THYROID DISEASE:
WHEN TO TREAT, AND HOW

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OUTLINE OF TALK

(1) INTRODUCTION

(2) GOITRE / THYROID NODULES

(3) HYPOTHYROIDISM

- PRIMARY HYPOTHYROIDISM
- SUBCLINICAL HYPOTHYROIDISM
- IN PREGNANCY
- IN THE ELDERLY
- MYXOEDEMA COMA

OUTLINE OF TALK (CONT)

(4) HYPERTHYROIDISM

- PRIMARY HYPERTHYROIDISM
- IN PREGNANCY
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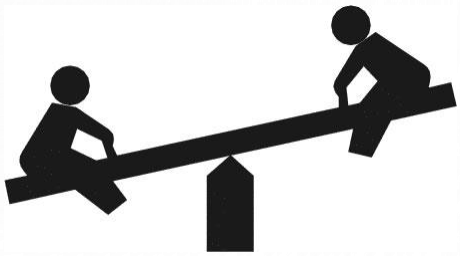
(1) INTRODUCTION

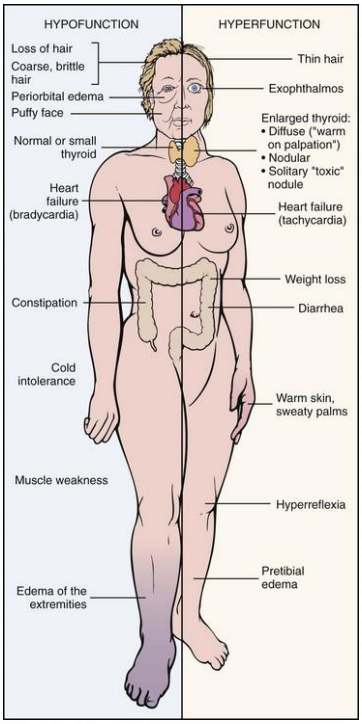
- IN COMMUNITY SURVEYS, HIGH SERUM ANTITHYROID PEROXIDASE ANTIBODY CONCENTRATIONS ARE FOUND IN APPROXIMATELY 5 % OF ADULTS AND APPROXIMATELY 15 % OF OLDER WOMEN (UNITED STATES NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES III): 11%)
- THE FREQUENCY OF SUBCLINICAL HYPOTHYROIDISM IS ABOUT 5% AND THAT OF OVERT HYPOTHYROIDISM VARIES FROM 0.1 TO 2 %
- NHANES: HYPOTHYROIDISM WAS FOUND IN 4.6 % (0.3 % OVERT AND 4.3 % SUBCLINICAL)

- NHANES: HYPERTHYROIDISM WAS FOUND IN 1.3 % (0.5 % OVERT AND 0.7 % SUBCLINICAL)
- IN ONE POPULATION-BASED STUDY, THE OVERALL INCIDENCE OF AUTOIMMUNE THYROIDITIS WAS 46.4 PER 1000 SUBJECTS DURING A 20-YEAR PERIOD
- HYPOTHYROIDISM IS MUCH (5 – 8 X) MORE COMMON IN WOMEN THAN MEN

THYROID DISEASE (CONT)

- **HYPOTHYROIDISM:**
  - UNDERACTIVE THYROID
  - LOW T4; HIGH TSH
- **HYPERTHYROIDISM:**
  - OVERACTIVE THYROID
  - HIGH T4; LOW TSH
- **SUBCLINICAL "MILD" HYPOTHYROIDISM:**
  - NORMAL T4; ELEVATED TSH
- **SUBCLINICAL "MILD" HYPERTHYROIDISM:**
  - NORMAL T4; SUPPRESSED TSH





- 68-YEAR-OLD FEMALE
- HUSBAND NOTICED A "SWELLING IN HER NECK"
- HYPERTENSION X 10 YEARS
- BREAST CANCER 12 YEARS AGO: RECEIVED CHEMO- AND RADIOTHERAPY; NOW IN REMISSION
- NO OTHER PAST MEDICAL HISTORY OF NOTE

ON SYSTEMIC ENQUIRY:

- NO DYSPHAGIA
- NO SYMPTOMS SUGGESTIVE OF HYPERTHYROIDISM OR HYPOTHYROIDISM

(2) GOITRE
THYROID NODULES

- PALPABLE THYROID ENLARGEMENT IS COMMON: OCCURS IN 5% OF THE POPULATION
- COINCIDENTAL FINDING / RELATIVE NOTICES A LUMP IN THE NECK
- SOMETIMES PRESENTS WITH ACUTE PAINFUL ENLARGEMENT DUE TO HAEMORRHAGE INTO A NODULE
- PROPER EXAMINATION OF THE THYROID CAN DISTINGUISH BETWEEN THE DIFFERENT GROUPS OF ENLARGEMENT
- SHOULD ALWAYS DO THYROID FUNCTION TESTS IF THE THYROID IS ENLARGED

THYROID ENLARGEMENT

3 MAIN GROUPS OF CAUSES:

- DIFFUSE GOITRE
- MULTINODULAR GOITRE
- SOLITARY THYROID NODULE

CAUSES OF THYROID ENLARGEMENT

Diffuse goitre	
Simple goitre	Dyshormogenesis
Hashimoto's thyroiditis	Infiltrative
Graves' disease	- amyloidosis, sarcoidosis
Iodine deficiency (endemic goitre)	Riedel's thyroiditis
Suppurative thyroiditis	Drugs
Transient thyroiditis	- iodine, amiodarone, lithium
Multinodular goitre	
Solitary nodule	
Simple cyst	Medullary cell carcinoma
Colloid nodule	Anaplastic carcinoma
Follicular adenoma	Lymphoma
Papillary carcinoma	Metastasis
Follicular carcinoma	

SIMPLE DIFFUSE GOITRE

- USUALLY PRESENTS BETWEEN THE AGES OF 15-25 YEARS, OFTEN DURING PREGNANCY
- USUALLY NOTICED BY FAMILY / FRIENDS
- OCCASIONALLY TIGHT SENSATION IN THE NECK, ESPECIALLY WHEN SWALLOWING
- GOITRE IS SOFT, SYMMETRICAL, 2-3 TIMES ITS NORMAL SIZE
- NO TENDERNESS, LYMPHADENOPATHY, OR OVERLYING BRUIT
- T3, T4, TSH NORMAL
- NEGATIVE THYROID ANTIBODIES

IN THE ABSENCE OF HYPERTHYROIDISM OR HYPOTHYROIDISM A DIFFUSE GOITRE RARELY NEEDS FURTHER INVESTIGATION OR TREATMENT UNLESS:

- VERY LARGE
- COSMETIC SYMPTOMS
- COMPRESSION OF OTHER LOCAL STRUCTURES
  - STRIDOR
  - DYSPHAGIA
- IN MOST CASES THE GOITRE REGRESSES
- IN SOME CASES IT DEVELOPS OVER MANY YEARS INTO A MULTINODULAR GOITRE
- PRESENCE OF AUTOANTIBODIES MAY SUPPORT GRAVES' DISEASE OR HASHIMOTO'S THYROIDITIS

MULTINODULAR GOITRE

- PATIENTS WITH SIMPLE GOITRE MAY PROGRESS TO DEVELOP NODULES
- THESE NODULES GROW AT VARYING RATES AND SECRETE THYROID HORMONE AUTONOMOUSLY
- COMPLETE SUPPRESSION OF TSH OCCURS IN 25% OF CASES, WITH T3 AND T4 OFTEN NORMAL (SUBCLINICAL HYPERTHYROIDISM) OR SOMETIMES ELEVATED (TOXIC MULTINODULAR GOITRE)
- USUALLY BENIGN CONDITION

- USUALLY DIAGNOSED IN PATIENTS PRESENTING WITH THYROTOXICOSIS, A LARGE GOITRE WITH OR WITHOUT TRACHEAL COMPRESSION, OR SUDDEN PAINFUL SWELLING CAUSED BY HAEMORRHAGE INTO A NODULE OR CYST
- GOITRE IS NODULAR ON PALPATION AND MAY EXTEND RETROSTERNALLY
- VERY LARGE GOITRES MAY CAUSE MEDIASTINAL COMPRESSION WITH STRIDOR, DYSPHAGIA, SUPERIOR VENA CAVA OBSTRUCTION
- HOARSENESS DUE TO RECURRENT LARYNGEAL NERVE PALSY CAN OCCUR, BUT IS MORE SUGGESTIVE OF A MALIGNANCY

- USUALLY NECESSARY TO CONFIRM THE CLINICAL DIAGNOSIS WITH ULTRASONOGRAPHY AND A RADIOISOTOPE THYROID SCAN
- SOMETIMES ONE OF THE NODULES IS MUCH LARGER THAN ANY OTHER (A 'DOMINANT' NODULE)
- IF SUCH A NODULE IS 'COLD' ON ISOTOPE SCANNING, IT HAS AN INCREASED RISK OF MALIGNANCY: FNA IS THEN INDICATED

MANAGEMENT

- IF THE GOITRE IS SMALL: NO TREATMENT NECESSARY BUT CHECK YEARLY THE THYROID FUNCTION TESTS
- ^{131}I THERAPY IS USUALLY 1ST LINE THERAPY FOR TOXIC MULTINODULAR GOITRE (ALSO FOR SUBCLINICAL THYROTOXICOSIS)
- ^{131}I CAN RESULT IN SIGNIFICANT DECREASE IN THYROID SIZE
- PARTIAL THYROIDECTOMY CAN BE PERFORMED FOR LARGE GOITRES WITH COMPRESSION / COSMETICALLY UNATTRACTIVE / TOXIC MULTINODULAR GOITRE
- THYROXINE THERAPY IS OF NO BENEFIT TO SHRINK THE MULTINODULAR GOITRE

SOLITARY THYROID NODULE

- THYROID NODULES CAN BE PALPATED IN 4 - 7 % OF ADULTS
- ARE FOUND INCIDENTALLY IN UP TO 40 % OF PATIENTS WHO UNDERGO ULTRASONOGRAPHY OF THE NECK
- FOUND IN 36 – 50 % OF PATIENTS AT AUTOPSY
- 20 – 76 % OF THE POPULATION HAS AT LEAST ONE THYROID NODULE
- IT IS **NB** TO DETERMINE WHETHER THE NODULE IS **BENIGN OR MALIGNANT** (4 – 6.5 % IN NON-SURGICAL SERIES)
- RARELY POSSIBLE TO MAKE THIS DISTINCTION ON CLINICAL GROUNDS ONLY

- PRESENCE OF CERVICAL LYMPHADENOPATHY INCREASES THE LIKELIHOOD OF MALIGNANCY
- PRESENTING IN CHILDHOOD OR ADOLESCENCE, ESPECIALLY IF PAST HISTORY OF HEAD / NECK IRRADIATION, OR IN THE ELDERLY: SUSPECT MALIGNANCY
- RARELY, METASTASIS FROM RENAL, BREAST, OR LUNG CARCINOMA CAN PRESENT AS PAINFUL, RAPIDLY GROWING SOLITARY THYROID NODULE

CAUSES OF THYROID NODULES

BENIGN

- MULTINODULAR GOITER
- HASHIMOTO'S THYROIDITIS
- CYSTS: COLLOID/SIMPLE/ HAEMORRHAGIC
- FOLLICULAR ADENOMAS
- HURTLE-CELL ADENOMAS

MALIGNANT

- PAPILLARY CARCINOMA
- FOLLICULAR CARCINOMA
- MEDULLARY CARCINOMA
- ANAPLASTIC CARCINOMA
- PRIMARY THYROID LYMPHOMA
- METASTATIC CANCER (BREAST, RENAL CELL, COLON, MELANOMA)

EVALUATION OF PATIENTS WITH THYROID NODULES

1. **HISTORY AND PHYSICAL EXAM**

- LOW ACCURACY FOR PREDICTING CANCER
- BUT, ⇧ LIKELIHOOD OF MALIGNANCY WITH:

➢CHILDHOOD HEAD + NECK IRRADIATION

➢TOTAL BODY IRRADIATION FOR BONE MARROW TRANSPLANT

➢FAMILY HISTORY OF THYROID CANCER

➢THYROID CANCER SYNDROMES (MEN2, FAMILIAL ADENOMATOUS POLYPOSIS, COWDEN SYNDROME)

PREVALENCE OF CANCER HIGHER IN:

- CHILDREN
- ADULTS <30YRS OR >60YRS
- RAPID GROWTH OF NECK MASS
- FIXED HARD MASS, OBSTRUCTIVE SYMPTOMS, CERVICAL LYMPHADENOPATHY, VOCAL CORD PARALYSIS: SUGGEST MALIGNANCY

2. SERUM TSH

- SERUM TSH, T4, T3 TO BE DONE IN ALL PATIENTS WITH A SOLITARY NODULE
- LOW TSH (OVERT/SUBCLINICAL HYPERTHYROIDISM): VERY SUGGESTIVE OF BENIGN AUTONOMOUSLY FUNCTIONING FOLLICULAR ADENOMA: CONFIRM WITH THYROID ISOTOPE SCANNING
- HIGH/NORMAL TSH: EVALUATION FOR HYPOTHYROIDISM, AND FNA IF CRITERIA FOR SAMPLING MET

3. THYROID ULTRASOUND

- TO BE PERFORMED IN ALL PATIENTS WITH THYROID NODULES: MORE ANATOMIC DETAIL THAN SCINTIGRAPHY/ CT / PHYSICAL EXAM
- USED TO SELECT PATIENTS FOR FNA
- CAN IDENTIFY POSTERIOR/ PREDOMINANTLY CYSTIC NODULES

ULTRASOUND FEATURES ASSOCIATED WITH THYROID CANCER RISK

INCREASED RISK FOR CANCER

- HYPO ECHOIC
- MICRO CALCIFICATIONS
- CENTRAL VASCULARITY
- IRREGULAR MARGINS
- INCOMPLETE HALO
- NODULE TALLER THAN WIDE
- DOCUMENTED ENLARGEMENT OF THYROID
- "TWINKLING" ON B-FLOW IMAGING

LOW RISK FOR CANCER

- HYPER ECHOIC
- LARGE, COARSE CALCIFICATIONS (EXCEPT MEDULLARY CARCINOMA)
- PERIPHERAL VASCULARITY
- SPONGIFORM APPEARANCE
- COMET-TAIL SHADOWING
- RESEMBLES PUFF PASTRY

4. THYROID SCINTIGRAPHY

- USED TO SELECT NODES FOR FNA
- NOT USED TO SELECT PATIENTS FOR SURGICAL RESECTION
- RADIOISOTOPES: ^{123}IODINE (PREFERRED) OR TECHNETIUM-99M PERTECNETATE
- DETERMINE THE FUNCTIONAL STATUS OF A NODULE

5. FINE NEEDLE ASPIRATION BIOPSY

- PROCEDURE OF CHOICE: EVALUATING THYROID NODULES AND SELECTING CANDIDATES FOR SURGERY
- INDICATED IN THYROID NODULES:

➢> 1CM, SOLID HYPO ECHOIC

➢≥ 1-1.5CM, SOLID ISOECHOIC OR HYPER ECHOIC

➢≥ 1.5-2CM, MIXED CYSTIC AND SOLID NODULES, WITH SUSPICIOUS ULTRASOUND FEATURES

➢≥ 2CM

FNA

- CYTOLOGICAL EXAMINATION CAN DIFFERENTIATE BENIGN (80%) FROM DEFINITELY MALIGNANT OR INDETERMINATE (20%) OF WHICH 25-50% ARE CONFIRMED AS CANCER AT SURGERY

LIMITATIONS:

- CAN'T DIFFERENTIATE BETWEEN FOLLICULAR ADENOMA AND CARCINOMA
- IN 10-20% OF CASES AN INADEQUATE SPECIMEN IS OBTAINED
- ULTRASOUND-GUIDED NEEDLE ASPIRATION CAN BE HELPFUL IN INCREASING THE QUALITY OF SPECIMENS

THERAPY

- SOLITARY NODULES WITH A SOLID COMPONENT IN WHICH CYTOLOGY IS INCONCLUSIVE OR SHOWS MALIGNANT CELLS ARE TREATED BY SURGICAL EXCISION
- BENIGN LESIONS: MAJORITY OF PATIENTS CAN BE REASSURED, NO THERAPY NECESSARY
- IF TOXIC (HYPERFUNCTIONING) NODULE: RADIOIODINE ABLATION

THYROID NEOPLASIA

BENIGN

- TOXIC FOLLICULAR ADENOMA

MALIGNANT

■ **DIFFERENTIATED CARCINOMAS:**

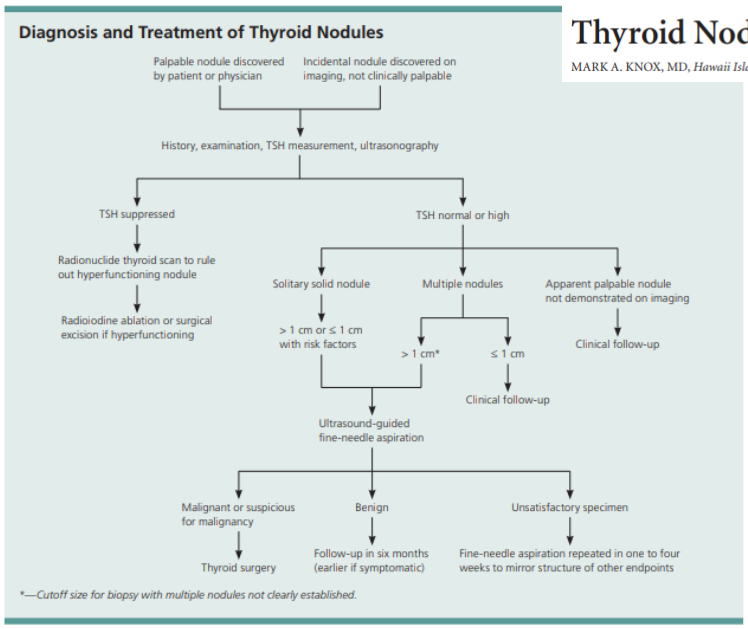
- PAPILLARY CARCINOMA
- FOLLICULAR CARCINOMA

■ **AGGRESSIVE CARCINOMAS:**

- MEDULLARY CARCINOMA
- ANAPLASTIC CARCINOMA

INDICATIONS FOR THYROIDECTOMY

- LARGE GOITRE
- PRESSURE SYMPTOMS (DYSPHAGIA, STRIDOR)
- COSMETIC REASONS
- POOR DRUG COMPLIANCE WITH ANTITHYROID THERAPY (IF HYPERTHYROID, AND CONTRAINDICATION FOR RADIOABLATION)
- SUSPECTED / CONFIRMED UNDERLYING MALIGNANCY
- 2ND TRIMESTER OF PREGNANCY IF HYPERTHYROID AND NOT RESPONDING TO MEDICAL THERAPY
- HYPERTHYROIDISM WITH CONTRAINDICATIONS FOR RADIOABLATION AND MEDICAL THERAPY



Thyroid Nodules

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Figure 1. Suggested diagnostic and treatment approach for thyroid nodules. (TSH = thyroid-stimulating hormone.)

Adapted with permission from Weiss RE, Lado-Abeal J. Thyroid nodules: diagnosis and therapy. Curr Opin Oncol. 2002;14(1):50.

(3) HYPOTHYROIDISM

- A 67-YEAR-OLD FEMALE PRESENTS WITH SLOWING OF MENTAL ACUITY, COLD INTOLERANCE, AND WEIGHT GAIN. ON EXAMINATION SHE HAS A RESTING HEART RATE OF 44/MINUTE, NON-PITTING OEDEMA OF HER LEGS, AND SHE APPEARS DEPRESSED AND LETHARGIC.

- **WHAT IS YOUR CLINICAL DIAGNOSIS?**
- POSSIBLE PRIMARY HYPOTHYROIDISM

WHAT OTHER INVESTIGATIONS WILL YOU REQUEST?

- TSH, FREE T4
- ANTI-TPO-ANTIBODIES

HOW WILL YOU CONFIRM THE DIAGNOSIS BIOCHEMICALLY?

- HIGH TSH
- LOW T4

WHAT IS THE ROLE OF THYROID ANTIBODIES IN A PATIENT WITH HYPOTHYROIDISM?

- TO DETERMINE WHETHER IT'S OF AUTOIMMUNE ORIGIN
- IF POSITIVE ANTI-TPO-ANTIBODIES (ANTI-THYRO-PEROXIDASE ANTIBODIES) POSITIVE: MOST LIKELY PAST HASHIMOTO'S THYROIDITIS
- ANTI-THYROGLOBULIN-ANTIBODIES LESS SPECIFIC
- IF AUTOIMMUNE, WATCH FOR OTHER ASSOCIATED AUTOIMMUNE DISEASES

HOW WILL YOU TREAT THE PATIENT?

- EUTHYROX / ELTROXIN (T4)
- IN THE ELDERLY OR PATIENTS WITH UNDERLYING IHD: "START LOW, GO SLOW": 12.5 - 25 MICROGRAM / DAY; CAN INCREASE AFTER 6 - 8 WEEKS AS DETERMINED BY TSH LEVELS
- YOUNGER / HEALTHY PATIENTS: CAN START WITH 75 - 125 MICROGRAM / DAY
- IN MYXOEDEMA COMA: LOAD WITH HIGH DOSE

Table 3. Levothyroxine Dosing Guidelines for Hypothyroidism in Adults

Population	*Dosing*
Nonpregnant patients	1.6 mcg per kg per day initial dosage[26]
Older patients; patients with known or suspected cardiac disease	25 or 50 mcg daily starting dosage; increase by 25 mcg every three to four weeks until full replacement dosage reached[19,20]
Pregnant patients	Increase to nine doses weekly (one extra dose on two days of the week) at earliest knowledge of pregnancy; refer to endocrinologist[21]
Patient with subclinical hypothyroidism	TSH < 10 mIU per L: 50 mcg daily, increase by 25 mcg daily every six weeks until TSH = 0.35 to 5.5 mIU per L TSH ≥ 10 mIU per L: 1.6 mcg per kg per day[26]

TSH = thyroid-stimulating hormone.

(*Am Fam Physician*. 2012;86(3):244-251. Copyright © 2012 American Academy of Family Physicians.)

Hypothyroidism: An Update

DAVID Y. GAITONDE, MD; KEVIN D. ROWLEY, DO; and LORI B. SWEENEY
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HOW WOULD YOU MONITOR A PATIENT RECEIVING THERAPY FOR HYPOTHYROIDISM?

- USUALLY WITH TSH ALONE
- WAIT 6 – 8 WEEKS BETWEEN DOSE ADJUSTMENTS BEFORE REPEATING TSH
- EXCEPTION: MYXOEDEMA COMA!
- DO THEN EVERY 1-2 DAYS A FREE T4, AND TITRATE DOSE UP ACCORDING TO THE T4 LEVEL (IT CAN TAKE WEEKS FOR THE TSH TO START GOING DOWN)

- AFTER RADIOABLATION FOR HYPERTHYROIDISM THE TSH CAN REMAIN SUPPRESSED FOR MONTHS
- ONCE THE PATIENT BECOMES HYPOTHYROID THE TSH CAN STILL BE LOW BUT THE T4 WILL ALSO BECOME LOW, AND THYROID HORMONE REPLACEMENT SHOULD BE STARTED

THE PATIENT STILL HAS PERSISTENT SYMPTOMS ON THERAPY?

Table 4. Alternative Causes of Persistent Symptoms in Patients with Normal-Range Thyroid-Stimulating Hormone Levels

- Adrenal insufficiency (rare)
- Anemia
  - B_{12} deficiency
  - Iron deficiency
- Chronic kidney disease
- Depression, anxiety disorder, and/or somatoform disorders
- Liver disease
- Obstructive sleep apnea
- Viral infection (e.g., mononucleosis, Lyme disease, human immunodeficiency virus/AIDS)
- Vitamin D deficiency

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COMBINATION T4 AND T3 THERAPY

- FOR THE VAST MAJORITY OF PATIENTS WITH HYPOTHYROIDISM, ALL GUIDELINES SUGGEST **NOT USING COMBINATION T4-T3 THERAPY**
- CONTROVERSY AROSE AS TO WHETHER T4 REPLACEMENT ALONE CAN MIMIC NORMAL PHYSIOLOGY
- T4 IS DEIODINATED IN PERIPHERAL TISSUES TO FORM T3, THE ACTIVE THYROID HORMONE
- SOME HYPOTHYROID PATIENTS REMAIN SYMPTOMATIC IN SPITE OF T4 REPLACEMENT AND NORMAL SERUM TSH CONCENTRATIONS
- IN A LARGE, COMMUNITY-BASED QUESTIONNAIRE STUDY OF PATIENTS TAKING T4 WHO HAD NORMAL SERUM TSH CONCENTRATIONS, 9 - 13 % MORE PATIENTS HAD IMPAIRED PSYCHOLOGICAL WELL-BEING AS COMPARED WITH NORMAL SUBJECTS

- THIS OBSERVATION RAISES THE QUESTION OF WHETHER HYPOTHYROID PATIENTS MIGHT BENEFIT FROM SUBSTITUTION OF SOME T3 FOR T4, AN IDEA THAT HAS NOW BEEN EVALUATED IN MULTIPLE RANDOMIZED TRIALS, ALMOST ALL OF WHICH SHOWED THAT COMBINATION T4-T3 THERAPY **DOES NOT APPEAR TO BE SUPERIOR** TO T4 MONOTHERAPY FOR THE MANAGEMENT OF HYPOTHYROID SYMPTOMS
- WELL-DESIGNED, BLINDED STUDIES ARE STILL NEEDED TO ADDRESS THIS ONGOING CONTROVERSY
- THE MAJORITY OF THE RANDOMIZED, CONTROLLED TRIALS USED EXCESSIVE AND NONPHYSIOLOGIC AMOUNTS OF T3 WHEN ASSESSING COMBINATION THERAPY
- IN ADDITION, A SLOW-RELEASE T3 PREPARATION, WHICH MAY AVOID SUPRAPHYSIOLOGIC PEAKS IN SERUM T3 CONCENTRATIONS, IS NOT YET COMMERCIALLY AVAILABLE

AMERICAN THYROID ASSOCIATION (ATA) GUIDELINES FOUND INSUFFICIENT EVIDENCE TO SUPPORT THE ROUTINE USE OF A COMBINATION OF T4 AND T3 THERAPY IN PATIENTS UNHAPPY WITH T4 MONOTHERAPY

- WHETHER A COMBINATION OF T4 AND T3 IS BENEFICIAL IN A SUBSET OF HYPOTHYROID PATIENTS HAS ALSO BEEN STUDIED
- ONE ANALYSIS SUGGESTED PATIENTS WITH A POLYMORPHISM IN THE TYPE 2 DEIODINASE, WHICH CONVERTS T4 TO T3, MIGHT BENEFIT
- CANDIDATES FOR COMBINED THERAPY INCLUDE PATIENTS WHO HAVE NOT FELT WELL ON T4 MONOTHERAPY:
  - SINCE THYROIDECTOMY
  - SINCE ABLATIVE THERAPY WITH RADIOIODINE, OR
  - WHO HAVE SERUM T3 AT OR BELOW THE LOWER END OF THE T3 REFERENCE RANGE
- PATIENTS WHO HAVE PREVIOUSLY FELT WELL ON T4 MONOTHERAPY BUT NOW FEEL POORLY ARE NOT LIKELY TO IMPROVE WITH COMBINED THERAPY

- IN ADDITION, THE USE OF COMBINED THERAPY IS DISCOURAGED IN OLDER PATIENTS, PATIENTS WITH UNDERLYING CARDIOVASCULAR DISEASE IN WHOM EXCESSIVE T3 LEVELS MIGHT PRECIPITATE AN ARRHYTHMIA, AND IN PREGNANT WOMEN
- FETAL NEUROGENESIS IS PRIMARILY DEPENDENT UPON MATERNAL FREE T4 CONCENTRATIONS UNTIL WEEK 16 TO 18 OF GESTATION
- REGIMENS CONTAINING EXCESSIVE T3 CAUSE HYPOTHYROXINAEMIA, WHICH HAS BEEN ASSOCIATED WITH IMPAIRED NEUROLOGIC DEVELOPMENT
- TEMPORARY TREATMENT WITH T3 MONOTHERAPY IS APPROPRIATE IN PATIENTS WITH THYROID CANCER WHO ARE TO UNDERGO RADIOIODINE IMAGING AND POSSIBLE TREATMENT
- TO SHORTEN THE PERIOD OF HYPOTHYROIDISM, THE PATIENT'S T4 THERAPY IS DISCONTINUED, AND T3 IS SUBSTITUTED FOR THREE TO FOUR WEEKS UNTIL THE T4 IS CLEARED

ABNORMAL TSH LEVELS ON A PREVIOUS STABLE DOSAGE?

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(*Am Fam Physician*. 2012;86(3):244-251.

Table 5. Common Reasons for Abnormal TSH Levels on a Previously Stable Dosage of Thyroid Hormone

Patient nonadherent to thyroid hormone regimen (missing doses)
Decreased absorption of thyroid hormone
Patient is now taking thyroid hormone with food
Patient takes thyroid hormone within four hours of calcium, iron, soy products, or aluminum-containing antacids
Patient is prescribed medication that decreases absorption of thyroid hormone, such as cholestyramine (Questran), colestipol (Colestid), orlistat (Xenical), or sucralfate (Carafate)
Patient is now pregnant or recently started or stopped estrogen-containing oral contraceptive or hormone therapy
Generic substitution for brand name or vice versa, or substitution of one generic formulation for another[25]
Patient started on sertraline (Zoloft), another selective serotonin reuptake inhibitor, or a tricyclic antidepressant[31]
Patient started on carbamazepine (Tegretol) or phenytoin (Dilantin)

NOTE: *Reasons are sorted by the clinically most important cause.*

TSH = thyroid-stimulating hormone.

WHEN TO RATHER REFER? (SPECIALIST PHYSICIAN +- ENDOCRINOLOGIST)

Table 6. Reasons for Endocrinology Consultation in Patients with Hypothyroidism

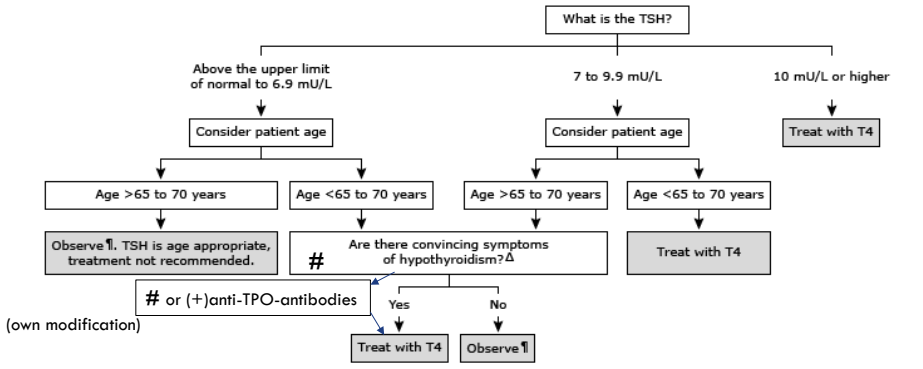
Age younger than 18 years	Presence of goiter, nodule, or other structural thyroid gland abnormality
Cardiac disease	Unresponsive to therapy
Coexisting endocrine diseases	
Myxedema coma suspected	
Pregnancy	

SUBCLINICAL HYPOTHYROIDISM

- SUBCLINICAL HYPOTHYROIDISM IS DEFINED BIOCHEMICALLY AS A NORMAL SERUM FREE THYROXINE (T4) CONCENTRATION IN THE PRESENCE OF AN ELEVATED SERUM THYROID-STIMULATING HORMONE (TSH) CONCENTRATION
- SOME PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM MAY HAVE VAGUE, NONSPECIFIC SYMPTOMS SUGGESTIVE OF HYPOTHYROIDISM, BUT ATTEMPTS TO IDENTIFY PATIENTS CLINICALLY HAVE NOT BEEN SUCCESSFUL
- THUS, THIS DISORDER CAN ONLY BE DIAGNOSED ON THE BASIS OF LABORATORY TEST RESULTS

- THE PREVALENCE IS DETERMINED BY THE UPPER LIMIT OF NORMAL FOR SERUM TSH
- IF THE UPPER LIMIT OF NORMAL RISES WITH AGE, AS APPEARS TO BE THE CASE, THEN THE PREVALENCE MAY NOT BE AS HIGH AS HAS BEEN PREVIOUSLY THOUGHT
- THE CAUSES OF SUBCLINICAL HYPOTHYROIDISM ARE THE SAME AS THOSE OF OVERT HYPOTHYROIDISM
- NB: ALWAYS FIRST REPEAT THE TFT IN 6 – 8 WEEKS TIME!
- OFTEN ELEVATED TSH DURING RECOVERY FROM EUTHYROID SICK SYNDROME (RARELY EVEN AS HIGH AS 20)

Indications for thyroid hormone replacement in nonpregnant adults with subclinical hypothyroidism*



(own modification)

TSH: thyroid-stimulating hormone; T4: levothyroxine; free T4: free thyroxine.
* Subclinical hypothyroidism is defined by a TSH above the normal reference range with a normal free T4, confirmed with repeat measurement.
¶ For patients not treated with T4, monitor TSH and free T4 initially at six months and, if stable, yearly thereafter.
Δ Convincing symptoms of hypothyroidism (new or worsening fatigue, constipation, cold intolerance) or growing goiter.

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Subclinical hypothyroidism in nonpregnant adults
Author:Douglas S Ross, MD Section Editor:David S Cooper, MD Deputy Editor:Jean E Mulder, MD
Literature review current through: Jul 2018. | This topic last updated: Apr 13, 2017

HYPOTHYROIDISM IN PREGNANCY

- A 32-YEAR-OLD WOMAN WITH HYPOTHYROIDISM DUE TO PAST GRAVES' DISEASE INFORMS YOU THAT SHE'S TRYING TO CONCEIVE. SHE'S ON EUTHYROX 100 MICROGRAM PER DAY. HER CURRENT TSH IS 2.5 MIU/L (0.5-5.00), AND HER T4 IS 15.1 PMOL/L (NORMAL: 11 – 22).

WHAT SHOULD SHE DO WITH HER EUTHYROX DOSE ON CONFIRMATION OF PREGNANCY, WHILE AWAITING HER FIRST ANTENATAL CONSULTATION?

- HYPOTHYROID WOMEN WHO ARE NEWLY PREGNANT SHOULD PRE-EMPTIVELY **INCREASE THEIR LEVOTHYROXINE DOSE BY APPROXIMATELY 30 PERCENT** AND NOTIFY THEIR CLINICIAN PROMPTLY
- CAN ACCOMPLISH THIS BY INCREASING THE DOSE FROM ONCE-DAILY DOSING TO A TOTAL OF **NINE DOSES PER WEEK** (DOUBLE THE DAILY DOSE TWO DAYS EACH WEEK)

- **EXCEPT FOR THE TFT, WHICH OTHER BLOOD TEST SHOULD BE REQUESTED DURING PREGNANCY WITH REGARDS TO HER PAST HISTORY, AND WHY?**
  - TSH-RECEPTOR ANTIBODIES
  - IF HIGH, THE BABY CAN DEVELOP INTRA-UTERINE/NEONATAL GRAVES' DISEASE
- **WHAT ARE THE TRIMESTER-SPECIFIC TSH TARGETS?**
- THE GOAL PRECONCEPTION SERUM TSH LEVEL IS BETWEEN THE LOWER REFERENCE LIMIT AND 2.5 MU/L (THUS ALSO FOR 1ST AND 2ND TRIMESTER)
- THE GOAL IS TO MAINTAIN TSH IN THE LOWER HALF OF THE TRIMESTER-SPECIFIC REFERENCE RANGE

- IF THE LABORATORY DOES NOT PROVIDE TRIMESTER-SPECIFIC REFERENCE RANGES FOR TSH (MU/L), THE FOLLOWING REFERENCE RANGES CAN BE USED:

THYROID DISEASE IN THE ELDERLY

- THE PREVALENCE OF THYROID DISEASE IN THE ELDERLY IS TWICE THAT IN YOUNGER PEOPLE
- **HYPOTHYROIDISM:** 2-7%; **HYPERTHYROIDISM:** 2%
- UP TO 9% OF HOSPITALIZED ELDERLY PATIENTS HAVE OVERT THYROID DISEASE
- **SUBCLINICAL HYPOTHYROIDISM:** 6-13% IN THE ELDERLY
- **SUBCLINICAL HYPERTHYROIDISM:** 2%

HYPOTHYROIDISM IN THE ELDERLY

- HYPOTHYROIDISM IN THE ELDERLY **MOST LIKELY DUE TO PAST:**
  - HASHIMOTO'S THYROIDITIS
  - THYROIDECTOMY
  - RADIOACTIVE IODINE ABLATION
- RISK OF DEVELOPING HYPOTHYROIDISM IS INCREASED IF POSITIVE SERUM ANTITHYROID ANTIBODIES

SYMPTOMS / SIGNS

- CAN **EASILY OVERLOOK** HYPOTHYROIDISM IN AN OLDER PATIENT; SYMPTOMS **NONSPECIFIC** AND COMMON IN OLDER PEOPLE (EG COLD INTOLERANCE, POOR APPETITE)
- MORE LIKELY THAN YOUNGER PATIENTS TO PRESENT WITH **CARDIOVASCULAR SYMPTOMS** (CCF, ANGINA)
- MORE OFTEN **NEUROLOGIC FINDINGS** (COGNITIVE IMPAIRMENT, CONFUSION, DEPRESSION, PSYCHOSIS, COMA)
- PHYSICAL FINDINGS OFTEN **NONSPECIFIC**
- PUFFY FACE, DELAYED DEEP TENDON REFLEXES, MYXOEDEMA SUPPORT DIAGNOSIS

THERAPY

- **DOSES** OF THYROID HORMONE REQUIRED **DECREASE** WITH AGE ("START LOW, GO SLOW")
- ELDERLY PATIENTS SHOULD BE STARTED ON 25-50 MICROGRAM PER DAY OF **LEVOTHYROXINE** (EVEN LOWER DOSES IF ISCHAEMIC HEART DISEASE IS PRESENT)
- DOSE SHOULD BE INCREASED BY 25 MICROGRAM EVERY 4-6 WEEKS UNTIL THE TSH IS WITHIN THE NORMAL LIMIT (SLOWER INCREASE IF IHD)
- AVOID T3; CAN BE CARDIOTOXIC

- ON AVERAGE, THE **DOSE** OF LEVOTHYROXINE IS 1 MICROGRAM/KG/D IN THE ELDERLY COMPARED TO1.7 MICROGRAM/KG/D IN YOUNGER PATIENTS
- THE **METABOLIC CLEARANCE OF OTHER DRUGS** IS DECREASED IN HYPOTHYROIDISM; THE DOSES OF THESE DRUGS MAY HAVE TO BE INCREASED ASHYPOTHYROIDISM IS TREATED

- **UNSURE** WHETHER TREATING **SUBCLINICAL** HYPOTHYROIDISM IN THE ELDERLY IS BENEFICIAL
- FOLLOW THEM UP CAREFULLY FOR DISEASE PROGRESSION, ESPECIALLY IF POSITIVE ANTIBODIES OR PAST RADIOABLATION

MYXOEDEMA COMA

- 3 MAIN CLINICAL FEATURES:
  - ALTERED MENTAL STATE
    - RANGE FROM POOR COGNITIVE FUNCTION TO PSYCHOSIS TO COMA
  - HYPOTHERMIA OR ABSENCE OF FEVER (EG WITH INFECTION)
  - PRESENCE OF A PRECIPITATING EVENT
- SIGNS OF INFECTION CAN BE MASKED
- EVEN WITH PROMPT RECOGNITION AND TREATMENT MORTALITY IS 20%

NEUROLOGIC MANIFESTATIONS

- DESPITE THE NAME, PATIENTS FREQUENTLY DO NOT PRESENT IN COMA, BUT MANIFEST VARYING DEGREES OF ALTERED CONSCIOUSNESS
- USUALLY TAKES THE FORM OF CONFUSION WITH LETHARGY AND OBTUNDATION
- ALTERNATIVELY, A MORE ACTIVATED PRESENTATION MAY OCCUR WITH PROMINENT PSYCHOTIC FEATURES, SO-CALLED MYXOEDEMA MADNESS
- UNTREATED, PATIENTS WILL PROGRESS TO COMA

Clinical features of myxedema coma

Decreased mental status
Hypothermia
Bradycardia
Hyponatremia
Hypoglycemia
Hypotension
Precipitating illness

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MANAGEMENT OF MYXOEDEMA

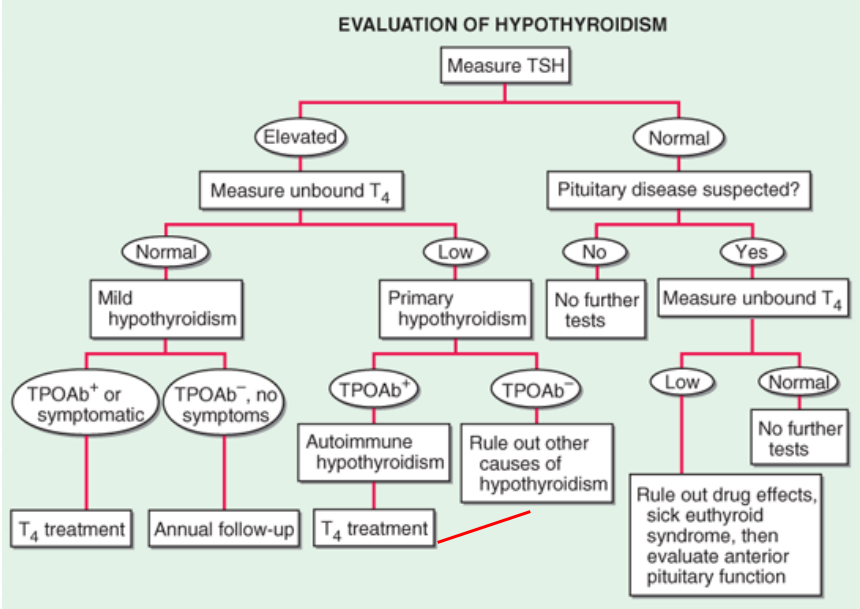
NB: ALL DRUGS ARE ABSORBED POORLY PER OS

- ICU ADMISSION MAY BE REQUIRED FOR VENTILATORY SUPPORT AND IV MEDICATIONS
- THYROXINE (T4) (PO OR NG)
  - LOADING DOSE OF 300 – 500 MCG PO
  - THEN 1.6MCG/KG DAILY PO
  - SMALL DOSES OF T3 (LOAD: 5-20 MCG; THEN 2.5-10 MCG 8HOURLY PO) CAN BE GIVEN (UP TO 20 MCG TDS PO) UNTIL PATIENT IS RESPONDING AND STABLE
- CAREFUL ECG MONITORING FOR ISCHAEMIC EVENTS

MANAGEMENT OF MYXOEDEMA COMA

- ELECTROLYTES
  - WATER RESTRICTION FOR HYPONATRAEMIA
  - AVOID FLUID OVERLOAD
- AVOID SEDATION
- HYPOTENSION MAY REQUIRE VASOPRESSOR DRUG
- MECHANICAL VENTILATION MAY BE NECESSARY
- GLUCOCORTICOIDS
  - CONTROVERSIAL BUT NECESSARY IN HYPOPITUITARISM OR MULTIPLE ENDOCRINE FAILURE
  - DOSE: HYDROCORTISONE 100 MG 8 HLY INITIALLY, THEN TAPER OVER 1 WEEK
- TREAT PRECIPITATING ILLNESS
- AVOID ACTIVE REWARMING

- CONTROVERSIAL WHETHER PATIENTS SHOULD BE TREATED WITH T4, T3, OR BOTH
- MOST EXPERTS PREFER TO GIVE BOTH BECAUSE THE BIOLOGIC ACTIVITY OF T3 IS GREATER, AND ITS ONSET OF ACTION IS MORE RAPID THAN T4
- ALSO, THE CONVERSION OF T4 TO T3 IS IMPAIRED DUE TO BOTH HYPOTHYROIDISM AND ANY NONTHYROIDAL ILLNESS
- THE DECREASE IN T4 TO T3 CONVERSION MAY BE A PROTECTIVE ADAPTATION IN THE FACE OF SEVERE ILLNESS
- THEREFORE, PROPER DOSING OF T3 IS IMPORTANT; HIGH SERUM T3 LEVELS HAVE BEEN CORRELATED WITH MORTALITY



Source: D.L. Kasper, A.S. Fauci, S.L. Hauser, D.L. Longo, J.L. Jameson, J. Loscalzo: Harrison's Manual of Medicine, 19th Edition, www.accessmedicine.com

(4) HYPERTHYROIDISM

- A 32-YEAR-OLD WOMAN PRESENTS WITH A FEW MONTHS' HISTORY OF FATIGUE, PALPITATIONS, LOSS OF WEIGHT AND INTERMITTENT DIARRHOEA. CLINICALLY SHE HAS A RESTING TACHYCARDIA OF 122/MIN, A FINE TREMOR, AND WARM EXTREMITIES. SHE ALSO HAS AN ENLARGED THYROID WITH AN AUDIBLE BRUIT OVER IT.

WHAT IS YOUR CLINICAL DIAGNOSIS?

- MOST LIKELY PRIMARY HYPERTHYROIDISM
- LOOK FOR FEATURES OF GRAVES' DISEASE:
  - OPHTHALMOPATHY, DERMOPATHY
- LOOK FOR COMPLICATIONS:
  - HEART FAILURE, PULMONARY HYPERTENSION, HYPERCOAGULOBILITY (DVT'S)

HYPERTHYROIDISM

- THYROID HORMONE CONTROLS THE **METABOLIC RATE** OF MANY TISSUES
- **CAUSES:** - GRAVES' DISEASE (MOST COMMON, ESPECIALLY YOUNG FEMALES)
  - MULTINODULAR OR SOLITARY TOXIC NODULE
  - DRUGS
  - THYROIDITIS

WHAT BIOCHEMICAL INVESTIGATIONS WILL YOU REQUEST?

- TSH, T4 (CONSIDER T3)
- TSH RECEPTOR ANTIBODIES (TRAB'S)
- ANTI-TPO(THYROPEROXIDASE)-ANTIBODIES

HOW WILL YOU BIOCHEMICALLY CONFIRM THE DIAGNOSIS?

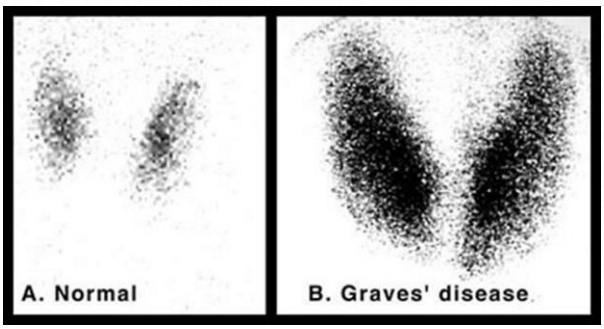
- LOW TSH
- HIGH FREE T4, T3

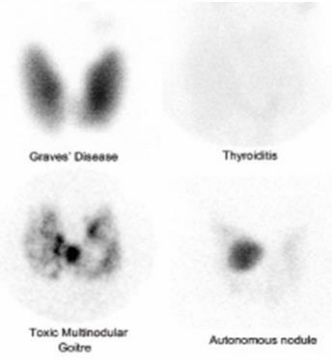
WHAT IS THE ROLE OF THYROID ANTIBODIES IN A PATIENT WITH HYPERTHYROIDISM?

- IF POSITIVE TRAB'S: GRAVES' DISEASE
- ANTI-TPO-ANTIBODIES CAN BE POSITIVE IN BOTH GRAVES' DISEASE OR HASHIMOTO'S THYROIDITIS (AUTOIMMUNE THYROID DISEASE)

WHAT IS THE ROLE OF A THYROID UPTAKE SCAN IN A PATIENT WITH HYPERTHYROIDISM?

- IF DIFFUSELY INCREASED UPTAKE: GRAVES' DISEASE
- IF NODULAR UPTAKE: TOXIC NODULE OR MULTINODULAR GOITRE
- IF NO UPTAKE: THYROIDITIS OR EXOGENOUS THYROID HORMONE





HOW WILL YOU TREAT THE PATIENT?

OPTIONS:

- MEDICALLY
- RADIOABLATION
- SURGERY

MEDICAL THERAPY

- **THIONAMIDE** (CARBIMAZOLE) (NO PROPYLTHIOURACIL IN SOUTH AFRICA)
- USUAL STARTING DOSE BETWEEN 10-30 MG PER DAY
- DEPENDING ON THE PATIENT'S CLINICAL PICTURE AND LEVEL OF THYROID HORMONE ELEVATION (CAN BE GIVEN AS SINGLE OR DIVIDED DOSES)

- **BETA BLOCKERS**: CAN START WITH PROPRANOLOL 20 MG THREE TO FOUR TIMES DAILY OR ATENOLOL 25 TO 50 MG DAILY (NOT IN ASTHMA OR SEVERE CCF)
- LUGOL'S IODINE ADDED FOR ABOUT A WEEK IF THYROID STORM PRESENT (COMBINED WITH ABOVE + CORTICOSTEROIDS, THIAMINE, CLEXANE)

RADIOABLATION

- **FIRST LINE THERAPY IF:**
- PAST THYROID STORM / PAST CCF (NB FIRST STABILISE THE PATIENT FOR SEVERAL MONTHS!)
- LARGE GOITRE / MNG
- MOST MEN
- ELDERLY
- ALLERGIC TO CARBIMAZOLE
- UNWILLING TO TAKE CARBIMAZOLE
- IF STILL NEEDS TO CONTINUE CARBIMAZOLE AFTER 18 MONTHS
- **NOT IF THE PATIENT IS PREGNANT OR HAS SEVERE / ACTIVE EYE DISEASE!**

INDICATIONS FOR THYROIDECTOMY

- LARGE GOITRE
- PRESSURE SYMPTOMS (DYSPHAGIA, STRIDOR)
- COSMETIC REASONS
- POOR DRUG COMPLIANCE WITH ANTITHYROID THERAPY (IF HYPERTHYROID, AND CONTRAINDICATION FOR RADIOABLATION)
- SUSPECTED / CONFIRMED UNDERLYING MALIGNANCY
- 2ND TRIMESTER OF PREGNANCY IF HYPERTHYROID AND NOT RESPONDING TO MEDICAL THERAPY
- HYPERTHYROIDISM WITH CONTRAINDICATIONS FOR RADIOABLATION AND MEDICAL THERAPY

Hyperthyroidism: Diagnosis and Treatment

IGOR KRAVETS, MD, *Stony Brook University School of Medicine, Stony Brook, New York*

(*Am Fam Physician.* 2016;93(5):363-370.

BEST PRACTICES IN ENDOCRINOLOGY: RECOMMENDATIONS FROM THE CHOOSING WISELY CAMPAIGN

Recommendation	*Sponsoring organization*
Do not order multiple tests in the initial evaluation of a patient with suspected thyroid disease. Order TSH, and if abnormal, follow up with additional evaluation or treatment depending on the findings.	American Society for Clinical Pathology
Do not routinely order a thyroid ultrasound in patients with abnormal thyroid function tests if there is no palpable abnormality of the thyroid gland.	The Endocrine Society/American Association of Clinical Endocrinologists

TSH = thyroid-stimulating hormone.

Source: For more information on the Choosing Wisely Campaign, see http://www.choosingwisely.org. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see http://www.aafp.org/afp/recommendations/search.htm.

SHE NOW INFORMS YOU THAT SHE'S PREGNANT. HOW WILL THAT CHANGE YOUR MANAGEMENT?

- **DON'T FORGET:**

  ~ HUMAN CHORIONIC GONADOTROPIN (HCG)-MEDIATED HYPERTHYROIDISM
- GESTATIONAL TRANSIENT THYROTOXICOSIS
- HYPEREMESIS GRAVIDARUM
- MULTIPLE GESTATION E.G. TWIN PREGNANCY
- TROPHOBLASTIC HYPERTHYROIDISM
  - HYDATIDIFORM MOLE (MOLAR PREGNANCY)
  - CHORIOCARCINOMA

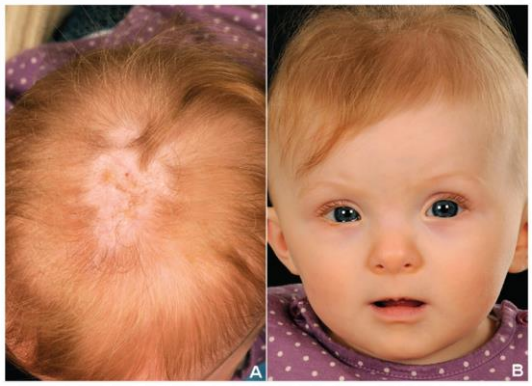
- TREATMENT OPTIONS FOR PREGNANT WOMEN WITH OVERT HYPERTHYROIDISM DUE TO GRAVES' OR NODULAR THYROID DISEASE ARE LIMITED BECAUSE THERAPY MAY BE HARMFUL TO THE FETUS
- HOWEVER, A GOOD FETAL AND MATERNAL OUTCOME DEPENDS UPON CONTROLLING THE MOTHER'S HYPERTHYROIDISM
- **NO THYROID UPTAKE SCAN OR RADIOABLATION DURING PREGNANCY!** (IT DESTROYS BABY'S THYROID)

- FOR WOMEN WITH MODERATE TO SEVERE HYPERTHYROIDISM COMPLICATING PREGNANCY, A **THIONAMIDE (CARBIMAZOLE)** IS THE FIRST CHOICE OF TREATMENT
- SHOULD TRY TO LIMIT THE DOSE OF CARBIMAZOLE TO 5 TO 20 MG PER DAY OR LESS: HIGHER DOSES (IN EXCESS OF 20 MG/DAY)
- CAN RESULT IN FETAL GOITRE AND HYPOTHYROIDISM

- **B-BLOCKERS:** OCCASIONAL CASES OF FETAL GROWTH RESTRICTION, HYPOGLYCAEMIA, RESPIRATORY DEPRESSION, AND BRADYCARDIA HAVE BEEN REPORTED AFTER MATERNAL ADMINISTRATION
- SHOULD CONSIDER **THYROIDECTOMY** IN HYPERTHYROID WOMEN DURING PREGNANCY WHEN THIONAMIDES ARE NOT TOLERATED BECAUSE OF ALLERGY OR AGRANULOCYTOSIS, OR IF NOT RESPONDING TO HIGH DOSE THIONAMIDES, PREFERABLY IN THE 2ND TRIMESTER

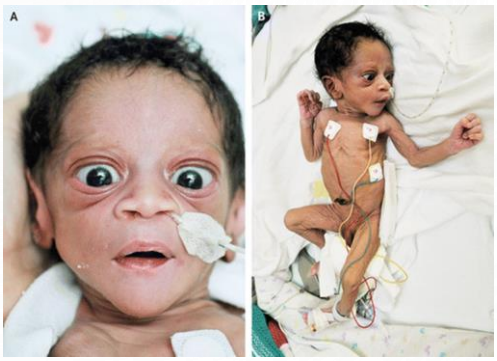
COMPLICATIONS OF THE THERAPY

- A **'SYNDROME OF METHIMAZOLE/CARBIMAZOLE EMBRYOPATHY'** WAS DESCRIBED, THAT ALSO INCLUDES DYSMORPHIC FACIES
- - DEFECTS WITH A STATISTICALLY SIGNIFICANT ASSOCIATION WITH THESE DRUGS INCLUDE:
  - APLASIA CUTIS
  - CHOANAL OR OESOPHAGEAL ATRESIA
  - TRACHEO-OESOPHAGEAL FISTULAS
  - VARIOUS TYPES OF ABDOMINAL WALL DEFECTS INCLUDING UMBILICOCOELE / OMPHALOCOELE, OMPHALOMESENTERIC DUCT ANOMALY, PATENT VITELLOINTESTINAL DUCT
  - CHOANAL ATRESIA
  - EYE DEFECTS
  - URINARY SYSTEM DEFECTS
  - VENTRICULAR SEPTAL DEFECTS



FETAL AND NEONATAL GRAVES' DISEASE

- 1 - 5 % OF NEONATES BORN TO WOMEN WITH GRAVES' DISEASE HAVE HYPERTHYROIDISM DUE TO TRANSPLACENTAL TRANSFER OF TSH RECEPTOR-STIMULATING ANTIBODIES



HOW WOULD YOU MONITOR A PATIENT RECEIVING THERAPY FOR PRIMARY HYPERTHYROIDISM?

- REMEMBER: TSH CAN REMAIN SUPPRESSED FOR MONTHS (EVEN RARELY UP TO A YEAR) AFTER PRESENTING WITH HYPERTHYROIDISM!
- NB: DURING THYROID STORM MEASURE FREE T4 EVERY 2ND DAY (ONLY TSH ON ADMISSION)

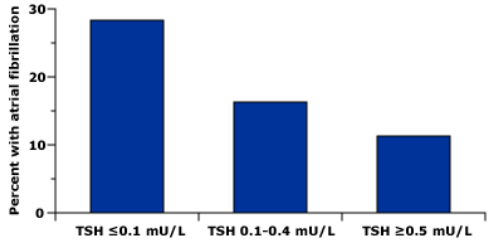
- USE THE FREE T4 TO ADJUST MEDICATIONS (NOT THE TSH) IN THE FIRST FEW MONTHS AFTER TREATMENT WAS STARTED, OR AFTER RADIOABLATION WAS DONE
- IF DISCREPANT RESULTS (EG BOTH T4 AND TSH LOW), USE THE T4 (NOT TSH)
- IN A STABLE PATIENT AFTER THE 1ST YEAR: CAN USE TSH ALONE AS SCREENING TO CHECK WHETHER THE PATIENT IS STILL EUTHYROID

SUBCLINICAL HYPERTHYROIDISM

- SUBCLINICAL HYPERTHYROIDISM IS MORE COMMON IN AREAS OF THE WORLD WITH MILD TO MODERATE IODINE DEFICIENCY
- IN ADDITION, SUBCLINICAL THYROID DYSFUNCTION IS MORE COMMON IN FEMALES, SMOKERS, AND OLDER ADULTS

- THE CAUSES OF SUBCLINICAL HYPERTHYROIDISM ARE THE SAME AS THE CAUSES OF OVERT HYPERTHYROIDISM, AND LIKE OVERT HYPERTHYROIDISM, SUBCLINICAL HYPERTHYROIDISM CAN BE PERSISTENT OR TRANSIENT
- COMMON CAUSES OF SUBCLINICAL HYPERTHYROIDISM INCLUDE EXCESSIVE THYROID HORMONE THERAPY (EXOGENOUS SUBCLINICAL HYPERTHYROIDISM), AUTONOMOUSLY FUNCTIONING THYROID ADENOMAS AND MULTINODULAR GOITRES, OR GRAVES' DISEASE

Increased incidence of atrial fibrillation in subclinical hyperthyroidism



Cumulative incidence of atrial fibrillation in subjects over age 60 years according to the serum concentration of TSH. The risk of atrial fibrillation was increased almost threefold in the subjects with marked suppression of TSH (left panel) as compared with those who had normal serum TSH concentrations and were presumably euthyroid (right panel); patients with slightly low serum TSH concentrations (middle panel) had a lesser increase in risk.

TSH: thyroid-stimulating hormone.

Data from: Sawin CT, Geller A, Wolf PA, et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. N Engl J Med 1994; 331:1249.

Table 2. American Thyroid Association Recommendations for Treating Adults with Subclinical Hyperthyroidism

Subclinical Hyperthyroidism: When to Consider Treatment

INES DONANGELO, MD, PhD, and SE YOUNG SUH, MD, *Allegheny Health Network, Pittsbu*

Factor	*TSH < 0.1 mIU per L*	*TSH 0.1 to 0.4 mIU per L**
Age ≥ 65 years	Treat	Consider treating
Age < 65 years in asymptomatic patient	Consider treating	Observe
Age < 65 years with comorbidities		
Heart disease	Treat	Consider treating
Hyperthyroid symptoms	Treat	Consider treating
Osteoporosis	Treat	Consider treating
Postmenopausal (no estrogen or bisphosphonate therapy)	Treat	Consider treating

TSH = thyroid-stimulating hormone.

**—0.4 mIU per L is the lower limit of the normal range.*

Adapted with permission from Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. Thyroid. *2016;26(10):1377.*

Subclinical Hyperthyroidism: When to Consider Treatment

INES DONANGELO, MD, PhD, and SE YOUNG SUH, MD, *Allegheny Health Network, Pittsburgh, Pennsylvania*

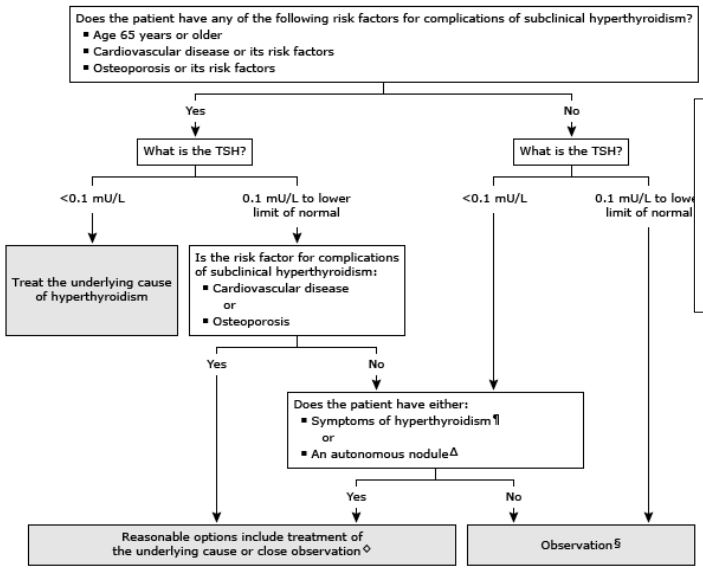
SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Physicians should not routinely screen for subclinical thyroid disease.	C	1
To reduce the risk of atrial fibrillation, heart failure, and mortality, physicians should treat adults with subclinical hyperthyroidism who are 65 years or older and have TSH levels less than 0.1 mIU per L.	C	34
To decrease the risk of further bone loss, physicians should treat postmenopausal women with TSH levels less than 0.1 mIU per L and osteoporosis.	C	34

TSH = thyroid-stimulating hormone.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

Indications for treatment of endogenous subclinical hyperthyroidism in nonpregnant adults*



TSH: thyroid-stimulating hormone.

* Subclinical hyperthyroidism is defined as a normal serum free thyroxine (T4) and triiodothyronine

Subclinical hyperthyroidism in nonpregnant adults
Author:Douglas S Ross, MD Section Editor:David S Cooper, MD Deputy Editor:Jean E Mulder, MD
Literature review current through: Jul 2018. | This topic last updated: Jun 29, 2018

HYPERTHYROIDISM IN THE ELDERLY

- TEND TO PRESENT WITH SYMPTOMS / SIGNS IN THE **MOST VULNERABLE ORGAN SYSTEM**
- USUALLY **CARDIOVASCULAR SYSTEM**: ATRIAL FIBRILLATION, CONGESTIVE CARDIAC FAILURE, ANGINA, ACUTE MYOCARDIAL INFARCTION **OR:**
- **CENTRAL NERVOUS SYSTEM**: APATHY, DEPRESSION, CONFUSION, LASSITUDE

MORE COMMON THAN IN YOUNGER PATIENTS:

- MUSCLE WASTING, FAILURE TO THRIVE, ANOREXIA, WEIGHT LOSS, OCCASIONALLY CONSTIPATION
- DEGENERATION OF THE SINUS NODE AND CARDIAC CONDUCTION SYSTEM: **LESS LIKELY TO HAVE PALPITATIONS** / SINUS TACHYCARDIA
- FALLS, BONE LOSS, FRACTURES
- OFTEN NORMAL THYROID SIZE OR NOT PALPABLE
- LID LAG OR OPHTHALMOPATHY LESS COMMON

THE SAME AS IN YOUNGER PATIENTS:

- WEIGHT LOSS I.S.O INCREASED APPETITE
- FINE TREMOR
- EYELID RETRACTION
- INCREASED PERSPIRATION
- INCREASED FREQUENCY OF BOWEL MOVEMENTS

"APATHETIC HYPERTHYROIDISM"

- REFERS TO HYPERTHYROIDISM WITHOUT CLEAR SYMPTOMS OF HYPERTHYROIDISM
- THE CARDINAL FEATURES ARE APATHY AND DEPRESSION
- CAN INCLUDE WEAKNESS, LETHARGY, WEIGHT LOSS
- DIAGNOSIS EASILY MISSED

THERAPY

- BETA-BLOCKERS TO ALLEVIATE SYMPTOMS
- **RADIOACTIVE IODINE IS THE THERAPY OF CHOICE IN THE ELDERLY**
- CAN USE ANTITHYROID DRUGS PRIOR TO ABLATION TO RENDER PATIENT EUTHYROID (NOT DEFINITIVE TREATMENT)
- HYPOTHYROIDISM DEVELOPS IN >80%
- RARELY SURGERY: INCREASED MORBIDITY
- **DOSES OF OTHER MEDICATIONS** MAY HAVE TO BE DECREASED ONCE PATIENT ISN'T HYPERTHYROID ANYMORE

THYROID STORM

- THYROID STORM IS A RARE, LIFE-THREATENING CONDITION CHARACTERIZED BY SEVERE OR EXAGGERATED CLINICAL MANIFESTATIONS OF THYROTOXICOSIS
- THE MORTALITY RATE OF THYROID STORM IS SUBSTANTIAL (10 TO 30 %); SHOULD BE MANAGED IN AN ICU
- ALTHOUGH THYROID STORM CAN DEVELOP IN PATIENTS WITH LONG-STANDING UNTREATED HYPERTHYROIDISM, IT IS OFTEN PRECIPITATED BY AN ACUTE EVENT SUCH AS THYROID OR NON-THYROIDAL SURGERY, TRAUMA, INFECTION, AN ACUTE IODINE LOAD, OR PARTURITION

Diagnostic criteria for thyroid storm*

Thermoregulatory dysfunction	
Temperature (°F | °C)	
99 to 99.9 | 37.2 to 37.7	5
100 to 100.9 | 37.8 to 38.2	10
101 to 101.9 | 38.3 to 38.8	15
102 to 102.9 | 38.9 to 39.4	20
103 to 103.9 | 39.4 to 39.9	25
≥104.0 | >40.0	30
Central nervous system effects	
Mild	10
Agitation	
Moderate	20
Delirium	
Psychosis	
Extreme lethargy	
Severe	30
Seizure	
Coma	
Gastrointestinal-hepatic dysfunction	
Moderate	10
Diarrhea	
Nausea/vomiting	
Abdominal pain	
Severe	20
Unexplained jaundice	

Cardiovascular dysfunction	
Tachycardia	
99 to 109	5
110 to 119	10
120 to 129	15
130 to 139	20
≥140	25
Atrial fibrillation	10
Heart failure	
Mild	5
Pedal edema	
Moderate	10
Bibasilar rales	
Severe	15
Pulmonary edema	
Precipitant history	
Negative	0
Positive	10

* A score of 45 or more is highly suggestive of thyroid storm; a score of 25 to 44 supports the diagnosis; and a score below 25 makes thyroid storm unlikely.
Adapted from: Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. Endocrinol Metab Clin North Am 1993; 22:263.

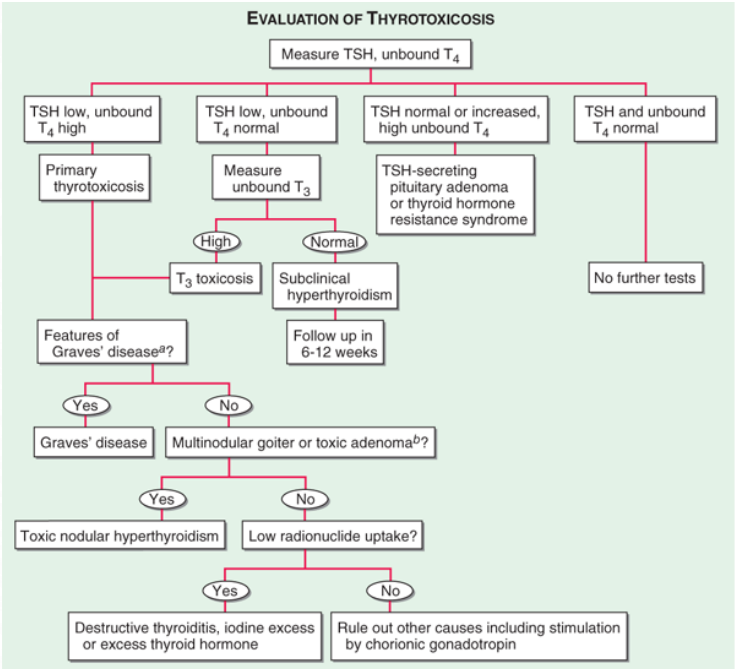
- THE TREATMENT STRATEGY FOR THYROID STORM CAN BE BROADLY DIVIDED INTO:
  - THERAPY DIRECTED AGAINST THYROID HORMONE SECRETION AND SYNTHESIS
  - MEASURES DIRECTED AGAINST THE PERIPHERAL ACTION OF THYROID HORMONE AT THE TISSUE LEVEL
  - REVERSAL OF SYSTEMIC DECOMPENSATION
  - TREATMENT OF THE PRECIPITATING EVENT OR INTERCURRENT ILLNESS
  - DEFINITIVE THERAPY

eTable C. Treatment of Thyroid Storm

- Supportive treatment
  - Airway maintenance
  - Oxygen
  - IV fluids
  - Cooling blanket (do not use salicylate to treat fever because salicylates increase free T_4 and free T_3 levels)
- Inhibit T_4 and T_3 synthesis
  - Methimazole (Tapazole) orally, rectally, via nasogastric tube, or IV, 20 to 40 mg every eight hours
  - Propylthiouracil orally, rectally, or via nasogastric tube, 200 to 400 mg every eight hours
- Inhibit T_4 and T_3 release
  - Saturated solution of potassium iodide, five drops orally every six hours to be started at least one hour after administration of an antithyroid agent
- Heart rate control
  - Esmolol (Brevibloc) IV, 50 to 100 mcg per kg per minute
  - Propranolol, 60 to 80 mg orally every four hours
  - Metoprolol IV, 5 to 10 mg every two to four hours
  - If beta-blockade is contraindicated, use diltiazem IV, 0.25 mg per kg over two minutes, then 10 mg per hour IV infusion or 60 to 90 mg orally every six to eight hours
- Inhibit T_4 to T_3 conversion
  - Hydrocortisone 100 mg IV every eight hours (also suppresses autoimmune process in Graves disease)
- Treat precipitating cause

IV = intravenous; T_3 = triiodothyronine; T_4 = thyroxine.

Information from Nayak B, Burman K. Thyrotoxicosis and thyroid storm. Endocrinol Metab Clin North Am. *2006;35(4):663-686, vii.*



(5) THYROIDITIS

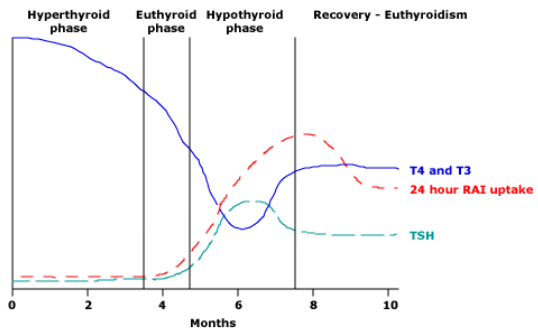
- THE TERM THYROIDITIS ENCOMPASSES A DIVERSE GROUP OF DISORDERS CHARACTERIZED BY SOME FORM OF THYROID INFLAMMATION
- THEY INCLUDE CONDITIONS THAT CAUSE ACUTE ILLNESS WITH SEVERE THYROID PAIN, AND CONDITIONS IN WHICH THERE IS NO CLINICALLY EVIDENT INFLAMMATION AND THE ILLNESS IS MANIFESTED PRIMARILY BY THYROID DYSFUNCTION OR GOITRE

Causes of thyroiditis according to the presence or absence of pain and tenderness

Disorder	Synonyms or causes
Thyroid pain and tenderness	
Subacute thyroiditis	Subacute granulomatous thyroiditis
	Subacute nonsuppurative thyroiditis
	de Quervain's thyroiditis
Infectious thyroiditis	Acute or chronic thyroiditis
Radiation-induced thyroiditis	
Palpation- or trauma-induced thyroiditis	
No thyroid pain and tenderness	
Painless thyroiditis	Silent thyroiditis
	Lymphocytic thyroiditis with spontaneously resolving hyperthyroidism
	Subacute lymphocytic thyroiditis
- Occurring postpartum	Postpartum thyroiditis
- Associated with drugs	Interferon-alpha
	Interleukin-2
	Lithium
	Tyrosine kinase inhibitors
	Checkpoint inhibitor immunotherapy
Chronic lymphocytic thyroiditis	Hashimoto's thyroiditis
- Postpartum exacerbation	Postpartum thyroiditis
Amiodarone-associated thyroiditis	
Fibrous thyroiditis	Riedel's thyroiditis
	Invasive thyroiditis

UpToDate: Overview of thyroiditis
Author:Kenneth D Burman, MD
Section Editor:Douglas S Ross, MD
Deputy Editor:Jean E Mulder, MD
Literature review current through: Jul 2018. | This topic last updated: Sep 12, 2017.

Characteristic course of thyroiditis (painless, postpartum, or subacute)



The initial thyroid inflammation damages thyroid follicles and activates proteolysis of the thyroglobulin stored within the follicles. The result is **unregulated** release of large amounts of T4 and T3 into the circulation and, therefore, hyperthyroidism. This state lasts only until the stores of thyroglobulin are exhausted because new hormone synthesis ceases. As the inflammation subsides, the thyroid follicles regenerate and thyroid hormone synthesis and secretion resume. There may be a transient period of hypothyroidism and increased TSH secretion before thyroid secretion becomes normal again. However, some patients have only a hyperthyroid or hypothyroid phase.

T4: thyroxine; T3: triiodothyronine; RAI: radioiodine; TSH: thyroid-stimulating hormone.

UpToDate®

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TREATMENT

- THERE ARE NO STUDIES ASSESSING THE OPTIMAL TREATMENT OF PAINLESS THYROIDITIS
- TREATMENT IS BASED UPON OBSERVATIONAL DATA AND CLINICAL EXPERIENCE
- MANY PATIENTS WITH THYROIDITIS NEED NO TREATMENT DURING EITHER THE HYPERTHYROID OR THE HYPOTHYROID PHASES, BECAUSE THYROID DYSFUNCTION IS RARELY SEVERE AND IT IS TRANSIENT

HYPERTHYROID PHASE

- PATIENTS WHO ARE SYMPTOMATIC OR WHO ARE AT INCREASED RISK FOR ATRIAL FIBRILLATION SHOULD BE TREATED WITH A BETA-BLOCKER DURING THE HYPERTHYROID PHASE, UNLESS THERE IS A CONTRAINDICATION TO THEIR USE
- OPTIONS INCLUDE PROPRANOLOL (40 TO 120 MG DAILY) OR ATENOLOL (25 TO 50 MG DAILY)
- THYROID FUNCTION SHOULD BE MONITORED EVERY FOUR TO EIGHT WEEKS TO CONFIRM RESOLUTION OF HYPERTHYROIDISM AND TO DETECT THE DEVELOPMENT OF HYPOTHYROIDISM
- BETA BLOCKERS SHOULD ONLY BE USED DURING THE HYPERTHYROID PHASE OF PAINLESS THYROIDITIS

- IN VERY RARE CASES OF SEVERELY DERANGED THYROID FUNCTION, GLUCOCORTICOID THERAPY HAS BEEN USED SUCCESSFULLY
- THERE IS NO ROLE FOR ANTITHYROID DRUGS (CARBIMAZOLE) OR RADIOACTIVE IODINE, BECAUSE THE HYPERTHYROIDISM IS NOT CAUSED BY EXCESS THYROID HORMONE SYNTHESIS AND BECAUSE UPTAKE OF RADIOIODINE IS VERY LOW

HYPOTHYROID PHASE

- AN OCCASIONAL PATIENT MAY HAVE SUFFICIENT SYMPTOMS OF HYPOTHYROIDISM TO WARRANT THYROXINE (LEVOTHYROXINE, T4) THERAPY
- IN ADDITION, MOST WOULD TREAT WHEN THE TSH EXCEEDS 10 MU/L, EVEN IN THE ABSENCE OF SYMPTOMS
- THE USUAL DOSE OF T4 IS 50 TO 100 MCG DAILY WITH PERIODIC MONITORING OF SERUM FREE T4 AND TSH
- THE EXOGENOUS T4 SHOULD BE DISCONTINUED AFTER THREE TO SIX MONTHS

- INITIALLY, THE DOSE CAN BE HALVED AND THYROID TESTS (TSH, FREE T4) REEVALUATED FOUR TO SIX WEEKS LATER TO INSURE NORMAL THYROID GLAND FUNCTION
- IF THYROID TESTS REMAIN NORMAL ON HALF DOSE, THYROID HORMONE CAN BE DISCONTINUED, WITH RETESTING OF THYROID FUNCTION IN FOUR TO SIX WEEKS
- IF THE TSH RISES ABOVE NORMAL ON HALF DOSE, THE PREVIOUS DOSE OF THYROID HORMONE SHOULD BE RESUMED

- AFTER RECOVERY FROM THYROIDITIS, THE PATIENT SHOULD BE TOLD OF THE RISK OF CHRONIC AUTOIMMUNE THYROIDITIS, ITS SYMPTOMS DESCRIBED, AND PERIODIC FOLLOW-UP ADVISED
- ALTHOUGH ABNORMALITIES IN THYROID FUNCTION RESOLVE IN MOST PATIENTS, 20 TO 30 % WILL DEVELOP PERMANENT HYPOTHYROIDISM
- PATIENTS SHOULD ALSO BE INFORMED ABOUT THE POSSIBILITY OF RECURRENT EPISODES OF THYROIDITIS, OFTEN MANY YEARS IN THE FUTURE (10 %)

Thyroiditis: An Integrated Approach

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Am Fam Physician. 2014;90(6):389-396.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Patients with elevated thyroid peroxidase antibody levels and subclinical hypothyroidism should be monitored annually for the development of overt hypothyroidism.	C	12
Women with postpartum thyroiditis and subclinical hypothyroidism should be treated with levothyroxine to achieve a thyroid-stimulating hormone level of less than 2.5 mIU per L if they are pregnant or desire fertility.	C	15
Patients with subacute thyroiditis should be started on high-dose acetylsalicylic acid or nonsteroidal anti-inflammatory drugs as first-line therapy.	C	25
Corticosteroid therapy for subacute thyroiditis should be initiated in patients with severe neck pain or minimal response to acetylsalicylic acid or nonsteroidal anti-inflammatory drugs after four days.	C	25
Patients with severe thyroid pain and systemic symptoms (e.g., high fever, leukocytosis, cervical lymphadenopathy) should undergo fine-needle aspiration to rule out infectious thyroiditis.	C	26

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.