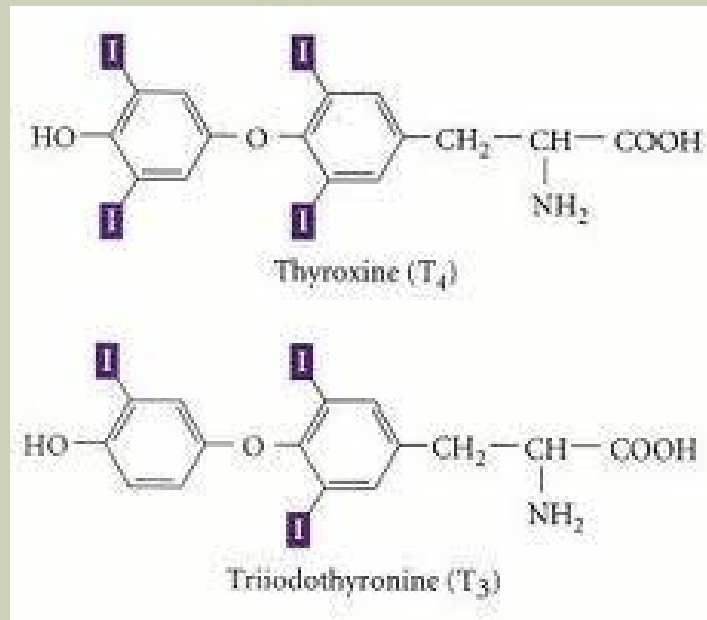
GRAVES' DISEASE: WHAT UNCOMMON FINDING CLINCHES THE DIAGNOSIS?



TESTING THYROID FUNCTION

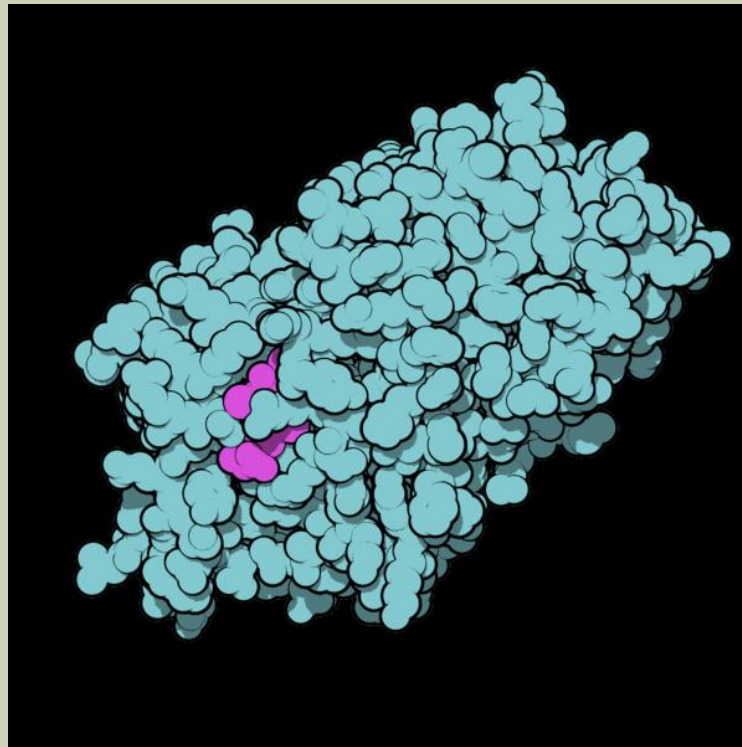
THYROID HORMONES

- Why do they call them T4 and T3?



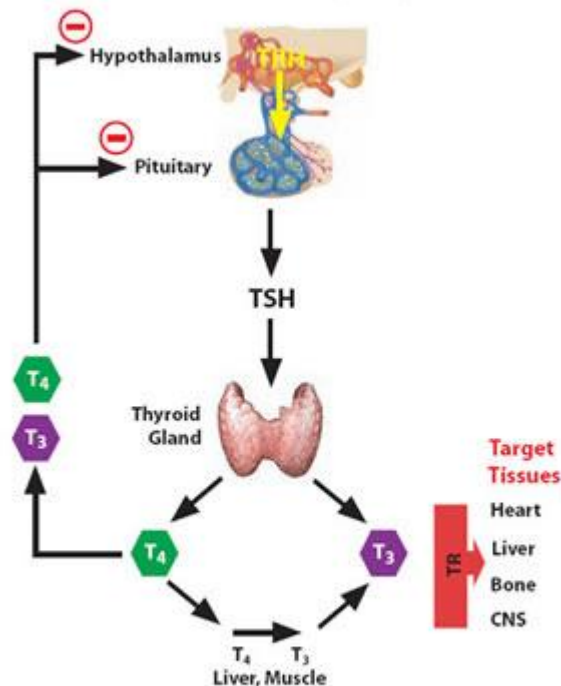
THYROID HORMONE BINDING

- Thyroxine binding globulin



THE HYPOTHALAMIC-PITUITARY-THYROID AXIS

Figure 1.
Hypothalamic-Pituitary-Thyroid Axis



Adapted from Berkow R, ed. The Merck Manual of Medical Information; 1997. CNS: central nervous system; TR: thyroid receptor; TRH: thyrotropin-releasing hormone; TSH: thyroid-stimulating hormone; T₃: triiodothyronine; T₄: thyroxine.

THYROID TESTS

- **Concentrations**
 - TSH (Thyroid stimulating hormone)
 - Total T4
 - Total T3
 - Free T4
 - Free T3
 - Reverse T3
- **Thyroid hormone binding**
 - TBG level
 - T3 uptake or thyroxine uptake
- **Autoimmunity**
 - Thyroperoxidase antibody (microsomal antibody)
 - Thyroglobulin antibody
 - Thyrotropin receptor antibody (TSH receptor antibody) for Graves' Dz

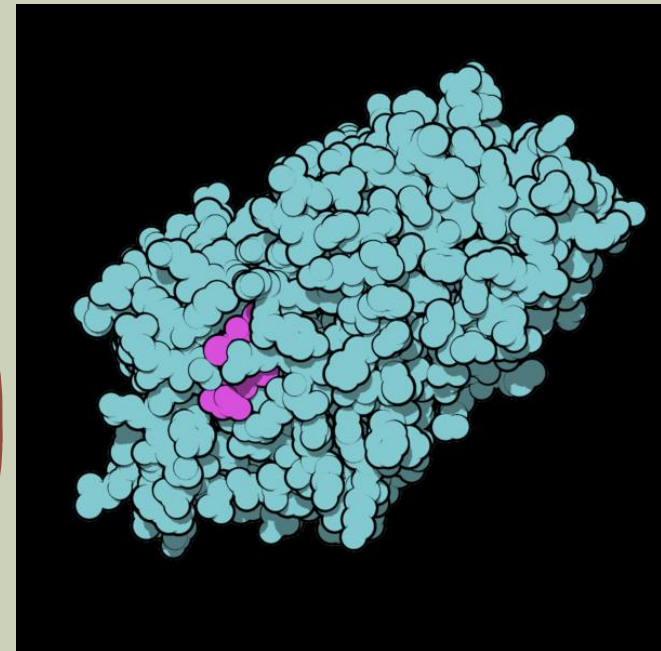
A WORD ABOUT THE THYROXINE UPTAKE OR T3 UPTAKE TEST...

Labeled T3 or T4
are added to serum

*T3

*T4

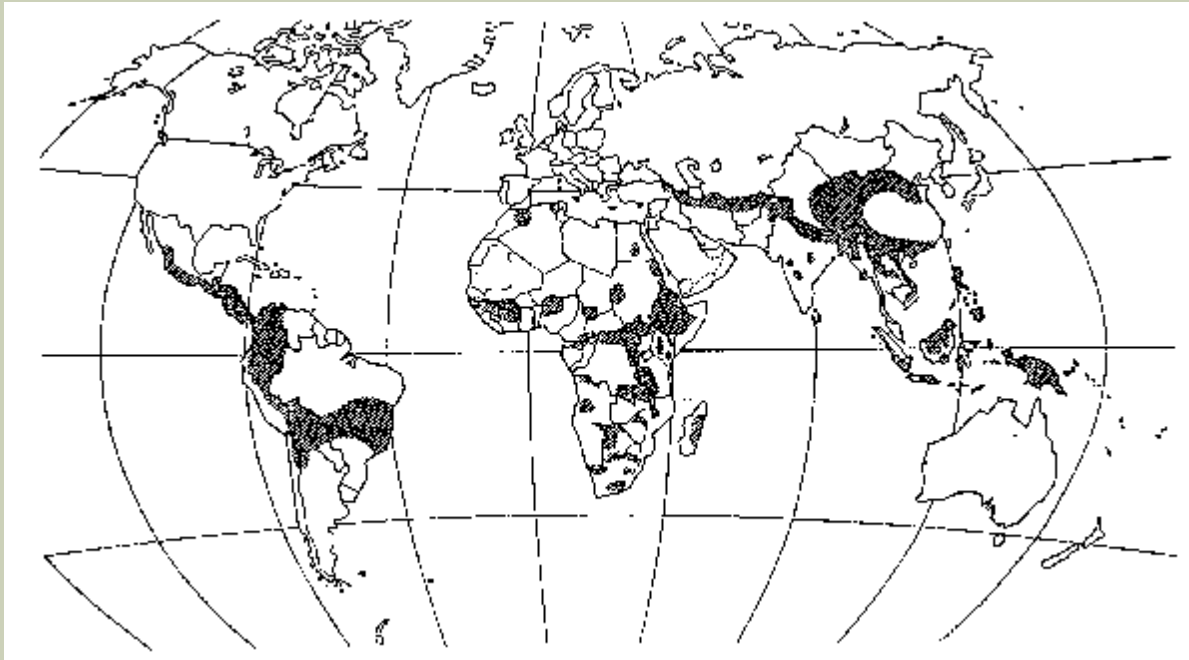
Serum Sample of
unbound *T3 or
*T4



Thyroxine binding globulin in serum

IODINE DEFICIENCY AREAS

- Do we need to suspect iodine deficiency and test for it?



Iodine deficiency areas (1987 map; UN Standing Committee on Nutrition)

SCENARIO: HYPERTHYROIDISM

■ Test pattern:

- Total T4 ↑
- Free T4 ↑
- Total T3 ↑
- Free T3 ↑
- T3 uptake ↑
- TSH ↓

SCENARIO: HYPOTHYROIDISM

■ Test pattern:

- Total T4 ↓
- Free T4 ↓
- Total T3 ↓
- Free T3 ↓
- T3 uptake ↓
- TSH ↑

SCENARIO: HIGH THYROXINE BINDING GLOBULIN (PREGNANCY, BCP'S, GENETIC)

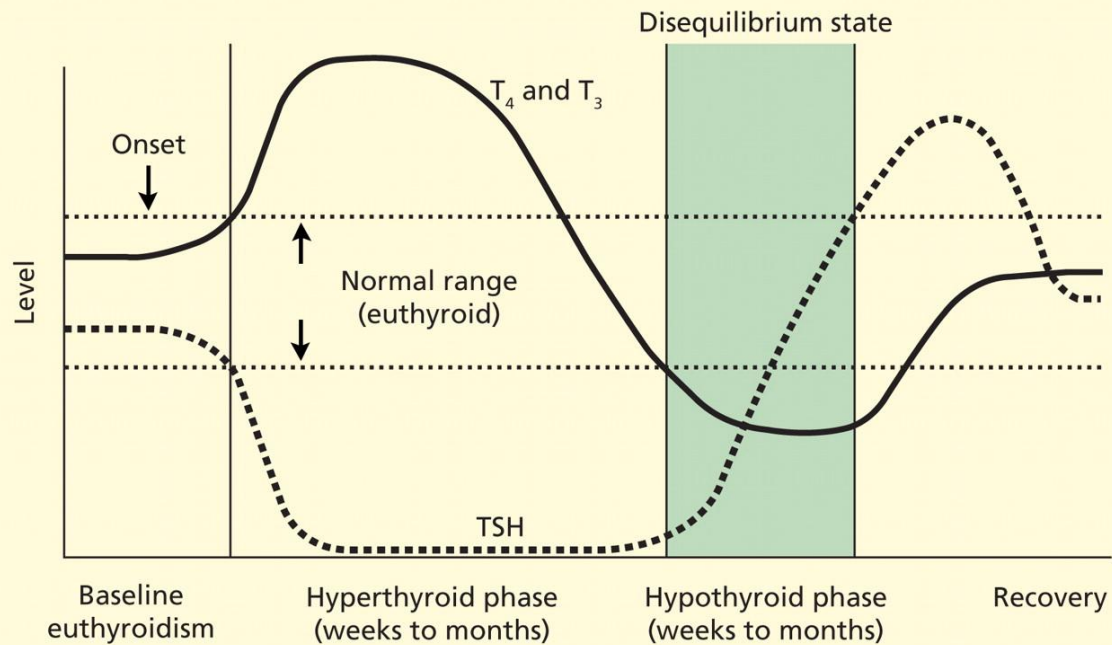
■ Test pattern:

- Total T4 ↑
- Free T4 **normal**
- Total T3 ↑
- Free T3 **normal**
- T3 uptake ↓
- TSH **normal**

INFLAMMATORY TRANSIENT THYROIDITIS

(SUBACUTE THYROIDITIS, MEDICATION INDUCED THYROIDITIS)

Natural history of thyroid function tests in patients with thyroiditis



Disequilibrium state = the period during the hypothyroid phase of thyroiditis in which the thyroid-stimulating hormone (TSH) level transiently remains low or inappropriately normal in the setting of low levels of free thyroid hormones; T_4 = thyroxine; T_3 = triiodothyronine

PANTALONE K M , NASR C Cleveland Clinic Journal of
Medicine 2010;77:803-811

Cleveland Clinic Journal of Medicine

**THYROID TEST
ABNORMALITIES DUE TO
NONTHYROID PROBLEMS**

THE EFFECT OF SERIOUS NONTHYROID ILLNESS ON THYROID TESTING

T4 AND T3 BINDING ARE INHIBITED IN SERIOUS ILLNESS

- 99.97% of T4 is bound to TBG, thyroxine binding prealbumin (TBPA), and albumin [most is bound to TBG] normally
- 99.7% of T3 is bound normally
- T4 and T3 binding are inhibited in serious illness
 - Possibly due to a binding inhibitor of thyroid hormone to TBG
 - Possibly due to desialylation of TBG (N-acetylneuraminic acid; sialic acid is removed from TBG structure)
- Hypothalamic TRH and pituitary TSH secretion are inhibited in serious illness—perhaps by cytokines
- The conversion of T4 to T3 is inhibited in starvation and serious nonthyroid illness—perhaps by poor transport of T4 into cells or perhaps by inhibition of type 1 deiodinase

T4 AND T3 BINDING ARE INHIBITED IN NTI, AND TSH IS SUPPRESSED, AND T4 TO T3 CONVERSION IS INHIBITED

- Sooooo. . .
 - The level of Total T4 in nonthyroid illness would be?
 - The level of Total T3 in nonthyroid illness would be?
 - The level of TSH would be?
 - The level of free T4 would be?
 - The level of free T3 would be?
 - The T4 uptake or T3 uptake test would be?

THYROID TESTS IN SERIOUS NONTHYROID ILLNESS

- TSH **LOW**
- Total T4 **LOW**
- Total T3 **LOW**
- Free T4 **HIGH OR NORMAL (OR LOW IF ASSAYED IMPROPERLY)**
- Free T3 **LOW**
- T4uptake or T3 uptake **HIGH**

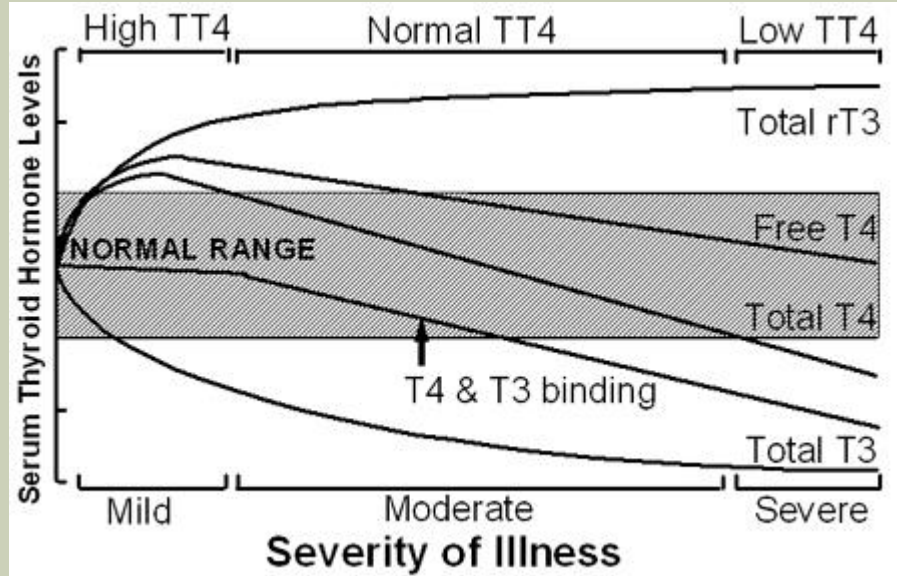
DURING RECOVERY FROM SERIOUS NONTHYROID ILLNESS, THYROID HORMONE BINDING IMPROVES

- Soooo . . .
 - What happens to Total T4?
 - What happens to Total T3?
 - What happens to free T4?
 - What happens to free T3?
 - What happens to TSH?
 - What happens to T4 uptake or T3 uptake?

THYROID TESTS IN SERIOUS NONTHYROID ILLNESS

- TSH **HIGH**
- Total T4 **NORMALIZING**
- Total T3 **NORMALIZING**
- Free T4 **BRIEFLY LOW**
- Free T3 **BRIEFLY LOW**
- T4uptake or T3 uptake **BRIEFLY LOW**

NONTHYROID ILLNESS



THE THYROID IN NON-THYROIDAL ILLNESS

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RECOVERY FROM NONTHYROID ILLNESS

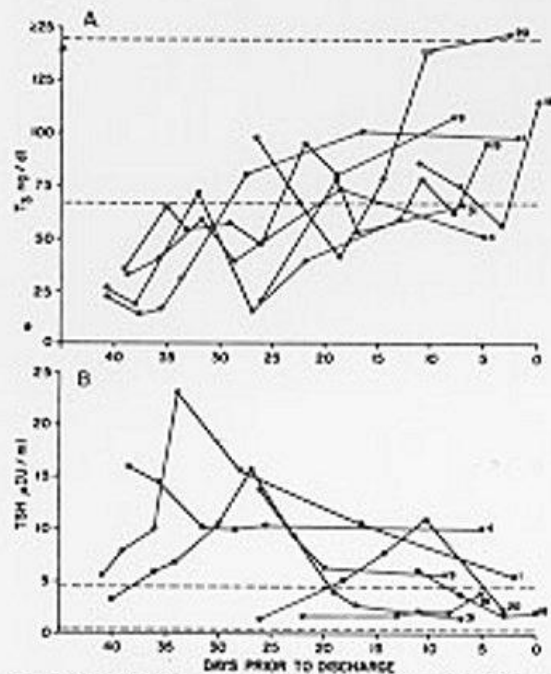


FIG. 1. T_3 and TSH concentrations in patients with nonthyroid illness who were eventually discharged. Patients are identified by case number. The broken lines indicate ± 2 SD of the mean value in the normal subjects. Divide T_3 by 65 to convert to nmol/liter.

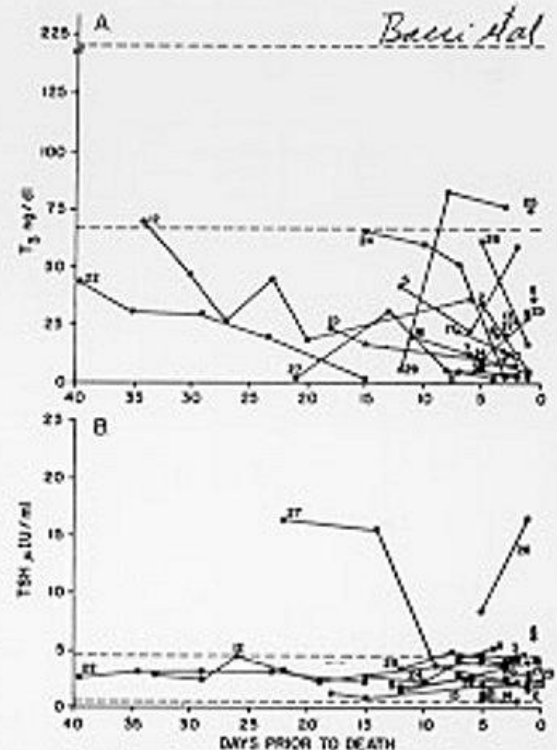
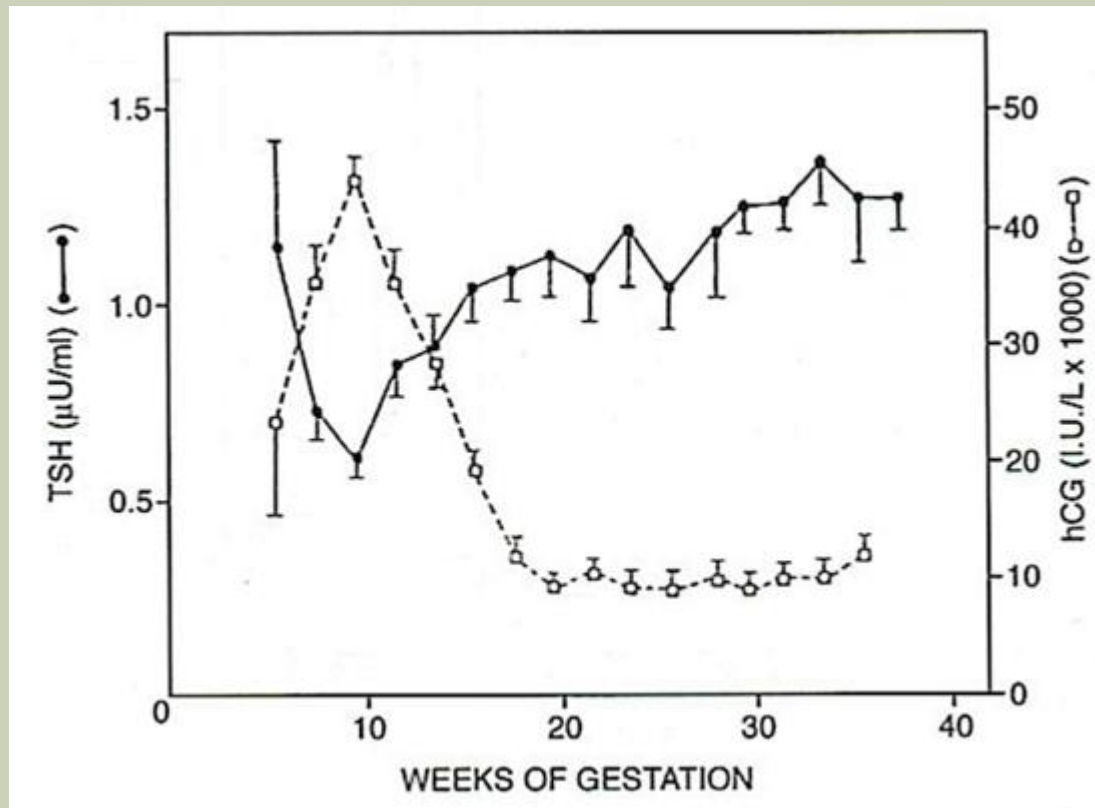


FIG. 2. T_3 and TSH concentrations in patients with nonthyroid illness who died. Numbers and broken lines as in Fig. 1.

Bacci V, Schussler GC, Kaplan TB 1982 The relationship between serum triiodothyronine and thyrotropin during systemic illness. *J Clin Endocrinol Metab* 54:1229-1235

THE THYROID IN PREGNANCY

THE SUPPRESSION OF TSH IN PREGNANCY



From Glinoe D, de Nayer P, Bourdoux P, et al. Regulation of maternal thyroid during pregnancy. *J Clin Endocrinol Metab* 1990; 71:276.

TREATMENT OF THYROID DYSFUNCTION

HYPOTHYROIDISM TREATMENT

- Use levothyroxine (T4)
 - Most adults need 100-150 mcg daily for full replacement
 - Requirements are lower after age 70
 - The body will convert the T4 to T3 as needed
 - In cases of myxedema coma, call an Endocrinologist. The patient will usually need IV levothyroxine at 300 mcg to 500 mcg first dose

HYPERTHYROIDISM TREATMENT

- Medication
 - Thionamides (methimazole, propylthiouracil/PTU) block the use of iodine by the thyroid
 - PTU can cause hepatitis, so methimazole is first choice
 - Methimazole has been associated with birth defects, so PTU is first choice in pregnancy
 - Beta blocker for adrenergic symptoms
 - In extreme hyperthyroidism, cold iodide can block thyroid hormone secretion (iopanoic acid, SSKI, Lugol's) and steroids can help the body compensate for the extreme condition.
- Radioiodine (^{131}I)
- Surgery/thyroidectomy—choice of last resort

- In the case of thyrotoxicosis without hyperthyroidism (subacute thyroiditis, exogenous T₄, etc), one can use a beta blocker and wait

THE FINAL EXAM

PATIENT #1 SEVERE ANEMIA

- A patient drives to the ER. She is pale and states she is very fatigued. She is dyspneic. She gives the history of excessive menstrual bleeding. She used to take levothyroxine, but she lost her insurance and has not used it for one year. While waiting in the ER, she becomes unresponsive.
- What is her clinical condition?
 - What would you expect on exam?
 - What would her thyroid tests look like?
 - How would you treat her?

PATIENT #2 – A PREGNANCY

- A 24yo young woman has had a goiter for several years. She has been to an Endocrinologist who initiated treatment with some pills. She stopped them a long time ago. She is now 8 weeks pregnant. She feels nauseated and tired.
- On exam: she has a smooth, symmetrical goiter that is 3x normal size. It has a bruit. She is tachycardic. Skin is very warm and diaphoretic. She has a tremor. DTR's relax very briskly. She is 5'5" and 101 lbs. She has deep, rapid ventilation and cardiac outflow murmurs.
- What is her clinical condition?
 - What will her thyroid tests show?
 - How will you treat her?
 - What concerns you?

PATIENT #3—EAR ACHE

- A 36yo man felt a little shaky. You tested a TSH, and it was suppressed. In retrospect, he tells you his other symptoms include a sore throat and an ear ache.
- What is his clinical condition?
 - What else will you find on exam?
 - How will you treat him?

PATIENT #4–PNEUMONIA

- A 55yo woman came to you 3 weeks ago for chest pain and fever. A CXR showed a LLL pneumonia. She looked well enough to treat as an outpatient. You gave her antibiotics. Her fever abated, and her cough has improved, but she feels tired. You check a TSH, and it is elevated at 12.
- What is her clinical condition?
 - What other tests will you do?
 - How will you treat her?

EVALUATION AND MANAGEMENT OF THYROID DISORDERS

*You passed!
Thank you for
listening.*

Maine Medical
PARTNERS
Endocrinology &
Diabetes Center