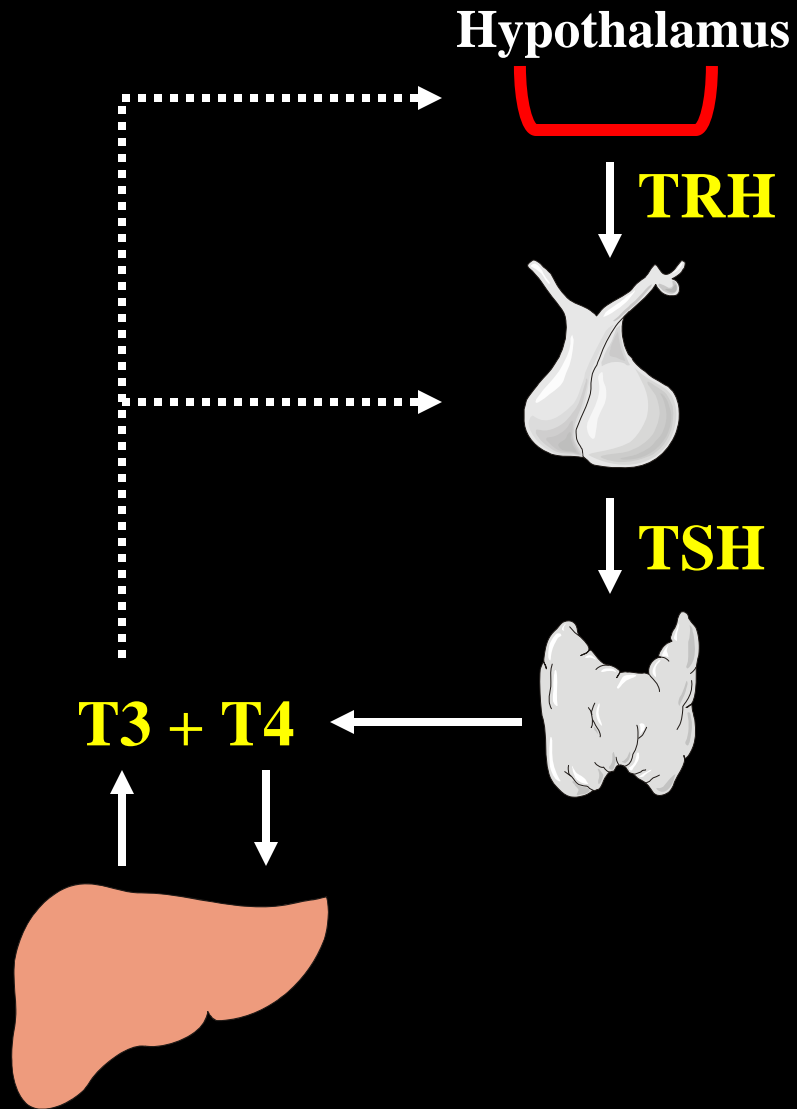


Disorders of Thyroid Function

Michael T. McDermott MD
Director, Endocrinology and Diabetes Practice
University of Colorado Hospital

Michael.mcdermott@ucdenver.edu

Thyroid Hormone Axis



Thyroid Function Testing

Testing / Screening

- ◆ **TSH: 1° Thyroid Disease (99%)**
- ◆ **TSH + Free T4: 2° Thyroid Disease (1%)**

↑ **TSH (1° Hypothyroidism)**

- ◆ **Free T4: Good Accuracy**

↓ **TSH (1° Hyperthyroidism)**

- ◆ **Free T4: Good Accuracy**
- ◆ **Total T3: Good Accuracy**
- ◆ **Free T3 Assays: Poor Accuracy - Avoid**

Case History

A 28 year old woman presents with 4 month history of fatigue, nervousness, palpitations and heat intolerance.

PE: BP 148/70 P 108 Ht 5'6'' Wt 115 lb.

Thyroid diffusely enlarged (3 x normal)

Lab: TSH: < 0.03 mU/L (nl: 0.5-5.0)

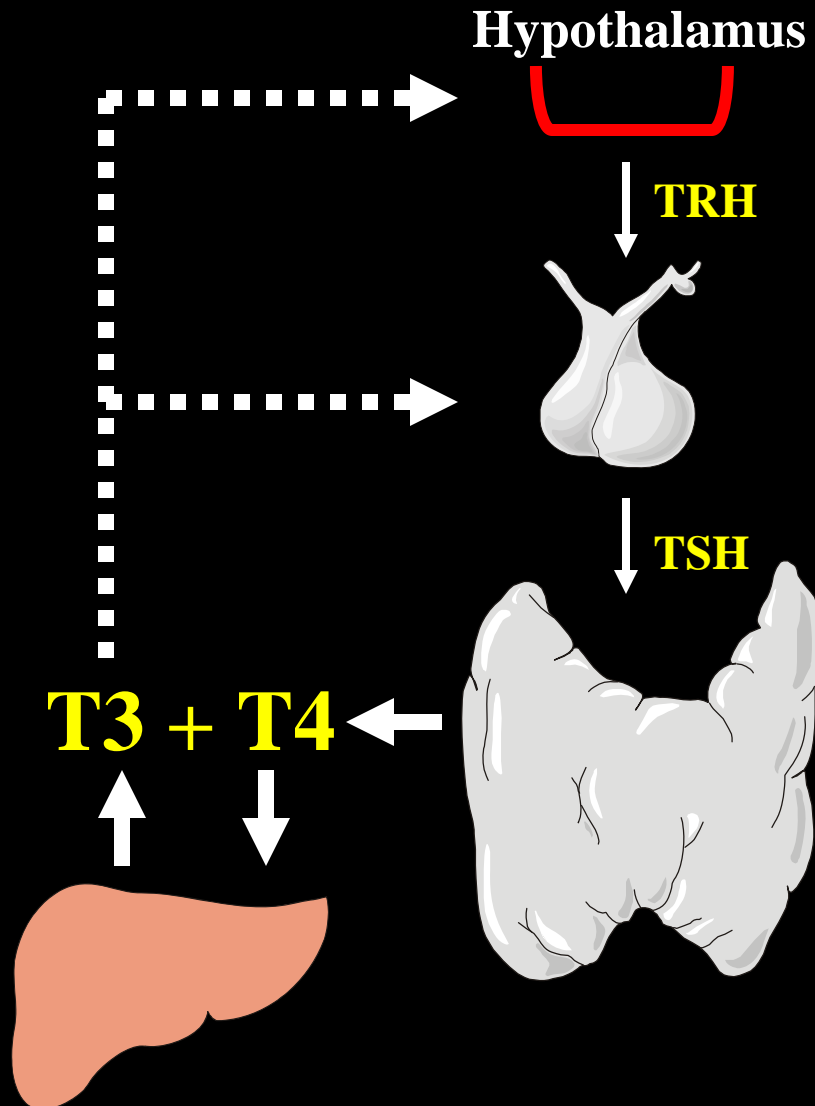
Free T4 7.8 ng/dl (nl: 0.7-2.7)

Total T3 698 ng/dl (nl: 90-190)

RAIU: 4 hr. = 62% 24 hr. = 74%

Thyroid Scan: Homogeneous Uptake

Hyperthyroidism



Overt Hyperthyroidism

↓ TSH
↑ Free T4
↑ Total T3

Subclinical Hyperthyroidism

↓ TSH
nl Free T4
nl Total T3

Thyrotoxicosis

Differential Diagnosis - RAIU

High RAIU

- Graves' Disease
- Toxic MNG
- Toxic Nodule
- HCG Secreting Tumor
- Central Thyrotoxicosis

Low RAIU

- Postpartum Thyroiditis
- Silent Thyroiditis
- Subacute Thyroiditis
- Factitious Thyrotoxicosis
- Iodine Induced
- Amiodarone Induced

Thyrotoxicosis

Differential Diagnosis - RAIU

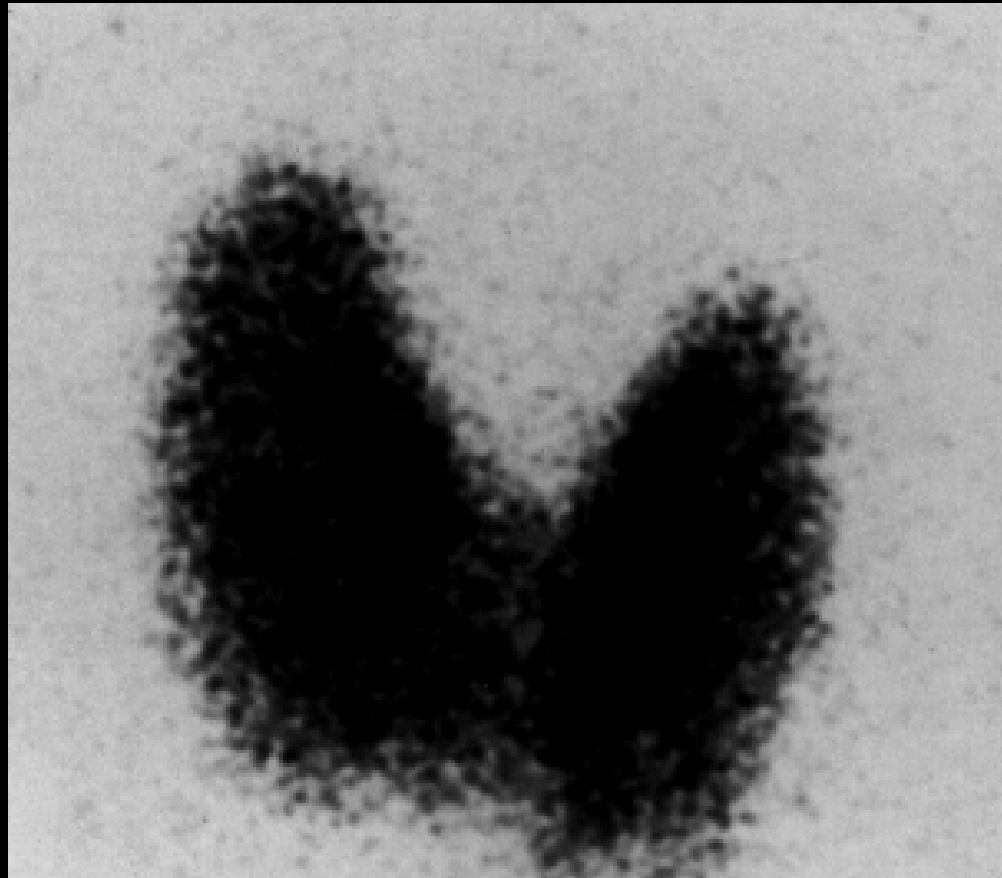
High RAIU

- Graves' Disease
- Toxic MNG
- Toxic Nodule
- HCG Secreting Tumor
- Central Thyrotoxicosis

Order Thyroid Scan

Graves' Disease

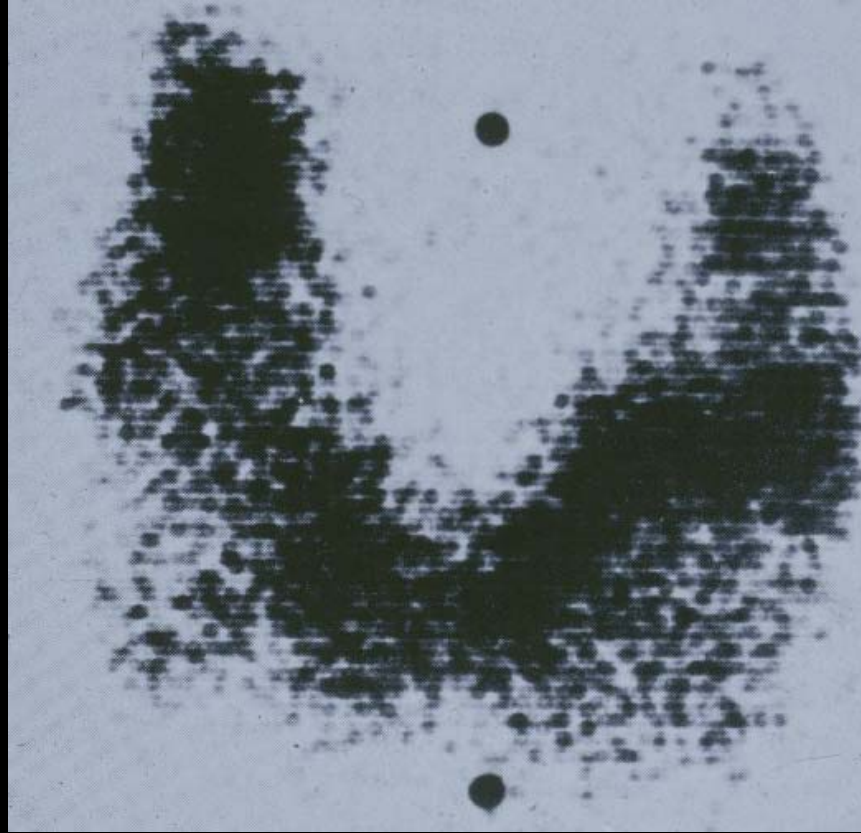
Diffuse Uptake



**TSH Receptor Antibodies Stimulate
Iodine Uptake and Thyroid Hormone Production**

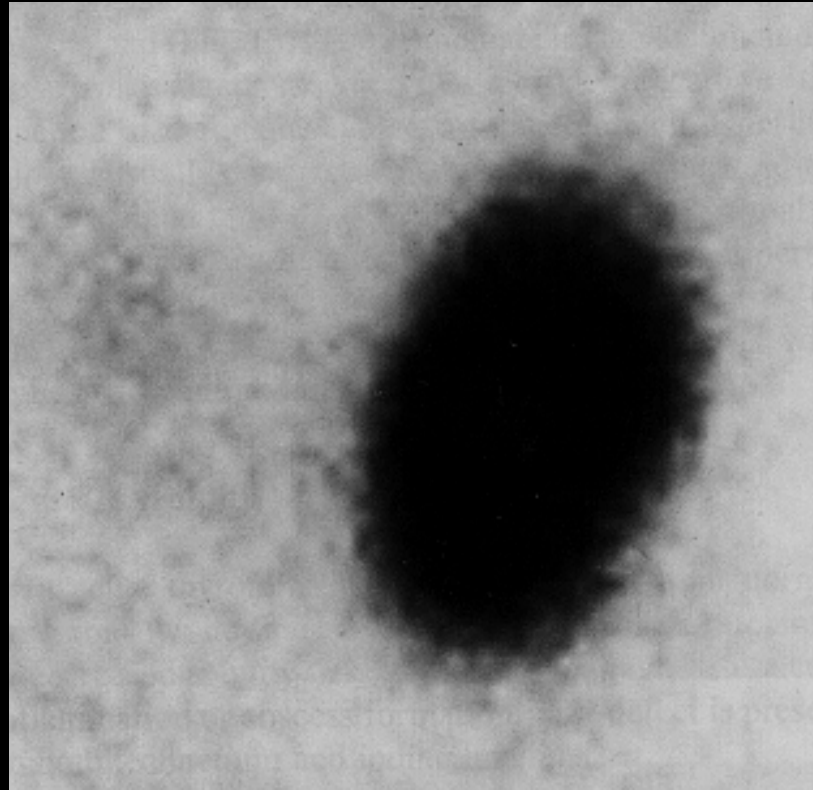
Toxic Multinodular Goiter

Patchy Uptake



**Mutation of TSH Receptor or α Subunit
Causing Autonomous Nodule Function**

Toxic Thyroid Nodule Solitary Uptake



**Mutation of TSH Receptor or α Subunit
Causing Autonomous Nodule Function**

Thyrotoxicosis

Differential Diagnosis - RAIU

Low RAIU

**Destructive
Thyroiditis**

- Postpartum Thyroiditis
- Silent Thyroiditis
- Subacute Thyroiditis
- Factitious Thyrotoxicosis
- Iodine Induced
- Amiodarone Induced

No Thyroid Scan Needed

Destructive Thyroiditis

Low RAIU

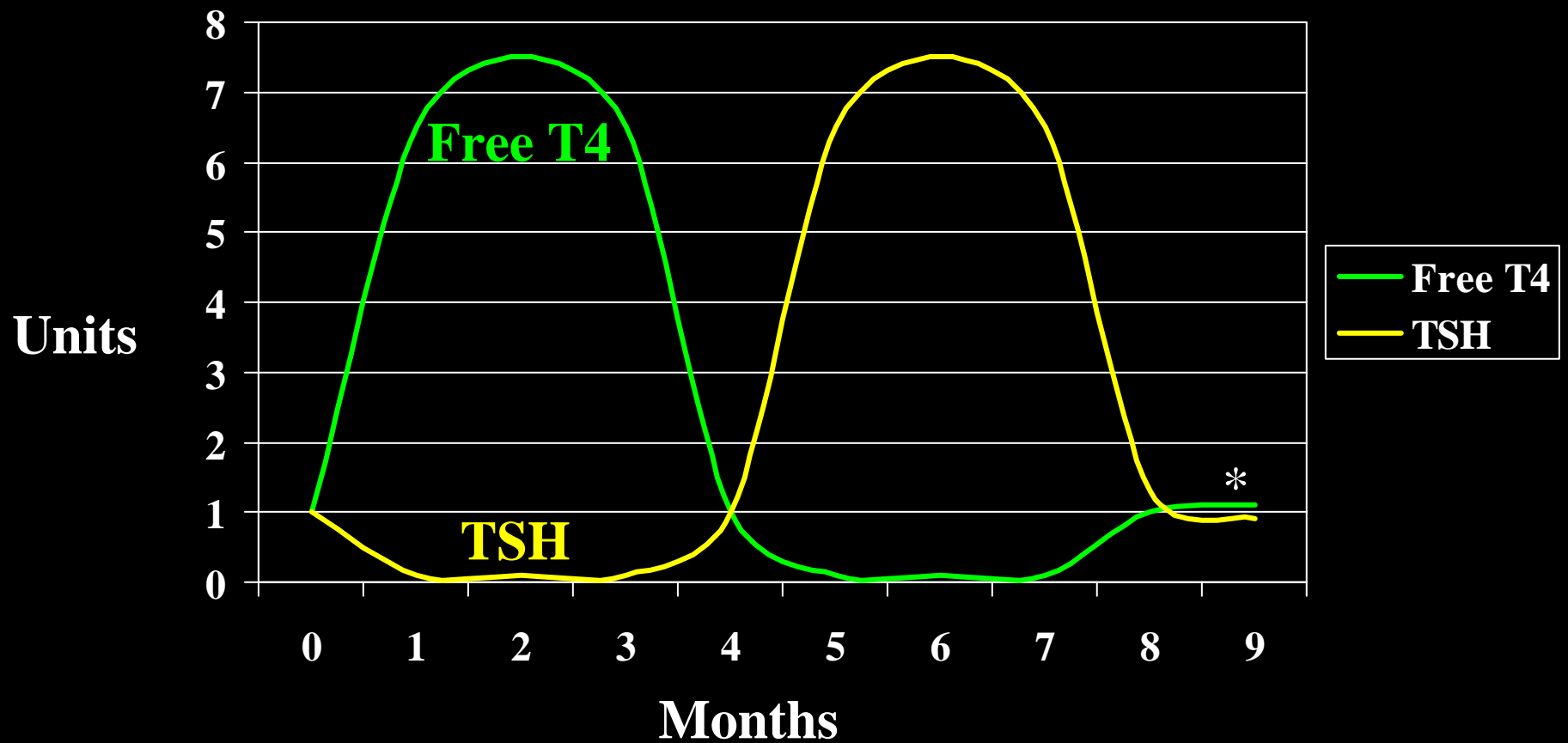
Destruction of
Thyroid Follicles
With Release of
T4 and T3 into
Circulation

- **Postpartum Thyroiditis**
Lymphocytic Thyroiditis
- **Silent Thyroiditis**
Lymphocytic Thyroiditis
- **Subacute Thyroiditis**
Granulomatous Thyroiditis
Pain and Tenderness
Elevated ESR

Destructive Thyroiditis

Clinical Course

Postpartum, Silent, and Subacute Thyroiditis



***20-25% Remain Hypothyroid**

Graves' Disease

Treatment

Anti-Thyroid Drugs for 12-18 Months

- ◆ Methimazole: 30 mg QD; ↓ in 1-2 months
- ◆ Propylthiouracil: 100 mg TID; ↓ in 1-2 months
- ◆ Beta Blocker: Atenolol 50 mg QD until euthyroid
- ◆ Goal: Rapid Symptom Relief; **Remission: ~ 20-40%**
- ◆ Liver Disease: PTU (AST, ALT, Liver Failure)
- ◆ Agranulocytosis: ~1/200 (Check CBC when Febrile)

Radioiodine (I-131) Therapy

- ◆ Hypothyroidism occurs in ~ 80-100% (Avg: 3 Months)

Surgical Therapy

- ◆ Hypothyroidism occurs in ~ 80-100% (1-2 Weeks)

Toxic MNG and Toxic Nodule

Treatment

Anti-Thyroid Drugs for 4-6 Weeks (prior to other Rx)

- ◆ Methimazole: 30 mg QD; ↓ in 1-2 months
- ◆ Propylthiouracil: 100 mg TID; ↓ in 1-2 months
- ◆ Beta Blocker: Atenolol 50 mg QD until euthyroid
- ◆ Goal: Rapid Symptom Relief; **Remission will not Occur**
- ◆ Liver Disease: PTU (AST, ALT, Liver Failure)
- ◆ Agranulocytosis: ~1/200 (Check CBC when Febrile)

Radioiodine (I-131) Therapy

- ◆ Hypothyroidism occurs in ~ 50% (Avg: 3-12 Months)

Surgical Therapy

- ◆ Hypothyroidism occurs in ~ 50% (1-2 Weeks)

Destructive Thyroiditis

Treatment

Postpartum, Silent, and Subacute Thyroiditis

■ Thyrotoxic Phase

Beta Blockers: if needed for symptoms

Anti-Thyroid Drugs: not effective

■ Hypothyroid Phase

Levothyroxine: if needed for symptoms

■ Resolution

75-80% return to Normal

20-25% remain Hypothyroid

Case Presentation

A 62 y.o. woman experiences occasional palpitations, fatigue and forgetfulness.

PMH: HTN, DJD, GERD

Meds: lisinopril, tylenol prn

PE: Ht 5'8" 180 lb. BP 145/80 P 84

Thyroid: nodular goiter

Lab: TSH < .01 mU/L

Free T4 1.8 ng/dl (nl, 0.7-2.7)

Total T3 165 ng/dl (nl, 90-190)

RAIU: 26% (24 hr.) Scan: patchy uptake

Subclinical Hyperthyroidism

Small Increase in Free T4 = Large Decrease in TSH

Free T4

Normal Range Change

2.7 ng/dl

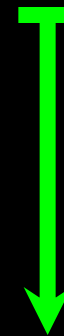


0.7 ng/dl

TSH

Normal Range Change

5.0 mU/L



0.5 mU/L

Subclinical Hyperthyroidism

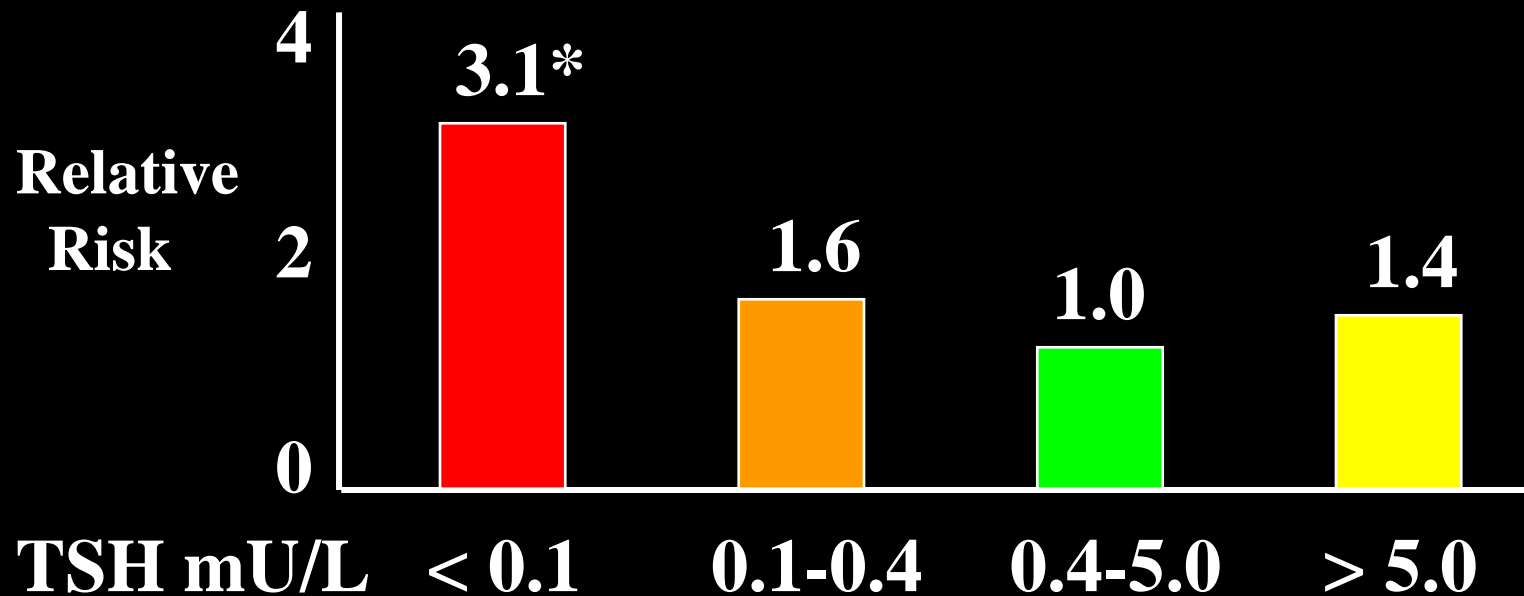
Clinical Concerns

- Symptoms
- Osteoporosis
- Atrial Fibrillation

Subclinical Hyperthyroidism

Risk of Atrial Fibrillation

2007 subjects > 60 yo (1193 women, 814 men)
TSH measured; 10 year follow-up



Subclinical Hyperthyroidism

Treatment – Consensus Recommendations

TSH 0.1-0.45 mU/L

- Not routinely recommended without symptoms
- On LT4 Rx: ↓ dose until TSH in normal range

TSH < 0.1 mU/L

- If ↑ RAIU: consider ATD or I-131 Rx
- On LT4 Rx: ↓ dose until TSH in normal range

Case History

A 33 year old woman presents for evaluation of fatigue and weight gain of 15 lb.

PMH: DM type 1

Meds: insulin

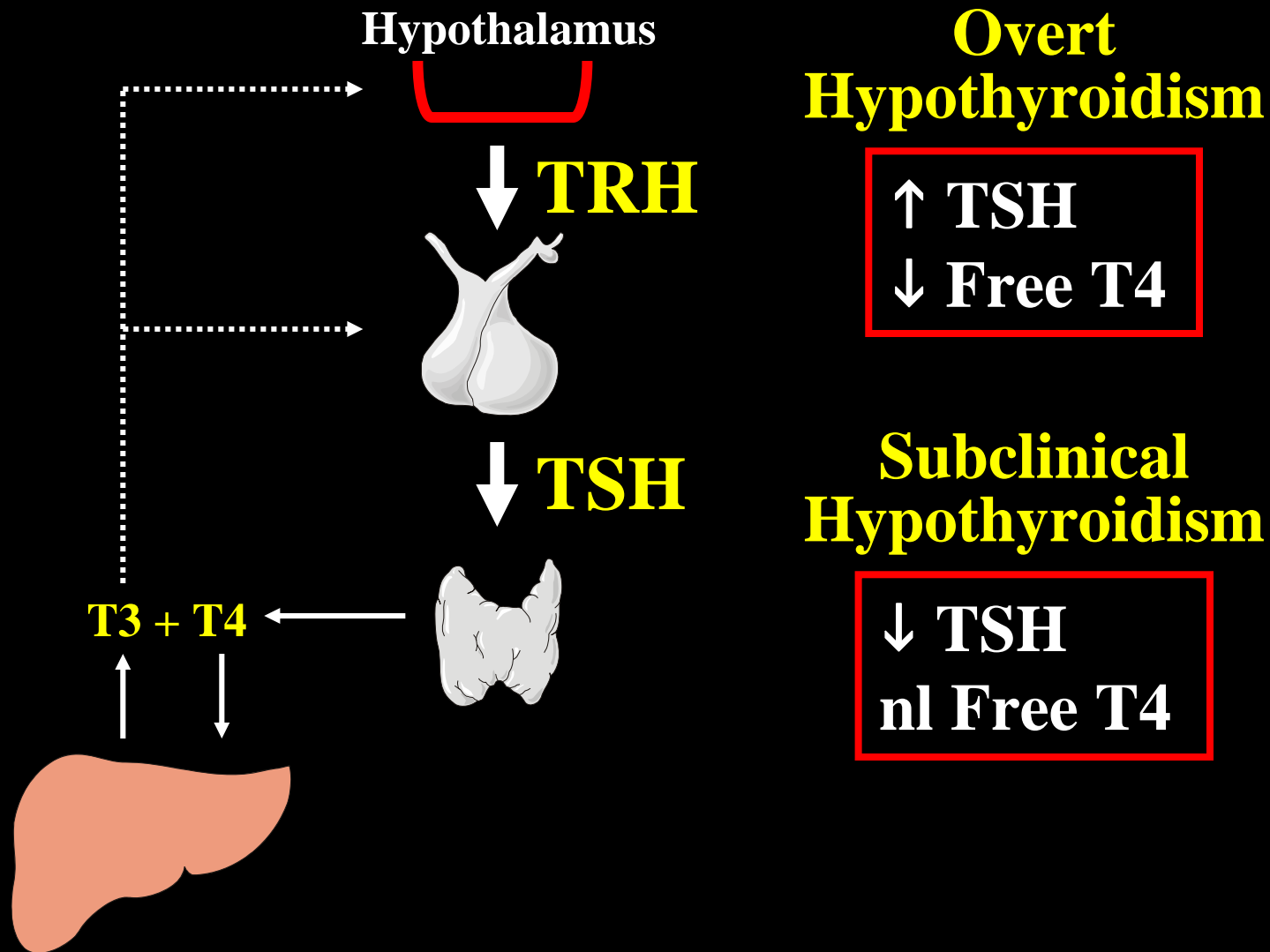
PE: BP 134/80 P 64 Ht 5'6'' Wt 154 lb.

moderate goiter, periorbital edema,
delayed reflex relaxation

Lab: TSH 112 mU/L (nl: 0.5-5.0)

TPO antibodies 72.5 units (nl: < 0.3)

Hypothyroidism



Primary Hypothyroidism

Etiology

- **Lymphocytic Thyroiditis**
- **Thyroidectomy**
- **I-131 Ablation**
- **Medications**
 - ◆ **Lithium**
 - ◆ **Amiodarone**
 - ◆ **Alpha Interferon**

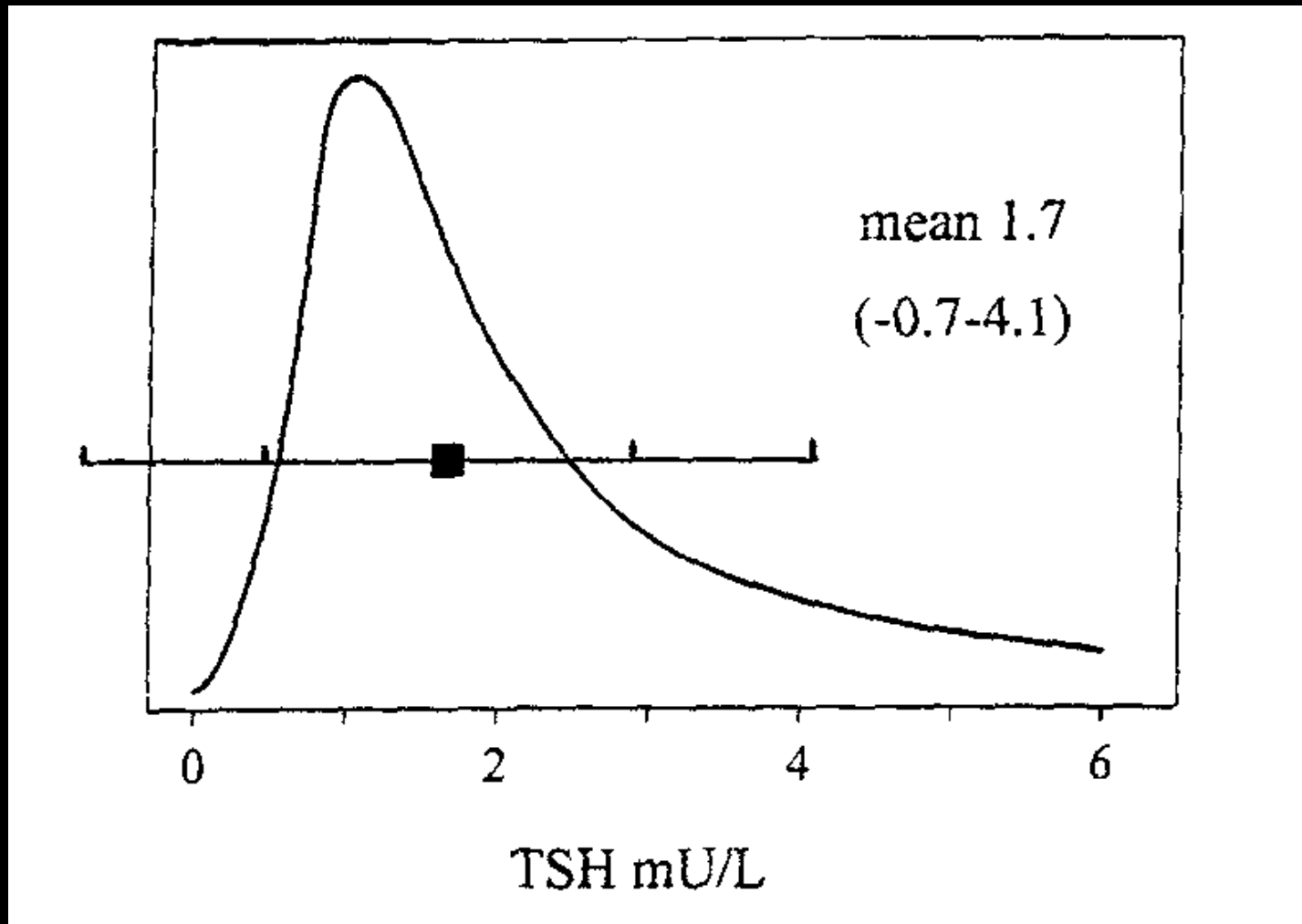
Hypothyroidism

Treatment

Age < 60 Years and No CAD

- **LT4 1.6 ug/kg: daily starting dose**
- **Recheck TSH: 6 weeks**
- **Titrate LT4 Until: $0.5 < \text{TSH} < 2.0$ mU/L**

TSH Distribution in Normal Population



TSH Goal (on LT4 Rx): 0.5-2.0 mU/L

Hypothyroidism

Treatment

Age > 60 Years or CAD

- **LT4 12.5-25 ug: daily starting dose**
- **Recheck TSH: 6 weeks**
- **Titrate LT4 Until: $1.0 < \text{TSH} < 3.0$ mU/L**

Case History

A 68 year old woman with progressive fatigue, mild depression and poor memory.

PMH: DJD, GERD Meds: tylenol

PE: BP 150/86 P 80 Ht 5'9" Wt 162 lb.

Complete exam normal

Lab: TSH 10.2 mU/L (nl: 0.5-5.0)

Free T4 0.9 ng/dl (nl: 0.7-2.7)

Chol 255 TG 165 HDL 45 LDL 177

Should she be treated for hypothyroidism?

Subclinical Hypothyroidism

Small Decrease in Free T4 = Large Increase in TSH

Free T4

Normal Range Change

2.7 ng/dl

0.7 ng/dl

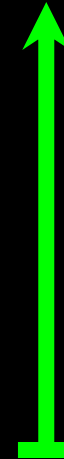


TSH

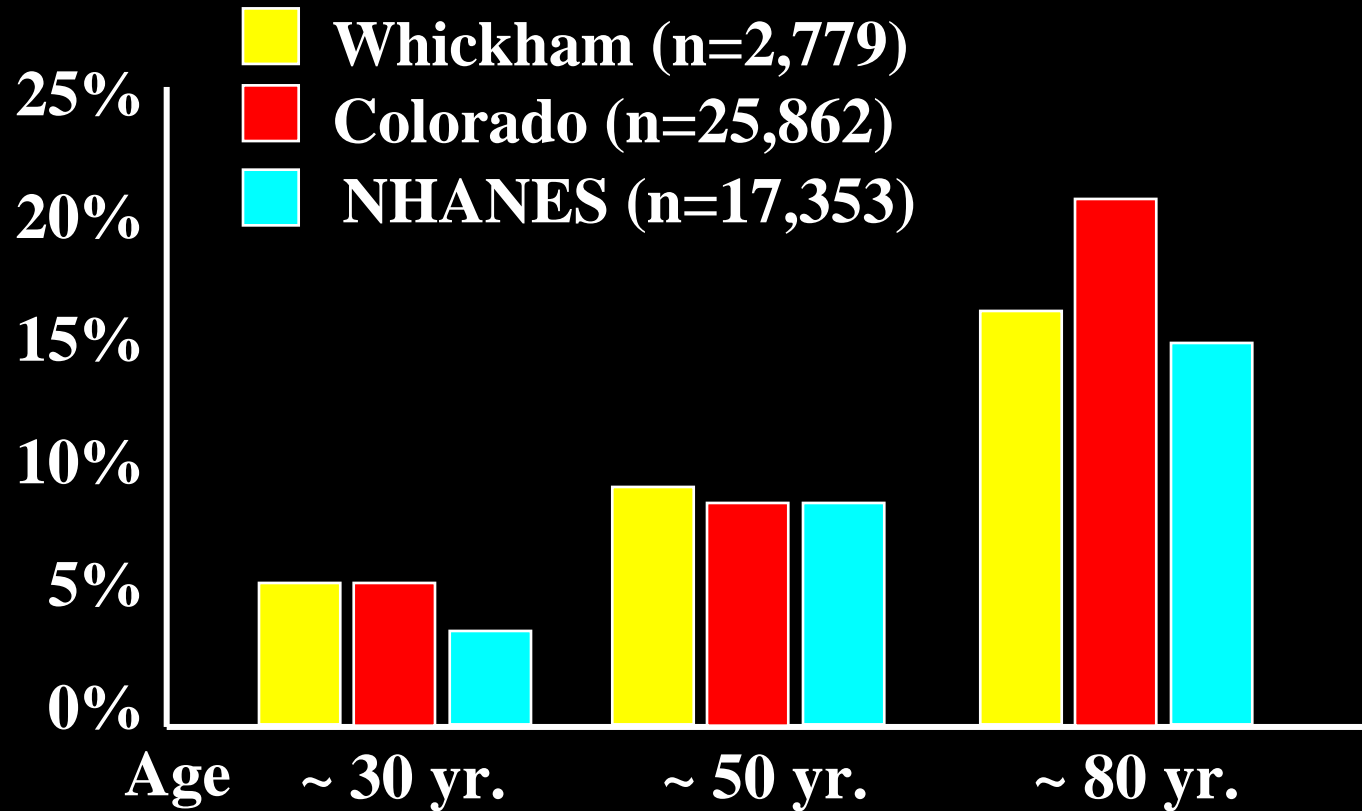
Normal Range Change

5.0 mU/L

0.5 mU/L



Mild Thyroid Failure Prevalence - Women



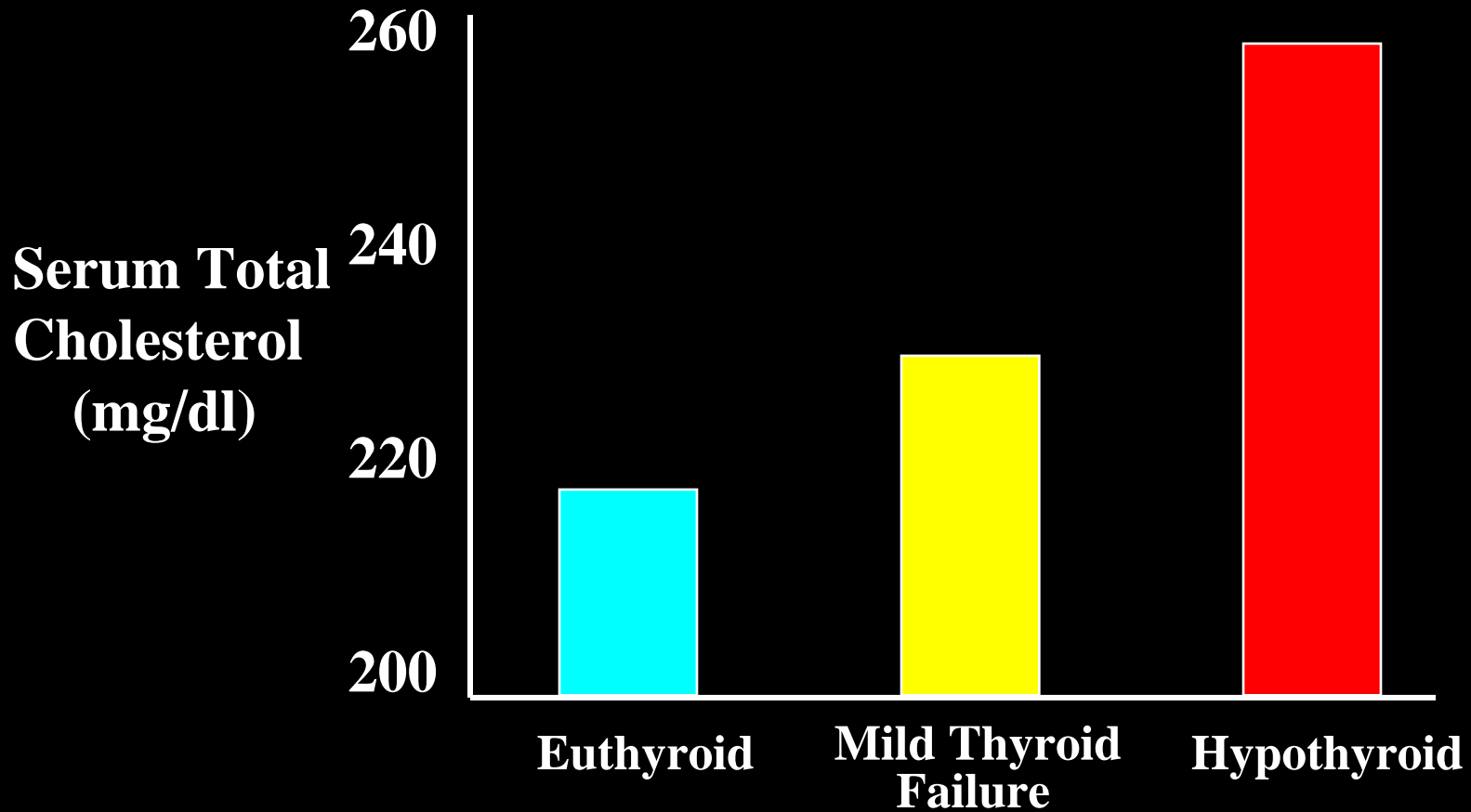
Tunbridge W, Clin Endo 7:481, 1977
Canaris G, Arch Intern Med 160:526, 2000
Hollowell J, J Clin Endo Metab 87: 489, 2002

Subclinical Hypothyroidism Issues

- Symptoms
- Lipid Elevation
- CVD Risk Factor

**Colorado
Study**

**Hypothyroidism
Cholesterol Elevation**

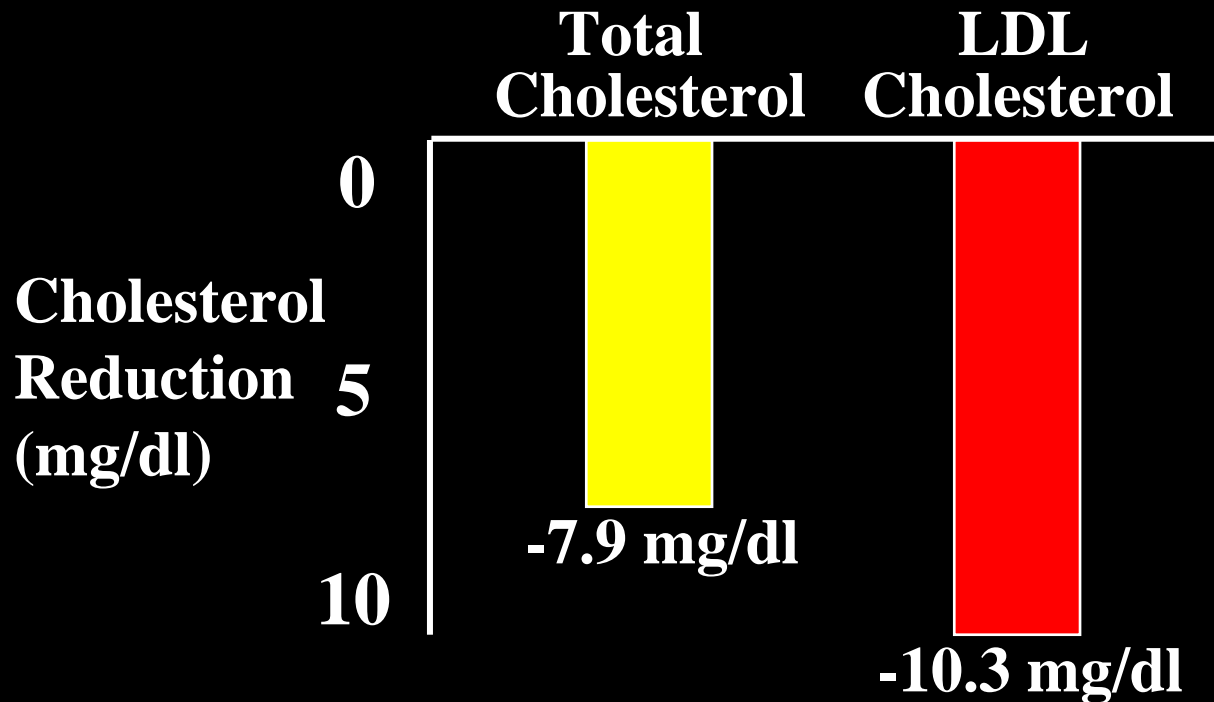


Mild Thyroid Failure

Lipid Changes with LT4 Therapy

Meta-Analysis: 13 Studies 247 patients

Mean TSH 4.8-19.0 mU/L



Subclinical Hypothyroidism

Treatment – Consensus Conference

TSH 4.5-10 mU/L

- LT4 Rx not routinely recommended without symptoms
- Clinical Judgment Advised
- Recommended: All Pregnant Women

TSH > 10 mU/L

- Routine LT4 Rx: Reasonable
- Clinical Judgment Advised
- Recommended: All Pregnant Women

Subclinical Hypothyroidism

Treatment

- **LT4 Rx: 25 ug daily starting dose**
- **Recheck TSH: 6-8 weeks**
- **Adjust LT4 dose: as needed to maintain**
 - ◆ **Serum TSH: 0.5-2.0 mU/L**

Case History

A 32 year old woman was diagnosed with hypothyroidism 6 months ago. Despite treatment she still complains of fatigue, mild depression and difficulty losing weight. **She requests T3 therapy.**

PMH: hypothyroidism **Meds**: LT4 125 ug/d

PE: BP 122/84 P 80 Ht 5'6" Wt 172 lb.

Complete exam normal

Lab: TSH 1.2 mU/L (nl: 0.5-5.0)

Free T4 1.3 ng/dl (nl: 0.7-2.7)

Total T3 104 ng/dl (nl: 90-190)

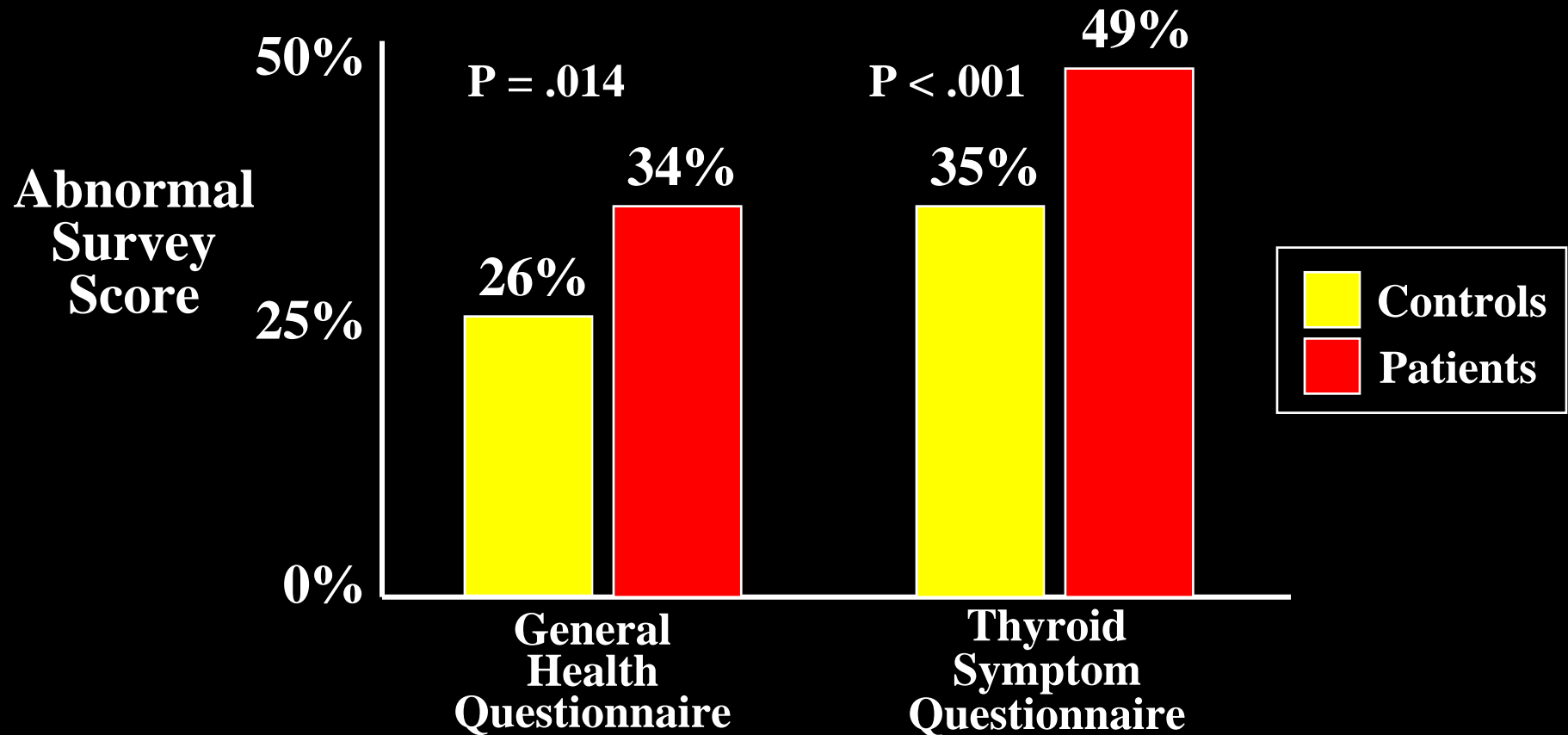
Should she be treated with LT3?

Persistent Symptoms on LT4 Rx

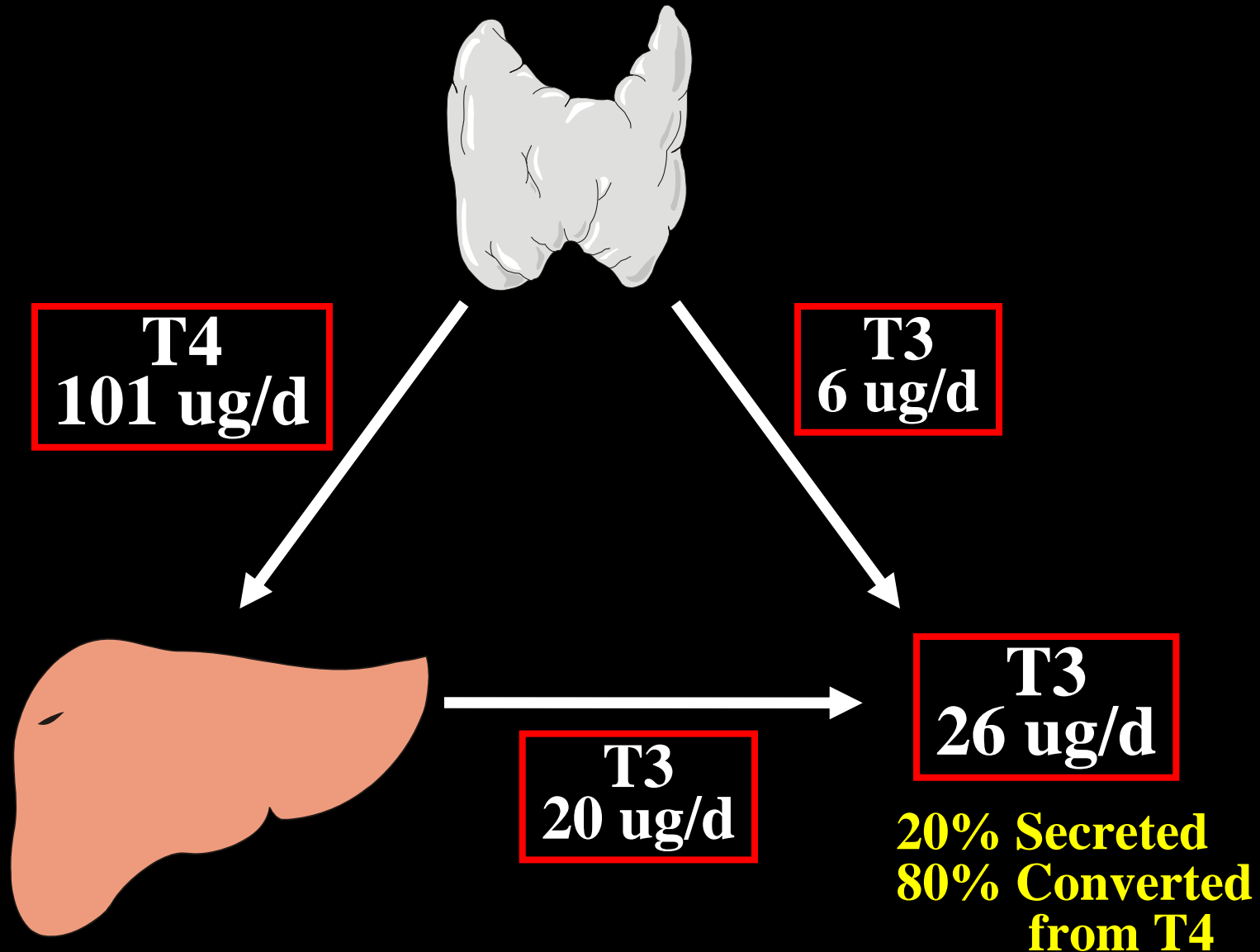
Community Based Questionnaire Study:

397 Hypothyroid Patients with normal TSH on LT4

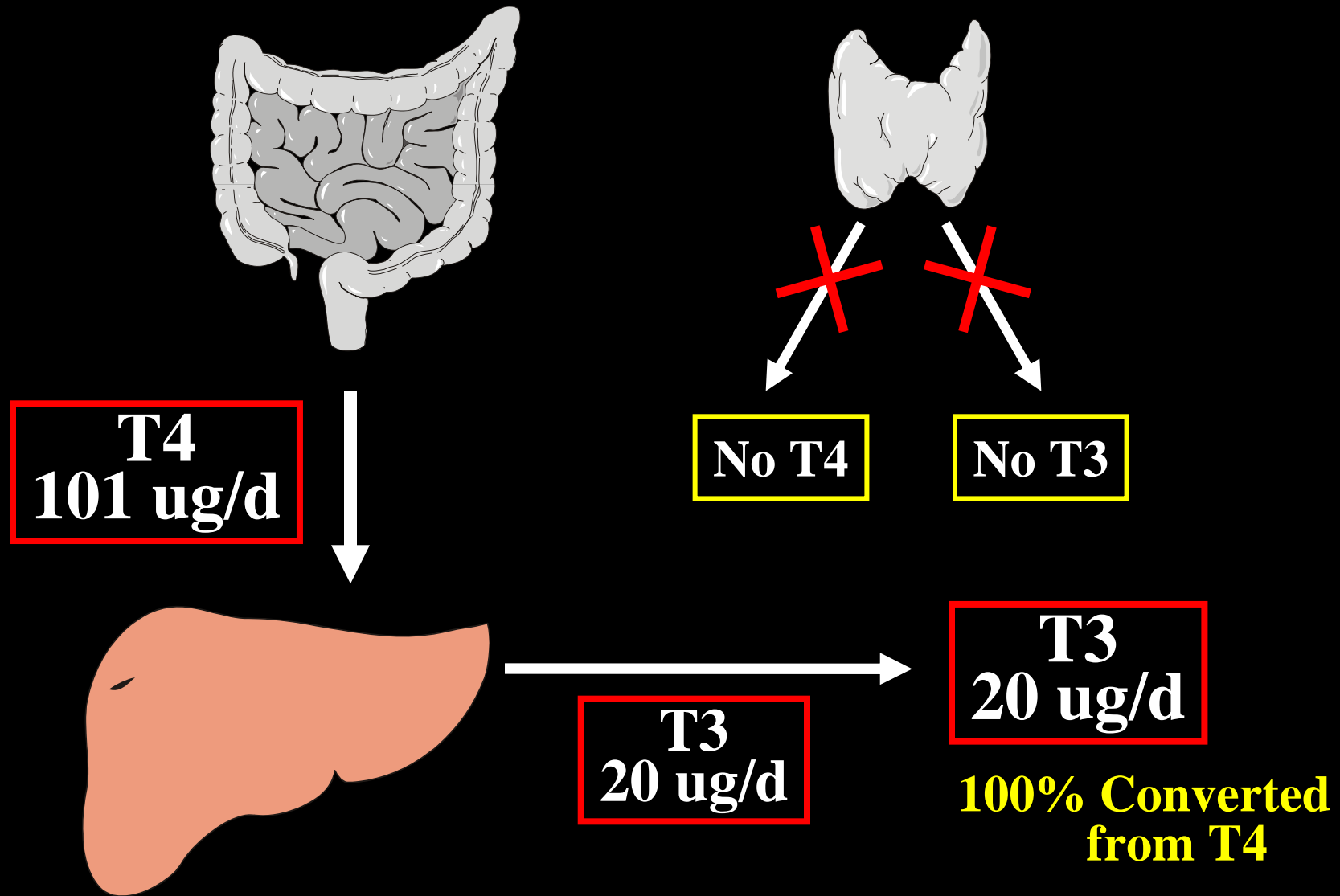
397 Control Subjects (matched for gender and age)



Thyroid Hormone Production



The T3 Hypothesis



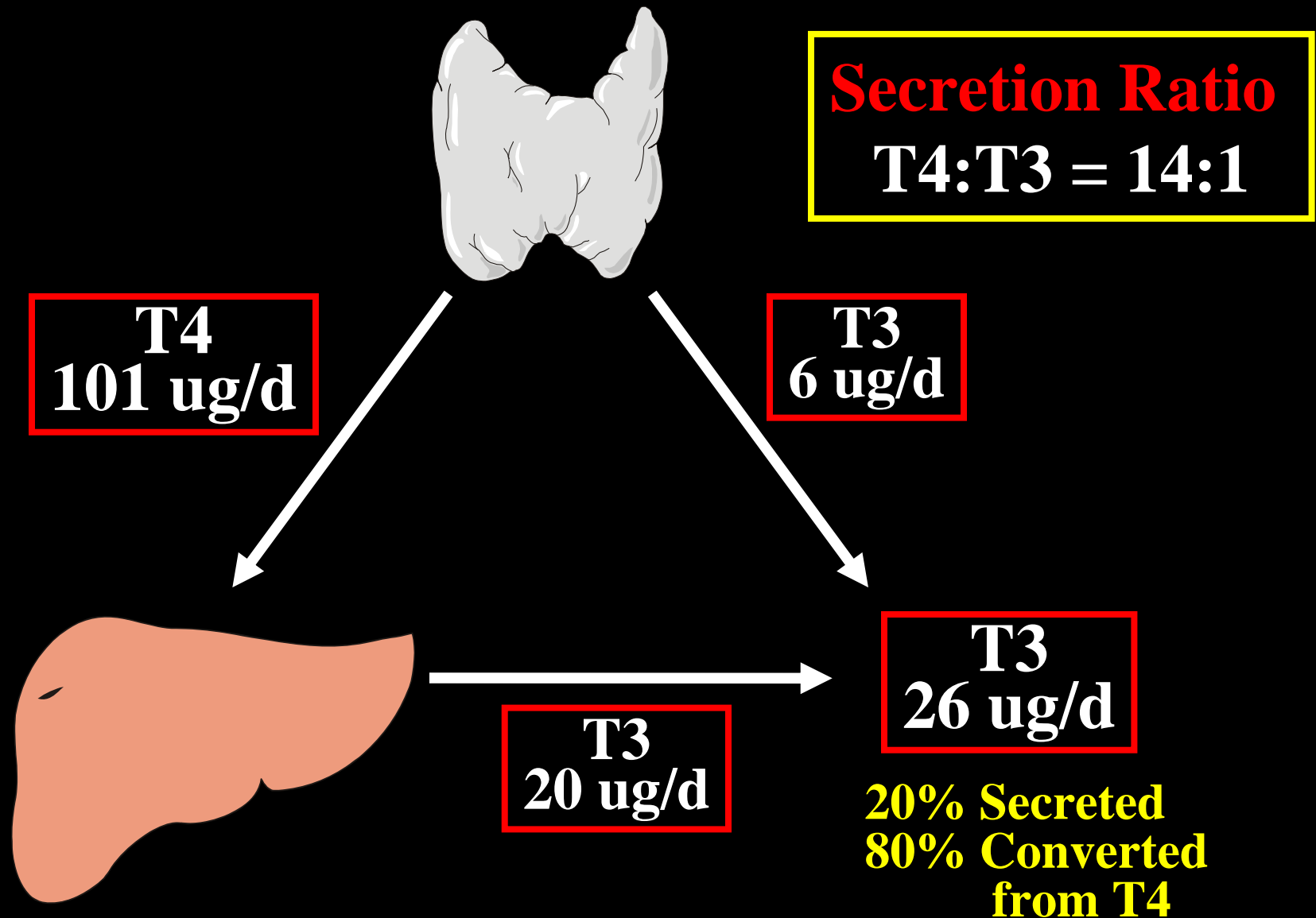
“Tissue T3 Deficiency”

Combined LT4 / LT3 Therapy

Randomized Controlled Trials

<u>Study</u>	<u>Objective Benefit</u>	<u>Subjective Benefit</u>	<u>T4/T3 Preference</u>
Bunevicious 1999	No	Yes	Yes
Walsh 2003	No	No	No
Sawka 2003	No	No	NA
Clyde 2003	No	No	NA
Siegmund 2004	No	No	NA
Saravanan 2005	No	No	NA
Escobar-Morreale 2005	No	No	Yes
Apelhof 2005	No	No	Yes
Rodriguez 2005	No	No	NA
Levitt 2005	No	No	NA
Regalbuto 2007	No	No	No
Slawik 2007 (Central)	No	No	NA
Escobar-Morreale 2005 Review:	No benefit of T4/T3		
Grozinsky-Glasberg 2006 Meta-Analysis:	No benefit of T4/T3		

Thyroid Hormone Production



Armour Thyroid

<u>Dose</u>	<u>LT4 + LT3</u>	<u>T4:T3*</u>
1/4 grains	9.5 + 2.25	2.8:1
1/2 grains	19 + 4.50	2.8:1
1.0 grains	38 + 9.0	2.8:1
1.5 grains	57 + 13.5	2.8:1
2.0 grains	76 + 18.0	2.8:1
3.0 grains	114 + 27.0	2.8:1
Normal	100 + 6	14:1

*Assumes 80% absorption LT4 and 100% absorption LT3

LT4/LT3 Therapy for Hypothyroidism **Recommendations**

Should all hypothyroid patients be treated with combination LT4/LT3 therapy?

◆ **No**

Should any hypothyroid patients be treated with combination LT4/LT3 therapy?

◆ **Reasonable if symptoms persist on optimal LT4 Rx**

The optimal T4:T3 ratio is ~ 10-14:1.

LT3 is best taken BID or as Slow Release

When using combination LT4/LT3 therapy, measure thyroid tests before meds are taken.

Thank You