Hyperthyroidism
Facts

- Prevalence 0.5-1.0%, more common in women
- Thyrotoxicosis is excess thyroid hormones from endogenous or exogenous sources
- Hyperthyroidism is excess thyroid hormones from thyroid gland
- Common causes include Graves' disease, TMNG, thyroiditis
- Diagnosis established by low TSH, high FT4, high T3, and RAIU

Hyperthyroidism
Etiology

Autonomous overactivity
- Graves' disease
- Hashimoto's thyroiditis
- Plummer's disease
- Toxic nodule

Hormonal discharge
- Granulomatous thyroiditis
- Lymphocytic thyroiditis

Pituitary TSH hypersecretion
- Inappropriate TSH secretion
- Thyrotrophic pituitary adenoma

Ectopic thyroid stimulators, eg, HCG

Metastatic follicular carcinoma

Struma ovarii

Hyperthyroidism
Common Causes

	%
Graves' disease	70-80
Toxic MNG	5-15
Thyroiditis	5-15

Graves' Disease

Symptoms	Signs
Nervousness	Goiter
↑ sweating	Exophthalmos
Heat intolerance	Tremor
Palpitations	Tachycardia
Fatigue	Atrial fibrillation
Weakness	
Weight loss	
Eye	

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Toxic Multinodular Goiter

- Elderly patient
- Longstanding goiter
- Heart disease: ↑ HR, AF, CHF
- Unexplained weight loss
- Depression
- Anxiety

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Comparison of Graves' Disease and Toxic MNG

	GD	TMNG
Goiter	Diffuse	Nodular
Size	Small	Large
Growth	Rapid	Slow
Age (yr)	<45	>50
Symptoms	Rapid onset	Slow onset
Histology	Parenchymatous, hyperplasia, uniform intense iodine metabolism in follicles	Variable follicular size and intensity of iodine metabolism

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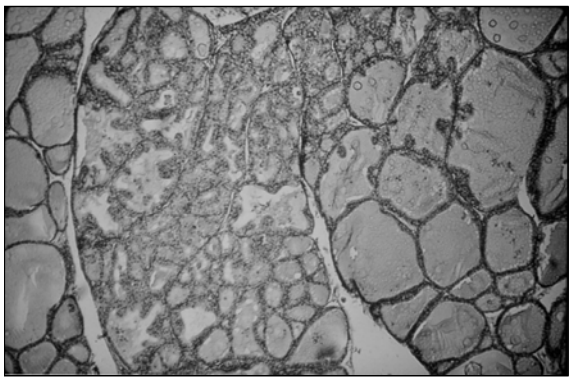

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Symptoms and Signs of Hyperthyroidism

Less common than younger pt

- Goiter and ophthalmopathy
- Heat intolerance
- Tachycardia, plapitations
- Muscular weakness

More common than younger pt

- Tremor
- Anorexia
- CHF, AF
- Muscular wasting

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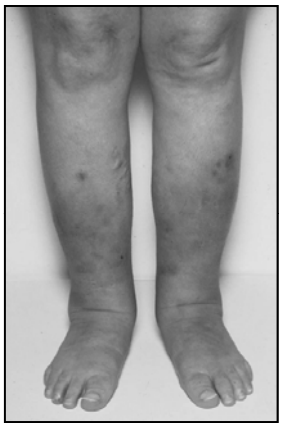

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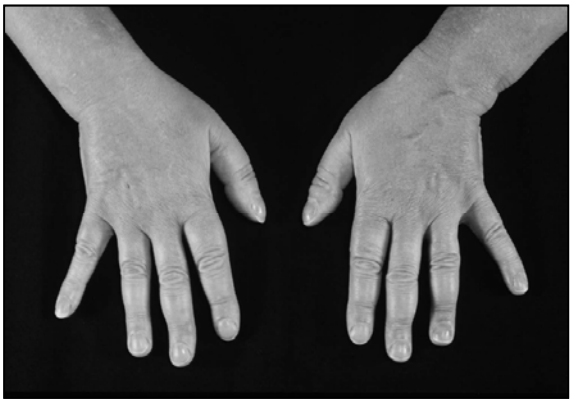

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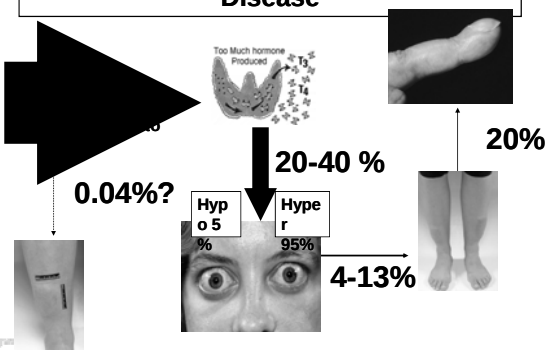
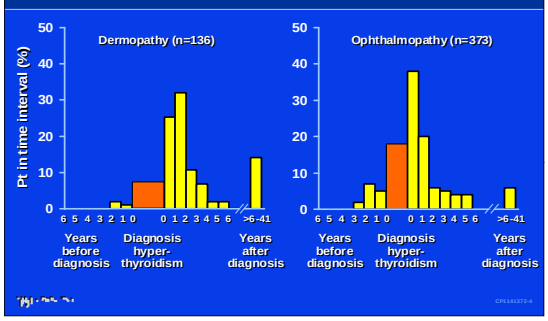
Fatourechi et al 1998-2002

Manifestations of Autoimmune Thyroid Disease

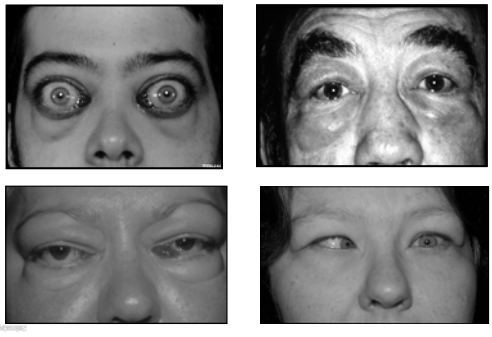


Onset of Dermopathy and Ophthalmopathy



Fatourechi V, Garrity JA, Gorman CA et al. J Endocr Invest 16:433-43?

Graves' Ophthalmopathy The Clinical Spectrum



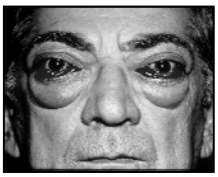
Pathophysiology of GO

Enlargement...

- **of muscles and adipose tissues in the confines of the bony orbit**

leads to….

- **proptosis, venous congestion, chemosis, injection, periorbital edema, and optic neuropathy**



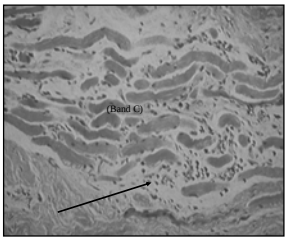
Pathophysiology of GO

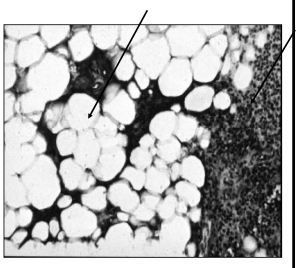
Fibrotic restriction of extraocular muscles

leads to...

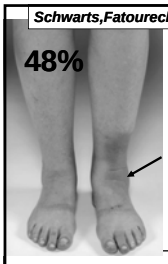
- **diplopia, increased intraocular tension**

Histopathology of GO



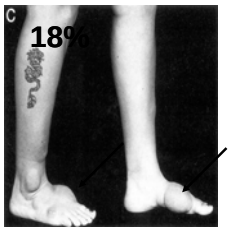


Schwarts,Fatourechi et al, 2002



Non-pitting Edema

Plaque Type



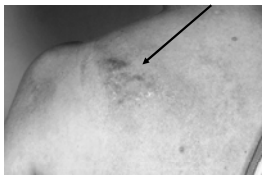
Nodular Thyroid Dermopathy

Thyroid Dermopathy

5 %

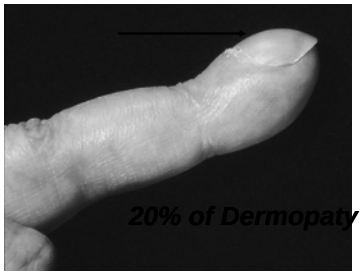
Elephantiasis

Dermopathy in scar tissue



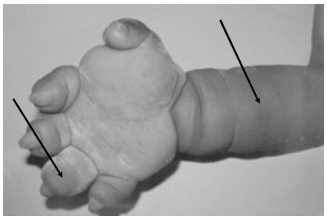
Dermopathy on the shoulder

Thyroid Acropachy
Clubbing in Thyroid Dermopathy



Thyroid Acropachy

Severe Acropachy with severe Dermopathy



Hyperthyroidism
Treatment Options

- **Thionamides**
- **Radioiodine (^{131}I)**
- **Stable iodine (^{127}I)**
- **Thyroidectomy**
- **Miscellaneous**

  Lithium, beta-adrenergic blockers, oral cholecystographic agents

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Thionamides

	Initial dose (mg/d)	Main-tenance dose (mg/d)	Serum half-life (hr)	Incidence of side effects (%) Major	Minor
Carbimazole	**30-60**	**5-20**	**–**	**0.7**	**2.0**
Methimazole	**30-60**	**5-20**	**6-9**	**0.3**	**5.0**
Propylthiouracil	**300-600**	**50-200**	**1-2**	**0.3**	**3.0**

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ATD Comparisons

Parameter	PTU	MMI
Response time	Slower	Faster
Toxicity	Dose related	Dose related
Compliance	Worse	Better
Effect on ^{131}I	Decrease	None

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ATD FAQs

Q	A
• Optimal duration of therapy?	12-18 mo
• Dose influences remission?	Probably not
• Higher dose causes more rapid control?	Yes
• Predictors of remission?	Small goiter, mild disease, low TRAb titer
• Prevents post RAI exacerbation?	Maybe
• Does T4 enhance remission?	No

Cooper DS: JCEM 88:3474, 2003

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ATD Remission?

Sign	Test
↓ goiter size	Palpation
↓ ATD dose	FT4
↓ RAIU	RAIU
↓ thyroid autonomy	TSH

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Why Not Antithyroid Drugs?

- Prolonged therapy
- At least 50% relapse after discontinuation of treatment
- Side effects

^{131}I Treatment

- Treatment of choice for
  - Hyperthyroid, nonpregnant adult pt with diffuse goiter and adequate ^{131}I uptake
- Complications
  - Persistent hyperthyroidism
  - Permanent hypothyroidism

^{131}I Treatment

- Simple
- Effective
- Economical
- Complications depend on ^{131}I dose used
  - Recurrent hyperthyroidism
  - Permanent hypothyroidism

Calculation of ^{131}I Dose

$$\text{Dose (mCi)} = \frac{\text{est thyroid wt x uCi/est gm x 100}}{\text{RAIU \%}}$$

Hyperthyroidism
Low RAIU

- Thyroiditis
- Graves' disease with I overload
- IIT
- Exogenous thyrotoxicosis
- Ectopic tissue, eg, struma ovarii

Painless Thyroiditis vs Graves' Disease

	PT	GD
Onset	Abrupt	Insidious
Clinical hyperthyroidism	Common	Universal
Goiter	Common	Universal
Exophthalmos	Absent	Common
Duration	Wk to mo	Mo to yr
Thyroid hormone (TSH, T3, FT4)	↓, ↑, ↑	↓, ↑, ↑
^{131}I uptake	Absent	Elevated
TPO	Infrequent	Common

Factors Limiting Usefulness of ^{131}I Therapy

- Low thyroid uptake of ^{131}I
- Toxic nodular goiter
- Pregnancy
- Childhood?

Hyperthyroidism
Surgery

- Choose an experienced surgeon
- Decreased experience with surgical treatment of hyperthyroid patient
- Bilateral subtotal thyroidectomy is preferred
- Complications include hemorrhage, hypopara, VC paralysis and hypothyroidism

Surgery

Complications	%
Mortality	0
Persistent or recurrent hyperthyroidism	<1-18
Vocal cord paralysis	0-4
Hypoparathyroidism	0-3.6
Hypothyroidism	4-30

Surgery

Preop preparation

- Need for Lugol's solution
- Cord check
- Discussion of general and specific risks
  - Incidence of hypoparathyroidism
  - Incidence of cord paralysis
  - Possibility of hypothyroidism
  - Eye problem
- Need for follow-up

Surgery

Indicated

- Plummer's disease (toxic nodular goiter)
- Pregnancy
- Children
- Graves' disease with large goiter
- When coexisting neoplasm suspected

Surgery

Contraindicated in

- Poor surgical risk pt
- Pt with recurrent thyrotoxicosis who is postop thyroidectomy with vocal cord paralysis

Surgery

Recommend for

- **Toxic nodular goiter**
- **Solitary nodules**
- **Pregnancy**
- **Children**

Why Not Surgery?

Why operate when there are acceptable alternatives?

Hypoparathyroidism	**1% at best**
Hypothyroidism	**Approximately 40% at 5 years**
Recurrent hyperthyroidism	**Varies inversely with postop hypo-thyroidism**

Beta-Adrenegic Antagonists

Popranolol (Inderal)	**10-40 mg qid**
Metoprolol (Lopressor)	**50-100 mg bid**
Atenolol (Tenormin)	**50-100 mg qd**
Nadolol (Corgard)	**400-200 mg qd**

Beta-Adrenegic Antagonists

- Thyroid crisis or near-crisis
- During interval prior to therapy
- Preoperative therapy, preferably with iodine
- Prepares pt for surgery in 1 wk
- Possibly as sole therapy in mild cases

Pregnancy

Potential complications

- Maternal

  Miscarriage, preterm delivery, HTN, thyroid storm

- Fetal

  Hyperthyroidism, prematurity, stillbirth, IU growth retardation

Pregnancy

- Antithyroid drugs or surgery equally effective
- Radioiodine contraindicated
- ATD cross the placenta
- With ATD maintain T4 in the upper normal range for pregnancy
- Surgery favored in second trimester
- Preoperative preparation with iodine and/or PTU

Pregnancy

Postpartum hyperthyroidism

- Autoimmune basis
- Has low RAIU
- Hypothyroidism may follow hyper-thyroidism
- May spontaneously resolve
- Treat symptomatic patients

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CP1124522-3

Hyperthyroidism
Children

- Graves' disease is most common cause
- MMI 0.5-1.0 mg/kg/day or PTU 5-10 mg/kg/day is treatment of choice
- Remission occurs in 30-60% in 2 years
- Subtotal thyroidectomy for those with large goiters
- ^{131}I appears to be safe

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Hyperthyroidism
Choice of Treatment

Toxic adenoma	^{131}I or surgery
Toxic nodular goiter	Surgery
Graves' disease in children	Drugs or surgery
Graves' disease in pregnancy	Drugs or surgery
Recurrent Graves' disease	^{131}I
Graves' disease in middle-aged or elderly patients	^{131}I
Increased surgical risk	^{131}I or drugs

CP1124522-43

Hyperthyroidism
Therapy

Personal comments

- ATD are accompanied by side effects and high relapse
- Surgical complications may be increasing as the numbers of trained surgeons decline
- ^{131}I is the preferred initial Rx for most patient with Graves' disease
- Surgery is preferred for large hot nodules
- Genetic hazards of ^{131}I have been overstated — younger patients can be safely treated
- Current findings do not support the contention that ^{131}I therapy is an important initiator of ophthalmopathy

CP1124522-44

CP1124522-45