

“Under and Over: Update on Thyroid Disorders, 2004”

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Monday, 13 June 2004**

COURSE OBJECTIVES

- 1. Review the pathophysiology of thyroid disorders and contemporary approach to thyroid testing.**
- 2. Review recent concepts regarding the management of hypothyroidism.**
- 3. Review overt and subclinical hyperthyroidism.**
- 4. Review pregnancy and thyroid disease.**

OUTLINE OF PRESENTATION

1. Normal thyroid physiology
2. Thyroid Function testing
3. Common thyroid disorders
 - hypothyroidism
 - hyperthyroidism
 - nodular thyroid disease
 - thyroiditis
 - thyroid neoplasms
4. Hypothyroidism
 - historical perspective
 - etiology
 - clinical presentations
 - associated disorders (ie, lipids, cardiac)
 - treatment
 - LT4
 - LT3 – recent trials
 - subclinical hypothyroidism
5. Hyperthyroidism
 - common etiologies
 - clinical features
 - treatment options
 - surgery
 - RAI therapy
 - antithyroid drug therapy
 - subclinical hyperthyroidism:
 - management
 - clinical features
6. Pregnancy and Thyroid Disorders
 - autoimmune thyroid disorders
 - post-partum thyroiditis



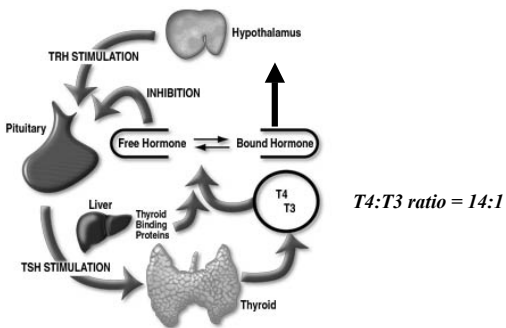
Under & Over: Update on Thyroid Disorders

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Common Thyroid Disorders

- Hypothyroidism
- Hyperthyroidism
- Nodular thyroid disease
- Thyroiditis
- Thyroid neoplasms

The Hypothalamic-Pituitary-Thyroid Axis



Tests of Thyroid Function

Tests	Normal Levels	When to Use
■ TSH	0.5 - 5.0 mU/L ¹	To assess thyroid status ¹
■ Free T ₄	0.7 - 2.1 ng/dL	With TSH, used to assess degree of hypothyroidism ¹
■ T ₄	4 - 12 µg/dL	Bound + free T ₄ ; with TSH used for definitive diagnosis of thyroid failure ²
■ Thyroid hormone binding ratio (THBR)	0.8 - 1.15	Estimates number of unoccupied serum protein-binding sites ¹
■ Free thyroxine index (FT ₄ I)	1 - 4	Estimates concentration of free T ₄
■ Total T ₃	75 - 175 ng/dL	Total T ₃ (Bound + free) more definitive test for hyperthyroid states
■ Anti-TPO, anti-Tg antibodies	Negative	May be recommended with slightly elevated TSH to predict prevalence of thyroid failure.

1. Stockigt JR. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:377.
 2. NACB. Standards of Laboratory Practice. 1996.

HYPOTHYROIDISM:

Historical Perspective

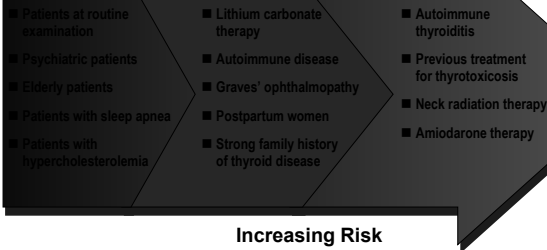
- **1656** – Wharton describes *glanudlae thyroidea*
- **1871** – Description of sporadic cretinism (termed "myxedema" to reflect the 'mixed edema')
- **1891** – myxedema treated with glycerine thyroid extract
- **1892** – oral thyroid extract given by mouth for myxedema:
"...have the patient take half a thyroid, lightly fried and minced, with currant jelly once a week."
 (Surks, MI in *The Thyroid*, 6th ed., 1991)
- 1893 – dessicated thyroid powder
- 1916 – thyroid USP (standardized .17 to .23% I)

Epidemiology of Hypothyroidism

- **>10 million Americans affected¹**
- **>10 times more common in women than men²**
- **Increased risk among women >40 years of age¹**
- **Elevated thyroid stimulating hormone (TSH) in 9.6% of women between ages 45-54, and 6.9% of men between ages 65-74²**
- **Elevated TSH in approximately 12% of women older than 60³**

1. Staub J-J. *Am J Med*. 1992;92:631.
 2. Tunbridge WMG et al. *Clin Endocrinol*. 1977;7:481.
 3. Sawin CT et al. *JAMA*. 1989;261:2653.

Overt Hypothyroidism: Who Is at Risk?



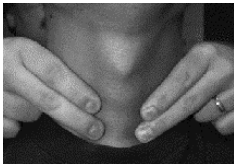
Ladenson PW. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996;76:878.

Clinical Symptoms of Hypothyroidism

- | | |
|--------------------------|--------------------------|
| ■ Arthralgias | ■ Fatigue |
| ■ Cold intolerance | ■ Hoarseness |
| ■ Constipation | ■ Lethargy |
| ■ Decreased memory | ■ Menstrual disturbances |
| ■ Decreased perspiration | ■ Memory impairment |
| ■ Depression | ■ Muscle cramps |
| ■ Dry skin | ■ Paresthesias |
| ■ Facial puffiness | ■ Weight change |

Braverman LE, Utiger RD. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:736.

Physical Examination of the Thyroid



Clinical Signs of Hypothyroidism

- Bradycardia
- Coarse hair
- Delayed relaxation of deep tendon reflexes
- Dry, cool, pale skin
- Goiter
- Hoarseness
- Nonpitting edema (myxedema)
- Puffy eyes and face
- Slow movements
- Slow speech
- Thinning lateral third of eyebrows

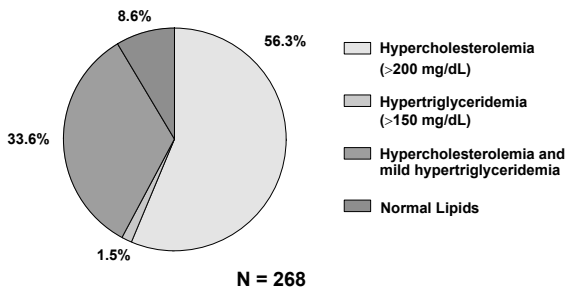
from Braverman LE, Utiger RD. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:736.

HYPOTHYROIDISM

Associated Disorders

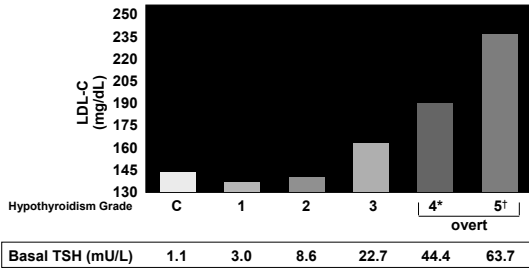
- Lipid abnormalities
- Cardiac disorders
- Mood disorders

Types of Lipid Abnormalities in Patients With Hypothyroidism



O'Brien T et al. *Mayo Clin Proc.* 1993;68:860.

LDL-C Levels Increase With Increasing Hypothyroidism Grade



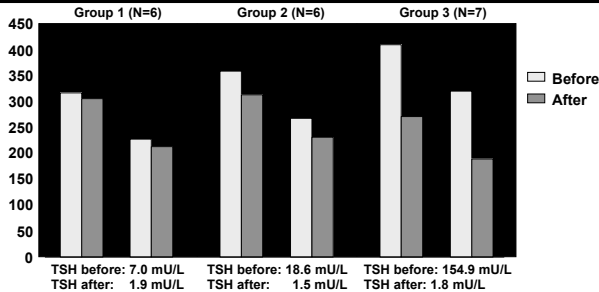
C=controls.
 *P<.01 vs controls. †P<.001 vs controls.
 Staub JJ et al. *Am J Med.* 1992;92:631.

Two Population-Based Studies of Hypothyroidism With Hypercholesterolemia

Total Cholesterol (mg/dL)	Number (%) Hypercholesterolemic	Number (%) with TSH ≥5
The Glasgow Study¹		
	N=2250	
>310	90 (4.0%)	12 (13.0%)
>270	351 (15.6%)	17 (4.8%)*
The England Study²		
	N=3277	
>310	83 (3.0%)	8 (9.6%)
>270	272 (8.0%)	16 (5.9%)

*Represents results from first 95 patients identified in screening program.
 1. Series JJ et al. *Clin Chim Acta.* 1988;172:217.
 2. Ball MJ et al. *J Roy Soc Med.* 1991;84:527.

Effect of L-Thyroxine Treatment on Lipid Levels in Dyslipidemia¹



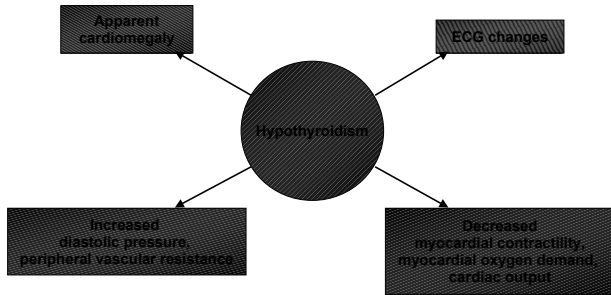
*=mg/dL. †Values are means ±SD.
 Diekman T et al. *Arch Intern Med.* 1995;155:1490.

Effect on Total Cholesterol of L-Thyroxine Therapy in Overt Hypothyroidism

Reference	N	TSH (mU/L)		Total Cholesterol (mg/dL)		
		Before Treatment	After Treatment	Before Treatment	Decrease After LT ₄ Therapy	% Change
Gorman (1979)	27	83 ± 73	6.2 ± 3.2	303.8 ± 73.1	-130.8	-38
Elder (1990)	56	98 ± 64	1.4 ± 1.3	346.2 ± 96.2	-123.1	-35
Wiseman (1993)	52	47 (6-260)	1.7 (0.1-6.3)	219.2 ± 42.3	-34.6	-15

Tanis BC et al. *Clin Endocrinol*. 1996;44:643.

Cardiovascular Changes Often Associated With Hypothyroidism



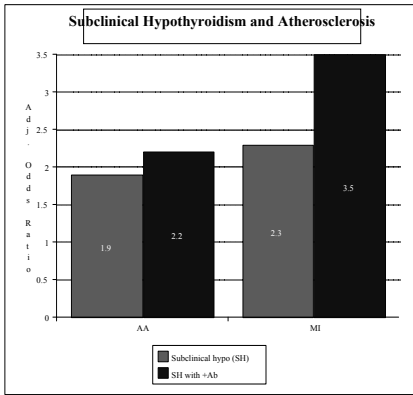
Klein I, Ojamaa K. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:799.

Hypothyroidism and CV Disease

The Rotterdam Study

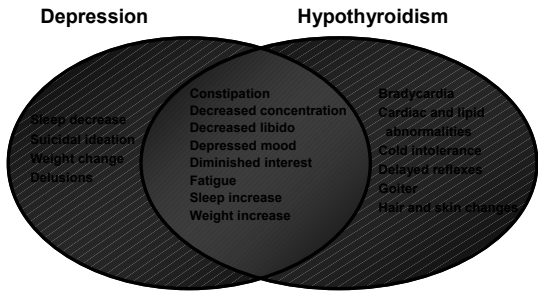
Hak E, Pols HAP, Vester TJ, et al. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and MI in elderly women: the Rotterdam Study. *Ann Int Med*. 2000; 132:270-6.

- Random sample of 1149 women (mean age, 69±7.5 y) screened for hypothyroidism; 11% had ↑TSH with normal free T4
- Age-adjusted prevalence of aortic atherosclerosis and MI: odds ratio=1.7)
- Attributable risk for subclinical hypothyroidism associated with MI was similar to that of known risk factors (age-adjusted relative risks: 2.5 for subclinical hypothyroidism, 2.4 for hypercholesterolemia, 1.6 for HTN, 2.0 for smoking, and 2.4 for diabetes mellitus).
- AUTHORS' CONCLUSION: "Subclinical hypothyroidism is a strong indicator of risk for atherosclerosis and MI in elderly women."



Hak E, Pols HAP, Visser TJ, et al. *Ann Int Med.* 2000; 132:270-8

Hypothyroidism and Depression Have Many Common Features



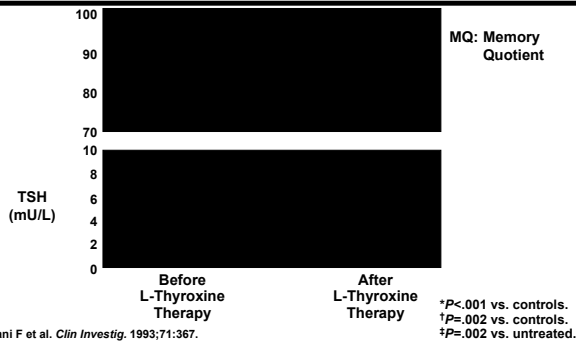
Adapted from Nemeroff CB. *J Clin Psychiatry.* 1989;50(suppl):13.

Hypothyroidism and Depression

- Depressive symptoms are common in hypothyroidism¹
- Many hypothyroid patients fulfill DSM-IV criteria for a depressive disorder²
- Depressed patients may be more likely than normal individuals to be hypothyroid³
- All depressed patients should be evaluated for thyroid dysfunction³

1. Nemeroff CB. *J Clin Psychiatry.* 1989;50 (suppl):13.
 2. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Copyright 1994 American Psychiatric Association.
 3. Jackson IMD. *Thyroid.* 1996;6:63.

Effect of L-Thyroxine Therapy on Memory Abilities in Mild Thyroid Failure



The Role of L-Thyroxine in Depression

- L-thyroxine therapy is recommended for any patients with depression who have persistently elevated serum TSH
- Antidepressants may be less effective if thyroid function not normalized

Hennessey JV, Jackson IM. *The Endocrinologist.* 1996;6:214.

Therapy of Hypothyroidism

- Choice of medication
- Adjustment of therapy
- Follow-up care

Which Thyroid Rx?

- Narrow therapeutic range for LT4
- Bioequivalence of thyroid preparations
 - * can't vary by more than $\pm 20\%$
- Name-brand versus generic L-thyroxine
(Fish, et.a NEJM, 1987)
- "Natural" vs. "synthetic" thyroid Rx

Pharmacologic Considerations in Treating Hypothyroidism

- Treatment of choice is L-thyroxine^{1,2}
- Brand-name L-thyroxine recommended^{1,2}
- Not recommended for *routine* use:
 - Desiccated thyroid hormone¹ (*thyroid USP*)
 - Combination of thyroid hormones¹
 - * *Thyrolar (T4/T3 = 4:1)*
 - Triiodothyronine (T₃) alone ¹
- TSH should be measured at 6 to 8 weeks after any change in L-thyroxine brand or dose^{1,2}

1. AACE. *Endocrine Pract.* 1995;1:56.
2. Singer PA et al. *JAMA.* 1995;273:808.

Older Thyroid Hormone Preparations

-Generally, most people do fine on levothyroxine sodium T4-only drugs. But some people do not. These people may be candidates for Armour or Thyrolar."

"My Own Experience:

After diagnosis, I spent a year and half on Thyrolar, as prescribed by my osteopathic MD, and was doing pretty well. After reading constantly about how the T4 only drugs were the "gold standard," I asked my doctor to switch me to Synthroid. Immediately, I started to lose my hair very rapidly. Within two months, despite my TSH test as showing still in the "normal" range, my usual 28-day menstrual cycle with normal 5 day periods went to every 22 days, lasting 7 days, and were unusually heavy and painful. Then I developed an ovarian cyst, which is associated with untreated hypothyroidism. After a few more months of hair loss, menstrual irregularities, and exhaustion, despite normal TSH levels, my doctor and I decided that I should go back to the Thyrolar. Symptoms resolved themselves within two months, and I was again back to normal. I stayed on Thyrolar for several years, before switching over to Armour—~~which~~ I've been on since the late 1990s, ever since. "

¹Here is descriptive information from the package inserts:

Armour Thyroid

Armour Thyroid tablets for oral use are natural preparations derived from porcine [pork] thyroid glands. Inactive ingredients are calcium stearate, dextrose, microcrystalline cellulose, sodium starch glycolate and gassy white (barium sulfate used as a whitening agent). Armour Thyroid is available in 1/4 grain, 1/2 grain, 1 grain, 1 1/2 grain, 2 grain, 3 grain, 4 grain and 5 grain tablet strengths.

Also, according to informational literature sent out by Forest Pharmaceuticals, Inc.,

"Because Armour Thyroid medications require a 4:22 to 1 ratio of T4 to T3, batches of desiccated thyroid are mixed until the desired ratio is obtained. This method ensures that each strength of Armour Thyroid will be consistent every time."



Hypothyroidism: Many Causes, One Treatment

- Goal: normalize TSH level regardless of cause of hypothyroidism¹
- Treatment: once daily dosing with L-thyroxine (0.75 mcg/lb, or 1.6 µg/kg/day)²
- Monitor TSH levels at 6 to 8 weeks, after initiation of therapy or dosage change³

1. Brent GA, Larsen PR. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:883.
2. AACE. *Endocrine Pract.* 1995;1:56.
3. Singer PA et al. *JAMA.* 1995;273:808.

Treatment of Overt Hypothyroidism

- Goal: normalize TSH level¹
- Starting dose for healthy patients (<50 years old) should begin at full dose
- Starting dose for healthy patients ≥50 years old *can* start at ≤50 µg/day. Dose can be increased by 25 µg/day, if needed, at 6- to 8-week intervals.¹ "Start low and go slow..."
- Starting dose for patients with heart disease should begin at 12.5 to 25 µg/day and increase by 12.5 to 25 µg/day, if needed, at 6- to 8-week intervals²

1. Brent GA, Larsen PR. In *Werner and Ingbar's The Thyroid*, 7th ed. 1996:883.
2. Singer PA et al. *JAMA.* 1995;273:808.

Modern (Third-Generation) TSH Assays

- Allow measurement of changes in serum TSH levels as small as 0.01 and 0.02 mU/L^{1,2}
- Virtually eliminate need for TRH testing¹
- Improve accuracy of titration of L-thyroxine therapy³

1. Stockigt JR. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:377.
2. Spencer CA et al. *J Clin Endocrinol Metab.* 1990;70:453.
3. Ross DS et al. *J Clin Endocrinol Metab.* 1990;71:764.

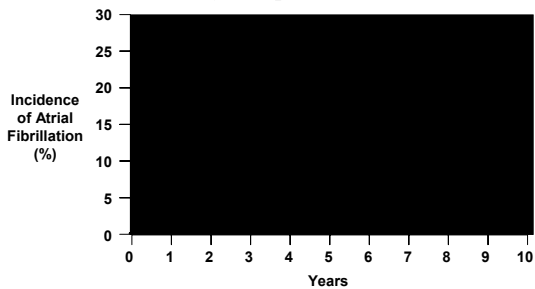
Follow-Up After 6 to 8 Weeks of L-Thyroxine Therapy

<i>TSH</i>	<i>Action</i>
HIGH	Increase daily L-thyroxine dose by 12.5-25 µg/d
NORMAL (TSH =0.5-3.5 mIU/L)	Continue dose; repeat TSH in 6 months and then annually or if symptomatic
LOW	Decrease daily L-thyroxine dose by 12.5 to 25 µg/d and repeat in 6 to 8 weeks

Singer PA. *JAMA*. 1995;273:808.

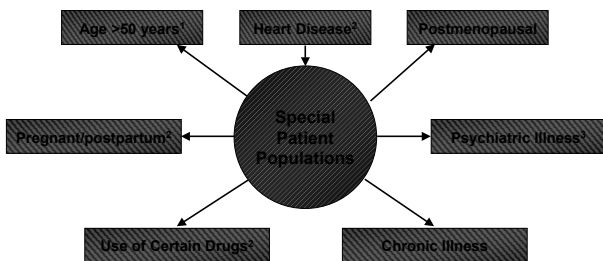
Cumulative Incidence of Atrial Fibrillation Among Subjects ≥60 Years of Age

Serum Thyrotropin Values at Baseline



Sawin CT et al. *New Engl J Med*. 1994;331:1249.

Management of Hypothyroidism: Special Patient Populations



- Singer PA et al. *JAMA*. 1995;273:808.
- Brent GA, Larsen PR. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:883.
- Whybrow PC. *AMA*. 1994;271:47.

L-Thyroxine Therapy: Compliance

- Can be problem for young, old, or depressed patients
- If poor compliance suspected
 - Measure TSH and FT4
(FT4 often normal with high TSH)
 - Review drug and diet regimens
 - Stress compliance benefits

Thyroid Rx for Normal Thyroid Function

- “Gilbert’s disease”
- LT4 used for weight loss in past
- LT4 therapy in patients with normal TFTs:
no improvement in well-being or cognitive functioning
with; no change
(BMJ 2001;323:891-5)
- LT4 may be used for suppressive therapy in selected cases

Controversial and/or Inappropriate Uses of Thyroid Hormone

- Uninodular and multinodular nontoxic goiter
- Prevent recurrence of nodules after thyroidectomy
- Rapid cycling bipolar depression with normal thyroid function tests
- Potentiate action of tricyclic drugs in depression
- Respiratory distress syndrome
- Hypothyroid fetus: dose and route controversial

- Chronic fatigue with normal thyroid function tests
- Obesity with normal thyroid function tests
- Hypercholesterolemia with normal thyroid function tests
- Severe systemic illness
- Premenstrual syndrome
- Treatment of infertility

Combined T3 and T4 Therapy for Hypothyroidism?

Bunevicius R, Kazanavicius G, Zalinevicius R, Prange AJ. Effects of thyroxine as compared with thyroxine plus triiodothyronine in patients with hypothyroidism. *NEJM* 1999; 340: 424-9.

- A ten-week crossover trial of LT4 vs. LT4/LT3 was performed in 33 patients with autoimmune thyroiditis or thyroid CA.
- Serum TSH was similar with both treatments, but mood and cognitive scores were better with combination therapy than with LT4 alone.
- POMS (mood) scores for fatigue, depression, and anger-hostility improved on combination therapy as did cognitive scores of pair recall and digit span.
- slight increase in pulse rate with elevated BP was noted while LT3/LT4 combination therapy was given.
- **AUTHORS' CONCLUSION:** "In patients with hypothyroidism, partial substitution of triiodothyronine for thyroxine may improve mood and neuropsychological function...."

Combined T3 and T4 Therapy for Hypothyroidism?

Clyde PW, et al. *JAMA* 2003;290:2952-58.

- Randomized, double-blind, placebo-controlled trial of T4 or T4 plus T3
- TSH levels were similar in both groups on Rx and remained normal during the study
- "...no beneficial changes in body weight, serum lipid levels, hypothyroid symptoms.....and standard measures of cognitive performance."

Why Treat Patients With Mild Thyroid Failure With L-Thyroxine?

- Prevent progression to overt hypothyroidism¹
- Alleviate symptoms^{1,2}
- Normalize serum lipids^{1,3}
- Normalize cardiac function^{2,4}
- May help depression⁵

1. Ayala AR, Wartofsky L. *The Endocrinologist*. 1997;7:44.
2. Cooper DS et al. *Ann Intern Med*. 1984;101:18.
3. Kinlaw WB. *Thyroid Today*. 1991;14:1.
4. Nystrom E et al. *Clin Endocrinol*. 1988;29:63.
5. Hennessey JU, Jackson IMD. *The Endocrinologist*. 1996;18:214.

Causes of Mild Thyroid Failure

- Autoimmune thyroiditis
- Treatment of Graves' hyperthyroidism
- Lithium carbonate therapy
- Iodide and iodide-containing medications
- External radiotherapy to the neck

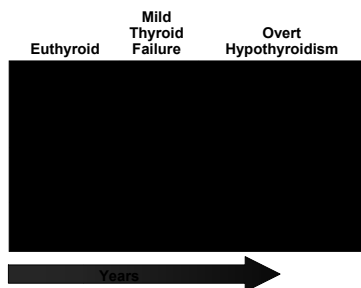
Ross DS. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1010.

Diagnosing Mild Thyroid Failure: The Challenge

- Insidious onset
- Patients often have few specific clinical symptoms or signs
- Symptoms are ordinary and nonspecific
- Specific age- and gender-related presentations

Ladenson PW. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:878.

Progression of Mild Thyroid Failure



Adapted from Ayala AR, Wartofsky L. *The Endocrinologist*. 1997;7:44.

When to Suspect Mild Thyroid Failure

- Hypercholesterolemia^{1,2}
- Refractory depression²
- Previous episode of postpartum thyroiditis²
- Goiter¹
- Family or personal history of thyroid disease¹
- Over 40 with nonspecific complaints²
- Insidious weight change
- Unexplained infertility²
- Overweight

1. Ayala AR, Wartofsky L. *The Endocrinologist*. 1997;44:401.
2. Weetman, AP. *British Journal Med*. 1997;314:1175.

When Should Mild Thyroid Failure Be Treated?

Case finding
to detect and treat
mild thyroid failure*

VERSUS

Managing symptoms
until overt disease
develops

*Defined as TSH ≥ 5.0 to 10 mU/L, normal FT₄ and FT₃.

Treatment of Mild Thyroid Failure

- Goal: normalize TSH level¹
- Starting dose may range from 12.5 $\mu\text{g/day}$ to full replacement dose²
- Reassess TSH after 6 to 8 weeks³
- If lipids are elevated, recheck when euthyroid⁴
- Euthyroid status may require 8 to 16 weeks to achieve²

1. Brent GA, Larsen PR. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:883.
2. AACE. *Endocrine Pract*. 1995;1:56.
3. Singer PA. *JAMA*. 1995;273:808.
4. De Groot LJ et al. *The Thyroid and Its Diseases*. 1996.

Effect of L-Thyroxine Therapy on Hypercholesterolemia in Patients With Mild Thyroid Failure

“The decrease in total cholesterol achieved with [L-thyroxine replacement] substitution therapy in patients with subclinical hypothyroidism [mild thyroid failure] may be considered as an important decrease in cardiovascular risk favoring treatment.”

Tanis BC et al. *Clin Endocrinol*. 1996;44:643.

Clinical Symptoms of Hyperthyroidism

- Appetite change
- Exertional shortness of breath
- Fatigue
- Headache
- Heat intolerance
- Hyperactivity
- Increased perspiration
- Irritability
- Menstrual disturbances
- Nervousness
- Palpitations
- Pelvic and pectoral girdle muscle weakness
- Sleep disturbance
- Tremor
- Weakness
- Weight change

Braverman LE, Utiger RD. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:522.

Clinical Signs of Hyperthyroidism

- Goiter
- Hyperactivity
- Hyperreflexia
- Muscle weakness
- Ophthalmopathy (only Graves' disease)
- Stare and eyelid retraction
- Systolic hypertension
- Tachycardia/atrial arrhythmia
- Tremor
- Warm, moist, smooth skin



Braverman LE, Utiger RD. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:522.

Subclinical Hyperthyroidism: Definition and Prevalence

- Usually asymptomatic¹
- Low or undetectable serum TSH¹
- Normal or borderline serum FT₄ and FT₃¹
- Variable prevalence (0.7% to 6.0%)²
- More common in women³
- More common in older people than overt hyperthyroidism⁴
- Most common cause is overtreatment with L-thyroxine

1. Ross DS. *Mayo Clin Proc.* 1988;63:1223. 2. Ross DS. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1016.
3. Sawin CT. *Adv Intern Med.* 1991;37:223. 4. Sawin CT et al. *N Engl J Med.* 1994;331:1249.

Common Causes of Subclinical Hyperthyroidism

Exogenous

- Excessive thyroid hormone replacement
- Thyroid hormone suppressive therapy

Endogenous

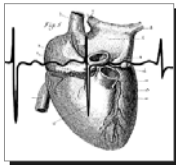
- Thyroid gland autonomy: thyroid adenoma or multinodular goiter
- Graves' disease

Ross DS. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1016.

Physiological Effects of Subclinical Hyperthyroidism



- ↓ bone density
- ↑ serum osteocalcin
- ↑ urinary hydroxyproline and pyrrolidine links



- ↑ heart rate
- ↑ risk of atrial fibrillation
- ↑ cardiac contractility²
- ↑ LV mass index
- ↑ intraventricular septal and posterior wall thickness

1. Ross DS. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1016.
2. Biondi B et al. *J Clin Endocrinol.* 1993;77:334.

Other Biological Effects of Subclinical Hyperthyroidism

Total and LDL cholesterol	↓
Liver enzymes	↑
Creatine kinase	↓
Sex hormone binding globulin	↑
Time asleep at night	↓
Mood (using multidimensional scale for state of well-being)	↑

Ross DS. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1016

Prevention and Treatment of Subclinical Hyperthyroidism

Endogenous

- Because low TSH is often transient, careful monitoring is needed
- Consider antithyroid drug treatment or radioiodine therapy (depending on etiology)

Exogenous

- Careful titration of L-thyroxine to maintain normal TSH
- Use smallest L-thyroxine dose needed to meet therapeutic goals

Ross DS. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1016.

Hypothyroidism in Pregnancy

- Often associated with infertility because of ovulatory disturbance¹
- Prevalence of 2.5%²
- Associated with increased risk of obstetrical complications²
- Women with positive thyroid antibodies are at risk for spontaneous miscarriage²



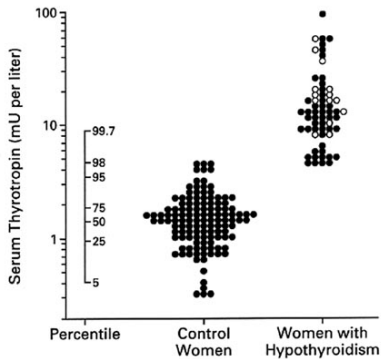
1. Grodstein F et al. *Epidemiology*. 1993;4:151.
2. Glinoe D. *Endocr Rev*. 1997;18:404.

Hypothyroidism and Pregnancy

Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *NEJM* 1999;341: 549-555.

- **SUMMARY:** Population-based study of 25,000 pregnant women screened; 62 had high TSH and 48 were untreated during the pregnancy.
- Children of these women performed slightly less well on all 15 tests of intelligence, attention, language, reading ability, school performance, and visual-motor performance.
- Full-scale IQ scores of the children of untreated women averaged 7 points less than matched control children.
- **AUTHORS' CONCLUSION:** "Undiagnosed hypothyroidism in pregnant women may adversely affect their fetuses; therefore screening for thyroid deficiency during pregnancy may be warranted."





Haddow JE, Palomaki GE, Allan WC, et al. *NEJM* 1999;341: 549-555.

Hypothyroidism in Pregnancy May Be Difficult to Diagnose

- Signs and symptoms (weight gain, fatigue) can overlap with common pregnancy complaints¹
- Among pregnant hypothyroid patients^{2,3}
 - one third have few or no symptoms
 - one third have moderate symptoms
 - one third have classical presentation of hypothyroidism



1. DeGroot LJ et al. *The Thyroid and Its Diseases*. 1996: chap 14.
2. Montoro MN. *Ann Intern Med*. 1981;94:31.
3. Leung AS et al. *Obstet Gynecol*. 1993;81:349.

Risk Factors for Hypothyroidism in Pregnant Women

- Previous therapy for hyperthyroidism
- Previous postpartum thyroiditis
- Goiter
- Family history of thyroid disease
- Type 1 diabetes mellitus
- Autoimmune disorder
- Hyperlipidemia
- Previous high-dose external neck irradiation

Montoro MN. *Clin Obstet Gynecol.* 1997;40:65.



Changes in Thyroid Function Tests During Pregnancy¹

Test	Change
TSH	No change*
Total T ₄	Increased
Free T ₄	No change
Total T ₃	Increased
Free T ₃	No change
Thyroglobulin	Increased
Thyroid hormone binding ratio (T ₃ -resin uptake)	Decreased
TPOAb	May become detectable ²

*May decrease in first trimester.

1. Emerson CH. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1021.
 2. Montoro MN. *Clin Obstet Gynecol.* 1997;40:65.



Possible Consequences of Hypothyroidism in Pregnancy

- Miscarriage¹⁻³
- Gestational hypertension³
- Preterm delivery¹
- Anemia³
- Placental abruption/postpartum hemorrhage³
- Fetal complications³

1. Montoro MN. *Clin Obstet Gynecol.* 1997;40:65.
 2. Glinoeer D. *Endocr Rev.* 1997;18:404.
 3. Roti E et al. *J Clin Endocrinol Metab.* 1996;81:1679.



Treatment of Hypothyroidism in Pregnancy

- Goal: normalize TSH level¹
- Women with established hypothyroidism often require L-thyroxine dose increase²
- L-thyroxine dose adjustment should occur in early pregnancy²
- Regular clinical and laboratory follow-up is essential²



1. Montoro MN. *Clin Obstet Gynecol.* 1997;40:65.
2. Glinoeer D. *Endocr Rev.* 1997;18:404.

Postpartum Thyroiditis (PPT)

Definition

- Occurrence of hyperthyroidism and/or hypothyroidism during the postpartum period in women who were euthyroid during pregnancy

Prevalence

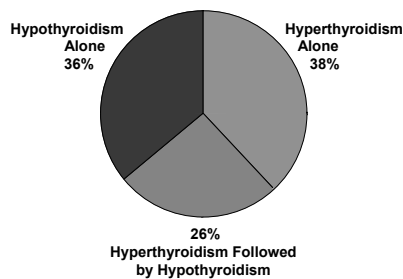
- Approximately 8% in the US

At Highest Risk

- Patients with type 1 diabetes, previous history of PPT or other autoimmune diseases such as Hashimoto's disease and Graves' disease

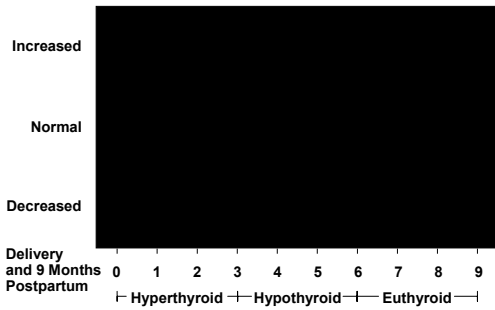
Stagnaro-Green A. *Thyroid Today.* 1993;16:1.

Biochemical Presentation of PPT*



*Based on 287 cases in 11 prospective studies from 1982-1992.
Stagnaro-Green A. *Thyroid Today.* 1993;16:1.

Clinical Course of Silent, Postpartum, and Subacute Thyroiditis



Treatment of Postpartum Hypothyroidism

- Symptomatic women require treatment with L-thyroxine¹
- Goal: Normalize TSH level²
- Close follow-up important because postpartum thyroid function is unstable²

1. Stagnaro-Green A. *Thyroid Today*. 1993;16:1.
2. Emerson CH. In: *Werner and Ingbar's The Thyroid*, 7th ed. 1996:1021.
