Hyperthyroidism: Guidelines and Beyond

Douglas S Ross MD

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Abbott Laboratories

Quest Diagnostics

Diagnosis

Biochemical Assessment
Biotin Interference Biotinylated Abs

	TSH	free T4	free T3
Biotinylated assays	mU/L	pmol/L	pmol/L
• Immunometric	0.01		
• Competitive binding		75.9	14.0
Non-biotinylated	3.96	15.5	4.5

Kwok et al Pathology 2012

Prescribed by Hairdressers

Biotin

- No “RDA”
- Adequate Intake (AI) 30 mcg

- Hair Skin and Nails 2,500 mcg tid
- Biotin 10,000 mcg

Prescribed by Neurologists

- Multiple Sclerosis
- Ataxia due to Multiple Carboxylase Deficiencies (MCD)

- Doses are up to 100 mg tid

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- Figure: time course of biotin effect

Case 1

- 39 year old woman with palpitations, tremulousness, increased sweating and 10 pound weight loss
- BP 120/60, pulse 98, no proptosis, thyroid 35 g, hyperdynamic precordium, trace pedal edema
- TSH <0.01, free T4 3.1, T3 343

What is the etiology of the hyperthyroidism?

2011

- A radioiodine uptake should be performed when the clinical presentation of hyperthyroidism is not diagnostic of Graves' disease; a thyroid scan should be added in the presence of thyroid nodularity. 1/+00

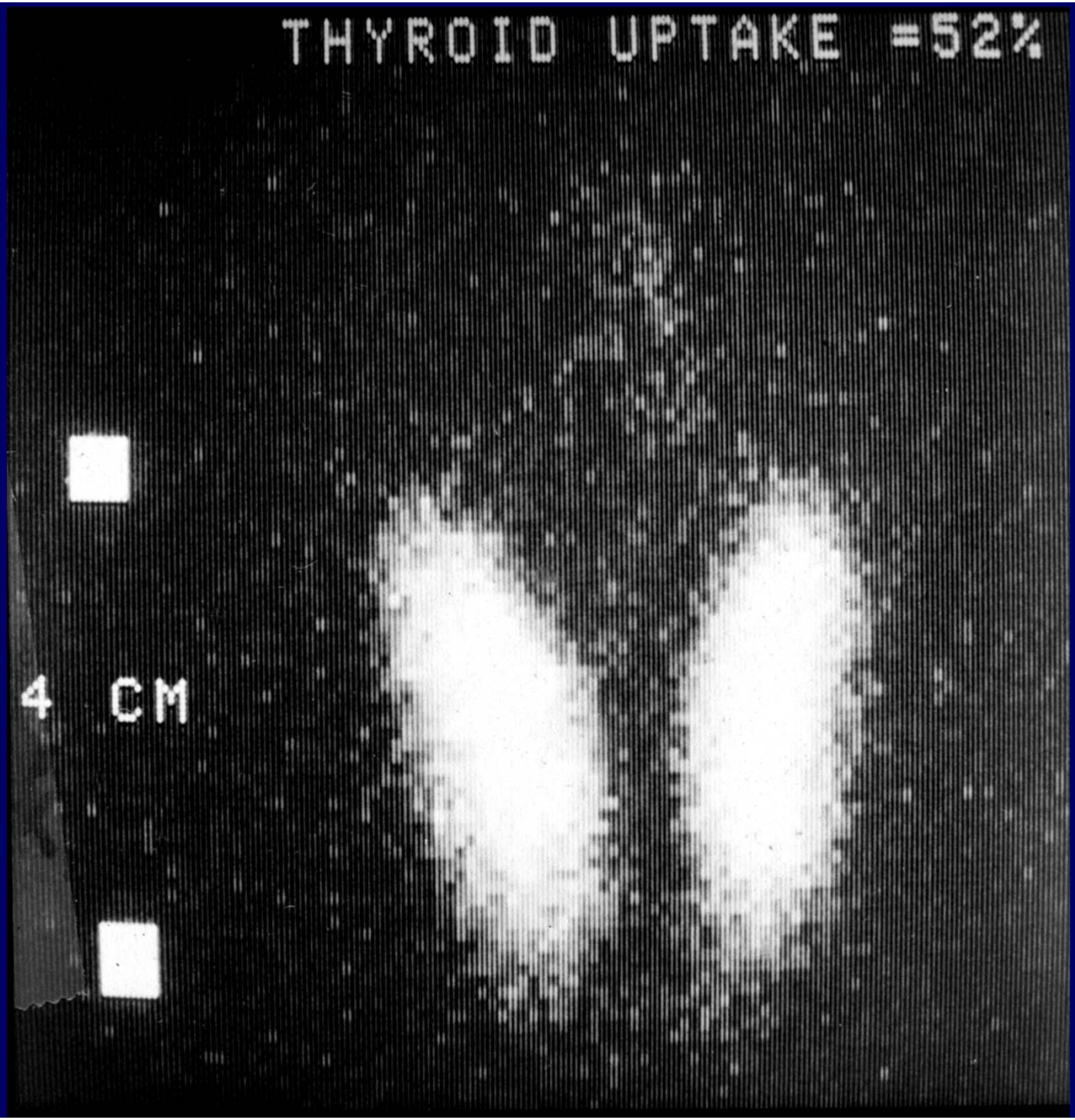
Hyperthyroidism

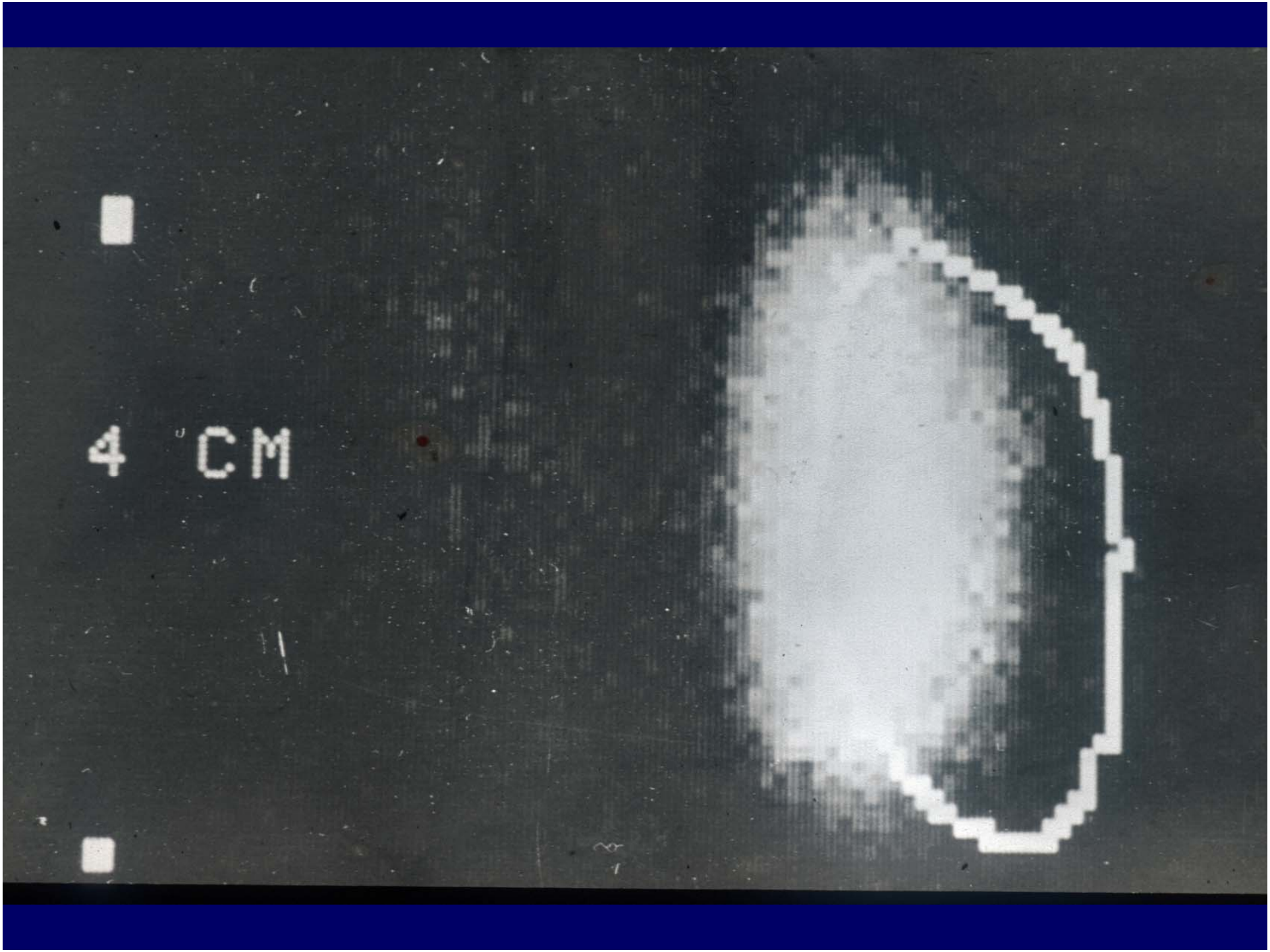
High radioiodine uptake

- Graves' disease
- Toxic adenoma
- Toxic multinodular goiter
- Trophoblastic disease
- TSH-mediated

Low radioiodine uptake

- Painless or postpartum thyroiditis
- Subacute thyroiditis
- Factitious ingestion of thyroid hormone
- Amiodarone induced
- Struma ovarii


THYROID UPTAKE =52%
4 CM


4 CM


UPTAKE= 0.03%
PALPATED BY DR. ROSS
4CM.
SSN.

Etiology: 2016 Update

- The etiology of thyrotoxicosis should be determined. If the diagnosis is not apparent based on the clinical presentation, diagnostic testing is indicated and can include, depending on available expertise and resources, (1) measurement of TRAb, (2) determination of the radioactive iodine uptake (RAIU), or (3) measurement of thyroidal blood flow on ultrasonography. A radionucleotide thyroid scan should be obtained when the clinical presentation suggests a toxic adenoma or toxic multinodular goiter. **Strong recommendation, low-quality evidence.**

Antibodies in Graves Disease

- Thyrotropin Receptor Antibodies (TRAb)
  - TSI: Thyrotropin Stimulating Antibodies
  - TBII: Thyrotropin Binding Inhibitory
    - Imunoblobulins
    - Blocking Antibodies

3rd Generation TSI Assays

- Chinese hamster ovary cells
- Transfected with hTSH receptor
- cAMP promotor attached to a luciferase expression construct
- Signal is read by chemiluminescense

3rd Generation TBII assays

- May be automated
- Competitive binding assays using

  porcine TSH receptor

  biotinylated anti-porcine TSH receptor ab

Automated 3rd Generation TRAb Assays

Meta-analysis of automated 3G assays

- Sensitivity 0.976
- Specificity 0.991
- Odds Ratio for diagnosis GD

  3129 (95% CI 1447-6766)

Tozzoli et al Autoimmun Rev 2012

Impact of TSI versus RAIU scan

- 47 % cost savings *
- 46 % faster time to diagnosis
- No radiation exposure to patient

* Analysis does not include indirect costs to patient (e.g. time lost from work)

McKee & Peyerl Am J Manag Care 2012

Color Flow Doppler

	Pattern	Peak Systolic Velocity cm/sec
Graves'	Prominent	25.5 ± 9.9
Hashimoto's	Moderate	9.7 ± 4.9
Controls	Mild	7.4 ± 3.2

Erdogan et al Thyroid 2007

Alternative Approaches

T3/T4 ratio [ng/dl / mcg/dl]

> 20 Graves' disease

< 20 painless and postpartum thyroiditis

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- Figure: T3/T4 ratio in hyperthyroidism

Treatment of Graves’ disease

Beta-blockers

- Beta-adrenergic blockade is recommended in all patients with symptomatic thyrotoxicosis, especially elderly patients and thyrotoxic patients with resting heart rates in excess of 90 bpm or coexistent cardiovascular disease. ***Strong recommendation. Moderate-quality evidence.***

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- Table: Beta-blockers in hyperthyroidism

Treatment

- Patients with Graves' disease can be treated with any of the following modalities:

  131I therapy,

  antithyroid medications,

  or thyroidectomy.

Strong recommendation. Moderate-quality evidence.

Treatment

The long term quality of life following treatment for GD was found to be the same in patients randomly allocated to one of the 3 treatment options.

Abraham-Nordling M 2005 Thyroid

Which Treatment?
Radioiodine

Favor

- **Definitive pre-pregnancy treatment**
- **Elderly, comorbidities**
- **Poor surgical candidate, surgical contraindications, lack of surgical expertise**

Oppose

- **Pregnancy, lactation**
- **Orbitopathy**
- **Nodules suspicious for thyroid cancer**
- **Inability to comply with radiation precautions**

Which Treatment?
Methimazole

Favor

- **High remission chance**
- **Elderly, co-morbities**
- **Poor surgical candidate, surgical contraindications, lack of surgical expertise**
- **Orbitopathy**

Oppose

- **Prior adverse reactions**
  - **Agranulocytosis**
  - **Abnormal liver tests**
- **PTU if first trimester pregnancy**

Which Treatment?
Surgery

Favor

- **Large glands / nodules**
- **Suspicious nodules**
- **Hyperparathyroidism**
- **Orbitopathy**
- **Definitive pre-pregnancy treatment**
- **Low RAIU**

Oppose

- **Elderly, co-morbidities**
- **Poor surgical candidate, surgical contraindications, lack of surgical expertise**
- **Pregnancy**

Radioiodine

Preparation for Radioiodine

- Because RAI treatment of GD can cause a transient exacerbation of hyperthyroidism, beta-adrenergic blockade should be considered even in asymptomatic patients who are at increased risk for complications due to worsening of hyperthyroidism, i.e., elderly patients and patients with co-morbidities. ***Weak recommendation, low quality evidence.***

Preparation for Radioiodine

- In addition to beta-adrenergic blockade, pretreatment with MMI prior to RAI therapy for GD should be considered in patients who are at increased risk for complications due to worsening of hyperthyroidism. MMI should be discontinued 2-3 days prior to RAI. ***Weak recommendation, moderate-quality evidence***

Rationale for Pretreatment

- Avoid exacerbation of hyperthyroidism
- Patients achieve euthyroidism more quickly:

  97% of patients given methimazole by 12 weeks

  radioiodine can take 6-18 weeks or longer
- 14% of patients fail the first radioiodine dose

Stopping ATD before RAI

- Pretreatment is assocated with lower levels of T3, but..
- Thyroid hormone levels become high transiently if one stops a week before radioiodine is given

Burch et al JCEM 2001

Stopping ATD before RAI

	On CMZ	3 days off CMZ	
Free T4 (mean)	18.7	17.1	pmol/l
Free T3 (mean)	2.2	2.4	nmol/l

Walter MA Eur J Nucl Med 2006

Stopping ATD before RAI

Toxic MNG

Graves' Disease

Success of RAI treatment was the same without or 3 days off CMZ

Walter MA Eur J Nucl Med 2006

Restarting ATD after RAI 2016

- In patients who are at increased risk for complications due to worsening of hyperthyroidism, resuming MMI 3-7 days after RAI administration should be considered. *Weak recommendation, low quality evidence.*

Radioiodine Dose

- Sufficient radiation should be administered in a single dose, typically 10–15 mCi (370-555 MBq), to render the patient with GD hypothyroid. ***Strong recommendation, moderate-quality evidence***

Radioiodine Dose

- Fixed Dose:

  10 mCi

  85% cured, 61% hypothyroid

- Calculated Dose:

  Grams tissue x 128-155 uCi/g / RAIU

  90% cured, 80% hypothyroid

Allahabdaia et al JCEM 2001; Alexander et al JCEM 2002

Radioiodine Dose

Dose	Cure Rates
5.4 mCi	61 %
8.2	69
10	74
15	81
15.7	86

Kung et al Thyroid 1995; Bonnema et al JCEM 2004; Santos et al Clin Nucl Med 2012; Braga et al Thyroid 2002

Radioiodine Dose

- Only 25% cure in large glands (>75g) with fixed doses

Semi-quantitative Fixed Dose Regimens

- 5 mCi small glands
- 10 mCi medium glands
- 15 mCi large glands

Peters et al Eur J Clin Invest 1995;Jarlov et al Clin Endocrinol 1995

Antithyroid Drugs

Antithyroid Drugs

- Methimazole should be used in virtually every patient who chooses antithyroid drug therapy for Graves' disease, except in the 1st trimester of pregnancy, when propylthiouracil is preferred, or in patients with minor reactions to MMI who refuse radioactive iodine therapy or surgery. *Strong Recommendation, Weak quality evidence.*

Methimazole (MMI) versus PTU

- Longer serum half-life
- Single daily dosing versus divided doses
- Cholestatic jaundice versus hepatocellular necrosis (FDA warning for PTU)
- ANCA associated vasculitis with PTU, rare with MMI
- Possible lower risk of agranulocytosis
- Resistance to radioiodine treatment after PTU, uncertain after MMI

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- Figure: Lower T3 after PTU versus methimazole after 5 days

PTU VS METHIMAZOLE

Drug	**Time to normalize T3**
PTU 100 tid	**16.8 +/- 13.8 weeks**
MMI 10 tid	**5.8 +/- 1.0 week**

Okamura et al 1987

Starting dose of antithyroid drugs

A rough guide to initial MMI daily dosing is as follows:

5-10 mg if FT4 is 1-1.5 times the upper limit of normal

10-20 mg for FT4 1.5-2 times the ULN

30-40 mg for FT4 2-3 times the ULN

…incorporating additional information on symptoms, gland size and T3 levels where relevant.

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- Dose of ATD versus time to normalize thyroid function: free T4 < 7 or ≥ 7

Remission Rates in Graves Disease

- 314 patients, 18 months carbimazole or PTU
- 37 % overall remission rate

- 20 % men
- 40 % women
- 33 % under age 40
- 48 % age 40 or older

Allahabadia et al JCEM 2000

Remission After Antithyroid Drugs Favorable Prognostic Factors

- **Female**
- **Small gland**
- **Mild hyperthyroidism**
- **Shrinkage of the gland on treatment**
- **Positive TPO antibodies**

“Remission” After Antithyroid Drugs Mechanism

- **TRAb disappear**
- **Thyrotropin blocking antibodies appear**
- **Lymphocytes destroy the gland (TPO abs)**

Duration of Antithyroid Drugs

Meta-analysis

Relapse rates were not lower when patients were treated with more than 18 months of anti-thyroid drugs RR 0.88 (0.67-1.16)

Prakash Abraham et al. Eur J Endocrinol 2005;153:489-498

Duration of ATD Therapy

2011

- If methimazole is chosen as the primary therapy for GD, the medication should be continued for approximately 12-18 months, then tapered or discontinued if the TSH is normal at that time. 1/+++

Duration: 2016 Update

- If methimazole is chosen as the primary therapy for GD, the medication should be continued for approximately 12–18 months, then discontinued if the TSH and TRAb levels are normal at that time. *Strong recommendation, high quality evidence.*

Outcome based on TRAb level after 18 months of MMI treatment

Overall rate of remission 35%

Relapse rate TRAb > 3.85 was 97%

Clear = euthyroid Grey = hyperthyroid Black = hypothroid

Carella et al Thyroid 2006

Summary
Recommendations for ATD

- Inform patients of side effects and symptoms in writing
- Baseline CBC with differential and LFTs
- Check CBC with differential at onset of febrile illness
- Insufficient evidence for monitoring CBC or LFTs

Adverse Effects from Anti-thyroid Drugs

13 % of 5136 experienced an adverse effect

Sundaresh et al, J Clin Endocrinol Metab 2013

Discontinuing Anti-thyroid Drugs due to Adverse Events

	Discontinuing
• Low dose (15 mg) methimazole	17 %
• High dose (30 mg) methimazole	29
• PTU	34

Otsuka et al Clin Endocrinol 2012

Agranulocytosis

Two studies from Japan

- Retrospective study
- 50,385 subjects
- 50 agranulocytosis
- 5 pancytopenia
- 1 death

- Incidence 0.29 %
- Mean onset 69 days (11-233 days)

Watanabe et al JCEM 2012

- Registry (30 years)
- 754 cases
- 89 % agranulocytosis
- 11 % pancytopenia
- 30 deaths

- Incidence 0.10 -0.15 %
- 7% > 120 days

Nakamura et al JCEM 2013

Hepatotoxicity

- Hepatocellular necrosis with PTU
  - 2010 FDA Black Box warning
  - 1 in 10,000 adults
  - 1 in 2,000 children

Hepatotoxicity

- ♦ hepatitis
- ■ liver failure
- ▲ cholestasis

73,000 patients
Taiwan

Higher hepatitis,
but lower failure
with methimazole

Presented prior to
180 days

Dose dependent
For MMI

Wang et al Br J Clinical Pharmacology 2014

Vasculitis

- More common with PTU
- More common with duration of therapy
- Anti-neutrophil cytoplasmic antibody (ANCA) in up to 40% of patients treated with PTU
- May be fatal

Vasculitis from PTU

Tsai et al Formos J Endocrinol Metab 2010

After 12-18 months of ATD 2016

- If a patient with GD becomes hyperthyroid after completing a course of methimazole, consideration should be given to treatment with radioactive iodine or thyroidectomy. Continued low-dose methimazole treatment for longer than 12–18 months may be considered in patients not in remission who prefer this approach. *Weak recommendation, low quality evidence.*

Long-term methimazole [CMZ] versus radioiodine

- Two studies:

- Azizi et al 2005 Iran
  Eur J Endocrinol
- Villagelin et al 2015 Brazil
  Thyroid

Long-term methimazole [CMZ] versus radioiodine (Iran)

- 104 patients with recurrence after an 18 month course of MMI, age > 40, Graves' disease
- Randomized trial but high dropout rate
- 26 patients on continuous MMI 10 years
- 41 patients received RAI 100 uCi/g (3.7mBq/g)
- At baseline, no difference among the groups or dropouts

Azizi et al Eur J Endorinol 2005

MMI [CMZ] versus RAI

Parameters that were the same after 10 yr

- Free T4, T3, TSH
- Bone density

- No serious side effects (minor allergic sx)

MMI [CMZ] versus RAI

Parameters that were different

- 50 % goiter
- 6 % TSH > 5 during f/u
- 52 % positive TPO

- Cost $ 631

- 25 % goiter
- 12 % TSH >5 during f/u
- 16 % positive TPO

- Cost $ 691

MMI [CMZ] versus RAI

"Long-term continuous treatment of hyperthyroidism with MMI is safe. The complications and expense of the treatment do not exceed those of radioactive iodine therapy"

Azizi et al Eur J Endocrinol 2005

Long-term methimazole versus radioiodine (Brazil)

- 238 patients with recurrence after a 12-24 month course of MMI, age > 18, Graves' Disease
- Retrospective analysis, few dropouts
- 114 patients on MMI 2.5 – 7.5 mg
- 102 patients fixed 15 mCi RAI
- Mean follow-up 81 months
- At baseline, no difference between groups

MMI [CMZ] versus RAI

- No difference in QOL

  assessed by SF-36 questionnaires
- Higher overt and subclinical hypothyroidism in the RAI group
- Worse orbitopathy in the RAI group
- Higher body weight in the RAI group

MMI [CMZ] versus RAI

"Use of prolonged low-dose MMI treatment may be a viable therapeutic alternative for relapsed Graves' Disease patients, particularly in Graves' Orbitopathy or patients who are opposed to ablative treatment with RAI or surgery."

Villagelin et al Thyroid 2015

Surgery

Surgery

- If surgery is chosen as treatment for GD, patients should be rendered euthyroid prior to the procedure with MMI pretreatment, with or without beta-adrenergic blockade. Potassium iodide should be given in the immediate preoperative period. *Strong recommendation, weak quality evidence.*

Surgery: 2016 update

- Calcium and 25-OH-vitamin D should be assessed preoperatively and repleted if necessary, or given prophylactically. Calcitriol supplementation should be considered preoperatively in patients at increased risk for transient or permanent hypoparathyroidism. ***Strong recommendation, weak quality evidence.***

Pre-operative calcium supplementation

1 gram tid for
2 weeks pre-op

No difference in post-op PTH
Less symptoms with treatment: 9% versus 26%

Oltmann et al Ann Surg Onc 2015

Surgery

- If surgery is chosen as the primary therapy for Graves' disease, near-total or total thyroidectomy is the procedure of choice. *Strong recommendation, moderate quality evidence.*

Surgery: total versus subtotal

- Meta-analysis % hyperthyroid

- 538 patients total 0 %
- 5542 patients subtotal 8 %

Palit et al 2000 J Surg Research

Surgery

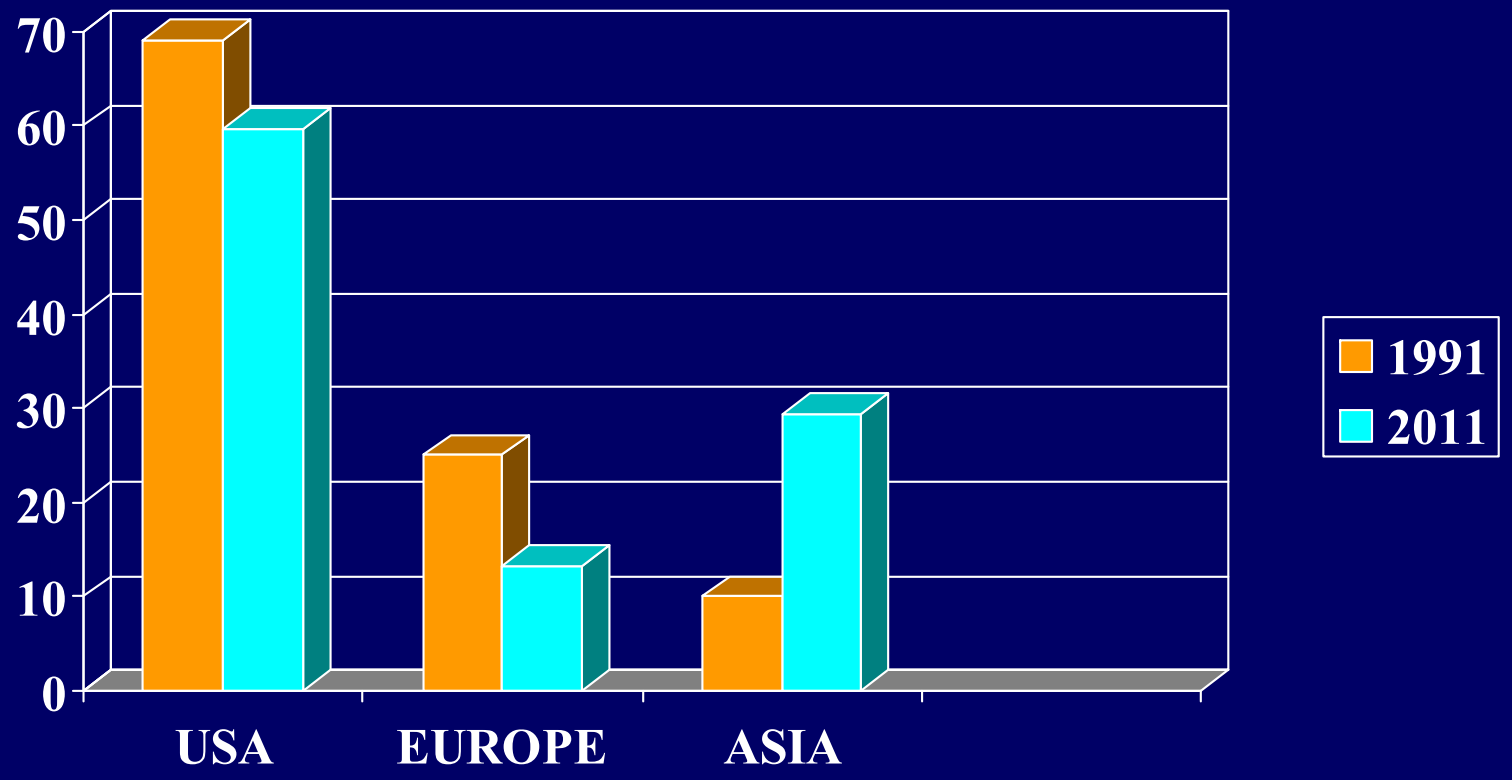
- If surgery is chosen as the primary therapy for Graves' disease, the patient should be referred to a high-volume thyroid surgeon. *Strong recommendation, moderate quality evidence.*

Surgical Complications

Procedures / year	1-9	10-29	30-100	>100
Adjusted rate	8.6	6.1	6.1	5.1* %

Sosa et al Ann Surg 1998

Physician Preference for Radioiodine



Solomn et al JCEM,1990; Burch et at JCEM 2012

Iodine as Primary Therapy 2016

- Potassium iodide may be of benefit in select patients with hyperthyroidism due to GD, who have had adverse reactions to ATD, and have a contraindication or aversion to RAI (or additional RAI) or surgery. Treatment may be more suitable for patients with mild hyperthyroidism, or a prior history of RAI. *Insufficient evidence to determine net benefits or risks.*

Iodine as Primary Therapy

- 44 Japanese patients
- 66 % controlled for 9-28 years (mean 18 yrs)
- 39 % achieved a remission after mean 7 years

- 10% no benefit
- 25% only transient benefit

Okamura et al JCEM 2014

Case 2

- 29 year old woman
- Graves disease diagnosed 7 months ago
- On methimazole 10 mg daily
- Free T4 1.5 ng/dl, T3 138, TSH 0.4
- She would like to become pregnant

Diagnosis of hyperthyroidism during pregnancy: a challenge

- TBG increases by week 7, peaks by week 16:

  increases total T4 and total T3
- HCG highest first trimester:

  stimulates T4 release and reduces TSH
- Low albumin and high FFA:

  spurious results in automated free T4 assays

Free T4 in pregnancy

	non-pregnant	1st	2nd	3rd
Total T4	8.7	10.6	10.5	11.0
Free T4 index	7.7	8.7	7.5	8.0
Free T4 "A"	1.1	1.2	0.85	0.89
Free T4 "B"	1.3	0.97	0.69	0.70

Lee et al Am J Obstet Gynecol 2009

Assessment of hyperthyroidism during pregnancy

- The diagnosis of hyperthyroidism in pregnancy should be made using serum TSH and either

  total T_4 and T_3, with total T4 and T3 reference ranges increasing to 1.5 times above the nonpregnant range by the 2nd and 3rd trimester,

  or free T_4 and free T_3 estimations with trimester-specific normal reference ranges.

  Strong recommendation, weak quality evidence.

Hyperthyroidism in pregnancy

- Transient hCG-mediated thyrotropin suppression in early pregnancy should not be treated with antithyroid drug therapy. *Strong recommendation, weak quality evidence.*

Hyperthyroidism during pregnancy Treatment

- Antithyroid drug therapy should be used for hyperthyroidism due to Graves' disease that requires treatment during pregnancy. PTU should be used when antithyroid drug therapy is started during the first trimester. Methimazole should be used when ATD therapy is started after the first trimester. *Strong recommendation, weak quality evidence.*

Teratogenesis from Anti-thyroid drugs

- Methimazole (MMI) and carbimazole (CMZ) have been associated with embryopathy
- Previously, reports of birth defects with PTU were rare
- But PTU has been associated with fulminant hepatocellular necrosis
- 2011 ATA guidelines: PTU first trimester, then MMI

Birth Defects
Danish Nationwide Study

- Danish Health Registries
- All births 1996-2008
- All ATD prescriptions 1995-2008
- 1820 children exposed to ATD early pregnancy
- All birth defects reported to age 2 (ICD-10)

Andersen et al JCEM 2013

Birth Defects with ATDs

811 730	no ATDs	5.7 %
3 543	controls	5.4
1 097	PTU	8.0
564	MTZ / CMZ	9.1

Control group: use of ATD > 12 months before or after the pregnancy

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- Figure: Odds ration for birth defects

Methimazole Embryopathy

- Choanal atresia
- Esophageal atresia
- Omphalocele
- Omphalomesenteric duct anomalies
- Aplasia cutis

Birth Defects after PTU

- Face and neck

  periauricular cysts
- Urinary tract

  congenital hydronephrosis

Most required a surgical procedure

Additional cases identified after age 2

Andersen et al Thyroid 2014

Patients switching ATDs per 2011 ATA Guidelines

- Based on prescriptions filled up to 10th week
- 159 patients (149 MMI to PTU)
- 10.1% had birth defects
- Defects include those from both groups of embryopathy
- Does switching expose the fetus to the risks of both drugs?

Imperfect Strategies for Anti-thyroid Drugs during Pregnancy

- Switching may result in transient maternal hypothyroidism during the 2nd trimester
- ATDs may also cause fetal hypothyroidism
- Should patients switch to PTU before they try to conceive?
- Should we discourage the elective use of ATDs during pregnancy?

2016 Updates

- In women who develop hyperthyroidism during their reproductive age range, the possibility and timing of future pregnancy should be discussed. Because of the risks of the hyperthyroid state on pregnancy and fetal outcome, we suggest that women should postpone pregnancy until they have become euthyroid with therapy. *Strong recommendation, weak quality evidence.*

2016 Updates

Women with Graves' hyperthyroidism who are planning a pregnancy could consider:

1) Changing to PTU prior to conception
2) Changing to PTU when hCG positive
3) Stopping ATD when hCG positive
4) Definitive therapy before conceiving

Weak recommendation; low quality evidence

2016 Updates

- We suggest that women with hyperthyroidism caused by Graves' disease that require high doses of ATD to achieve euthyroidism should be considered for definitive therapy before they become pregnant. *Weak recommendation, weak evidence.*

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- Figure: TRAb levels after radioiodine, surgery, or ATD

Factors favoring timing of switching or stopping ATD first trimester

SWITCHING

Young “fertile” woman:

Favor change to PTU preconception

Older less fertile woman:

Favor switch as soon as pregnancy diagnosed

STOPPING

Mild hyperthyrodism, low dose MMI, > 6 months on MMI, TRAb normal: favor stopping

Use of Iodine during pregnancy 2017 ATA Pregnancy Guidelines

- Excessive doses of iodine exposure during pregnancy should be avoided, except in preparation for the surgical treatment of GD. Clinicians should carefully weigh the risks and benefits when ordering medications or diagnostic tests that will result in high iodine exposure.

  Strong recommendation, moderate-quality evidence.

  "Excessive" = >500 mcg / day 1 drop SSKI = 50 mg

Iodine treatment during pregnancy

- 283 Japanese woman who stopped methimazole and shifted to iodine first trimester
- Hyperthyroidism was not as well controlled, but
- Fewer birth defects 1.53 versus 4.14 %
- More live births 92 versus 85%

Yoshihara et al 2015 Thyroid

Iodine treatment during pregnancy

- 35 Japanese patients taking 6 to 40 mg of iodine daily
- Only one infant was born with subclinical hypothyroidism

Momotani et al 1992 JCEM

2016 Update
Insufficient Evidence

Patients started on or switched to PTU during the first trimester could consider:

1) Switch to MMI at the beginning of the second trimester
2) Continue PTU as long as ATD treatment is needed for the duration of the pregnancy.

Titration of ATD during pregnancy

- The lowest possible dose of ATD needed to keep the mother's thyroid hormone levels at or slightly above the reference range and the TSH below the reference range.

- Thyroid function should be assessed monthly, and the ATD dose adjusted, as required.

Surgery during pregnancy

- When thyroidectomy is necessary for the treatment of hyperthyroidism during pregnancy, the surgery should be performed if possible during the 2nd trimester. *Strong recommendation, weak quality evidence.*

TRAb during pregnancy

- Patients found to have GD during pregnancy should have TRAb levels measured at diagnosis using a sensitive assay and, if elevated, again at 22–26 weeks of gestation.
- TRAb levels measured at 22–26 weeks of gestation should be used to guide decisions regarding neonatal monitoring. *Strong recommendation, weak quality evidence.*

Why is TRAb important during pregnancy complicated by hyperthyroidism?

- Indication of disease activity
- Disappearance suggests ATD can be stopped—avoid fetal hypothyroidism
- High levels 3rd trimester: Risk of fetal hyperthyroidism
- High levels 3rd trimester: Risk of neonatal hyperthyroidism

TRAb and Neonatal Hyperthyroidism

9 of 49 neonates were hyperthyroid

5 required treatment

All mothers had TRAB > 5

All had ATD during 3rd trimester

Abeillon-du Payrat et al
Eur J Endocrinol
2014

TRAb is also important in euthyroid woman s/p RAI or surgery

- Patients who were treated with RAI or thyroidectomy for GD prior to pregnancy should have TRAb levels measured using a sensitive assay either initially at 22–26 weeks of gestation, or initially during the first trimester and, if elevated, again at 22–26 weeks of gestation. *Strong recommendation, weak quality evidence.*

- Toxic adenoma and toxic nodular goiter
- Thyroid storm
- Pediatric thyrotoxicosis
- Graves’ orbitopathy
- Drug-induced thyrotoxicosis (amiodarone)
- Destructive thyroiditis
- Other causes of thyrotoxicosis