



# Thyroid Disorders

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Diabetes, Thyroid, Endocrinology and Metabolism

# Outline

- Diagnostic Tests
- Hyperthyroidism
- Hypothyroidism
- Thyroiditis
- Goiter
- Thyroid Cancer

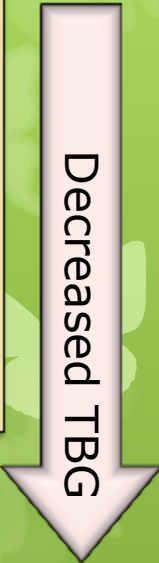
The background is a light green gradient with several white butterfly silhouettes scattered across it. The butterflies are of various sizes and orientations, some appearing as faint outlines and others as more solid shapes. The overall aesthetic is clean and nature-themed.

# Diagnostic Tests

# Thyroid Function Tests

- TSH
- Total Hormones (Total T3 & Total T4)
- Free Hormones (Free T3 and Free T4)

Elevated Total T4 & T3



Decreased Total T4 & T3

Total  
T3 & T4

Free  
T3 & T4

Highly protein  
bound

Affected by TBG  
levels, acute  
illness and drugs

Unbound form

Biologically  
available  
hormone pool

Not affected by  
TBG levels

**Measurement of the free unbound hormones are preferable**

# Thyroid patterns

Thyroid Disorder	TSH	Free T4	Total T4	Signs and Symptoms
<b>Hyperthyroidism</b>	Low	High	High	Present
<b>Subclinical Hyperthyroidism</b>	Low	Normal	Normal	Absent
<b>Isolated T3 Toxicosis</b>	Low	Normal	High	Present
<b>Primary Hypothyroidism</b>	High	Low	Low	Present
<b>Secondary Hypothyroidism</b>	Low or Inappropriately Normal	Low	Low	Absent/Present
<b>Subclinical Hypothyroidism</b>	High	Normal	Normal	Absent
<b>Increased TBG</b>	Normal	Normal	Increased	Absent
<b>Decreased TBG</b>	Normal	Normal	Decreased	Absent

# Thyroid Proteins & Antibodies

- Thyroglobulin (Tg)
  - Follow up of thyroid cancer
  - To rule out thyrotoxicosis factitia
  - Elevated in thyroiditis
- Antibodies to thyroid proteins
  - Anti thyroglobulin (Anti Tg)
    - Follow up of thyroid cancer patients
    - Autoimmune thyroid illness (not routinely included)
  - Anti Thyroid Peroxidase (Anti TPO)
    - Autoimmune thyroid illness
  - Anti TSH receptor (TRAB)
    - TSH stimulating – Hyperthyroidism
    - TSH blocking - Hypothyroidism

Patient Group	TSH receptor Antibody	Thyroglobulin (Tg) Antibody	Thyroid Peroxidase (TPO) Antibody
General Population	0%	5-20%	8-27%
Grave's Disease	80-95%	50-70%	50-80%
Autoimmune thyroiditis	10-20%	80-90%	90-100%

# Radionuclide Imaging

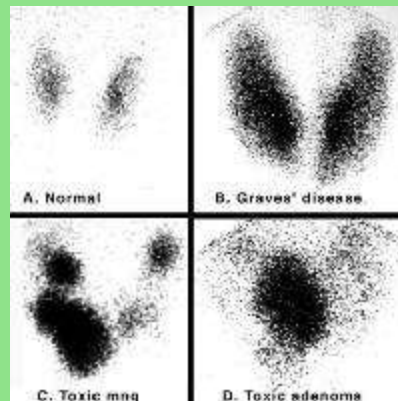
The thyroid gland selectively transports radioisotopes of iodine ( $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ) and  $^{99\text{m}}\text{Tc}$  pertechnetate, allowing thyroid imaging and quantitation of radioactive tracer fractional uptake.

## Thyroid Uptake

- Iodine uptake measures thyroid function
- High in Graves' Disease
- Low in Thyroiditis (hyperthyroid phase)

## Thyroid Scan

- Imaging

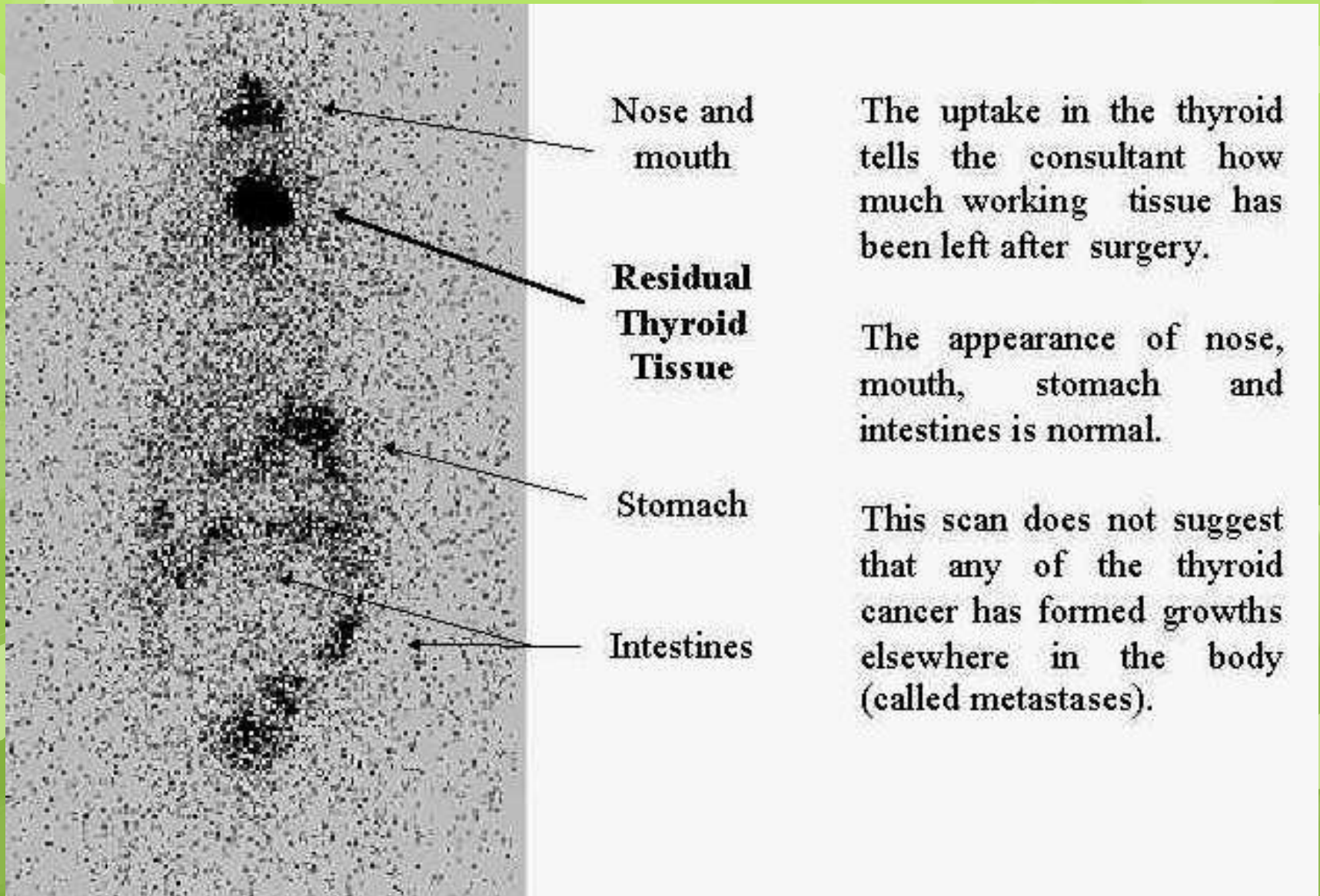


## Whole Body Scan

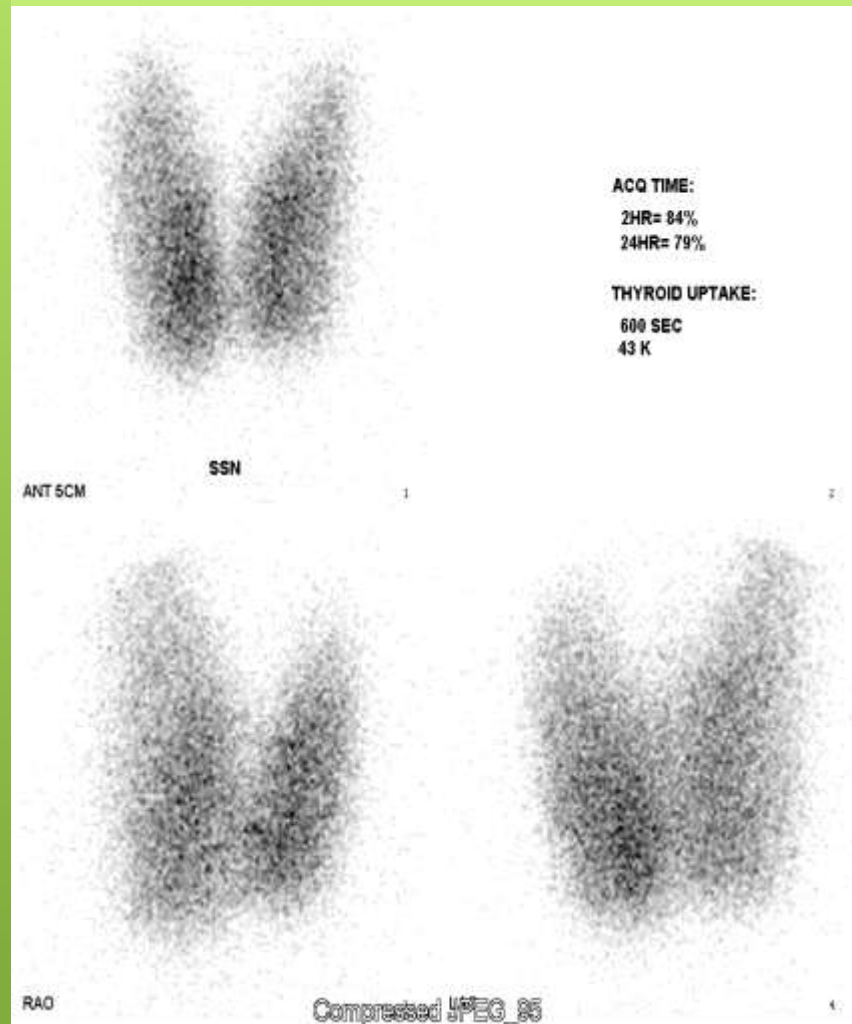
- Follow up in Thyroid Cancer



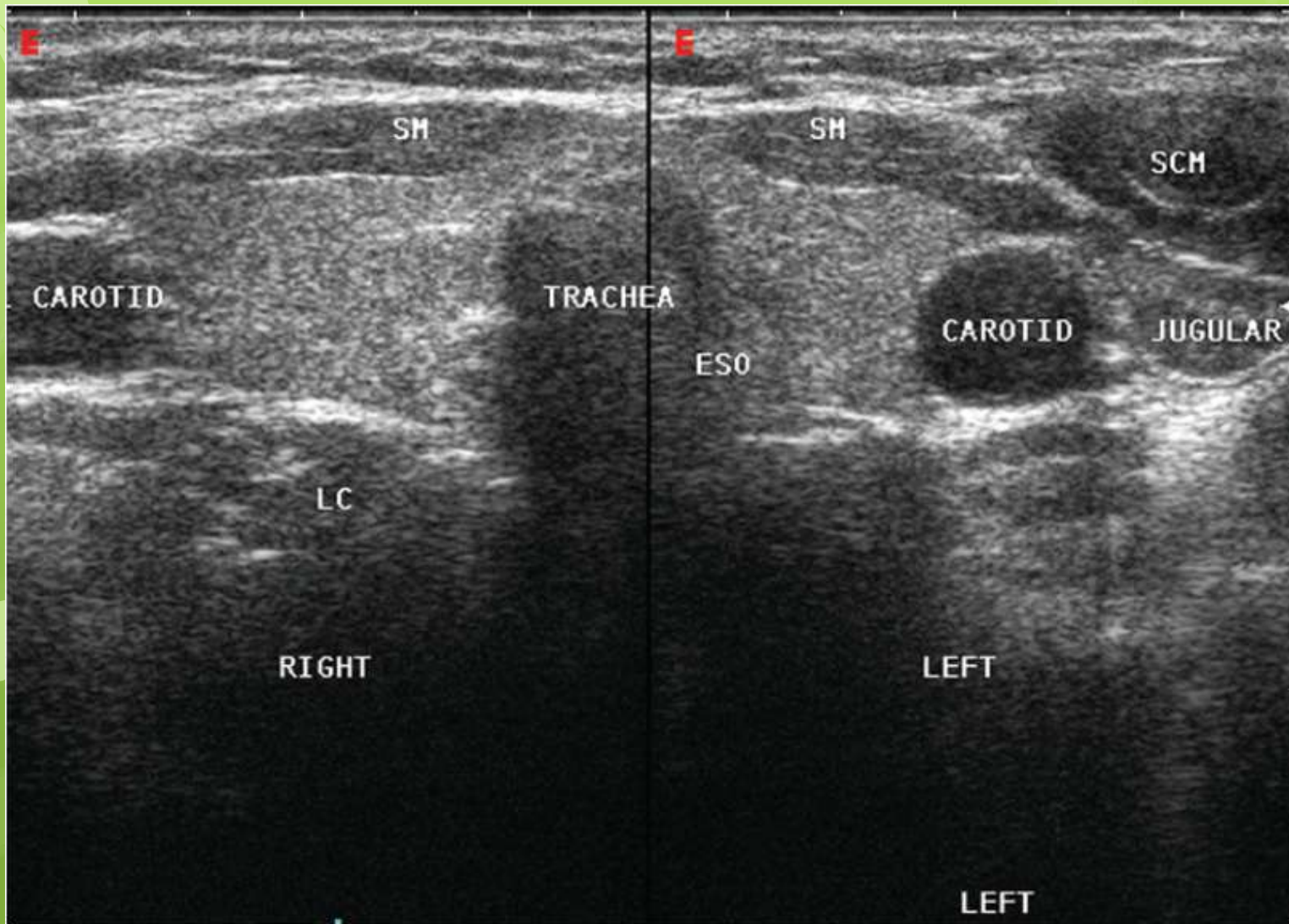
# Radionuclide Imaging: Whole Body Scan



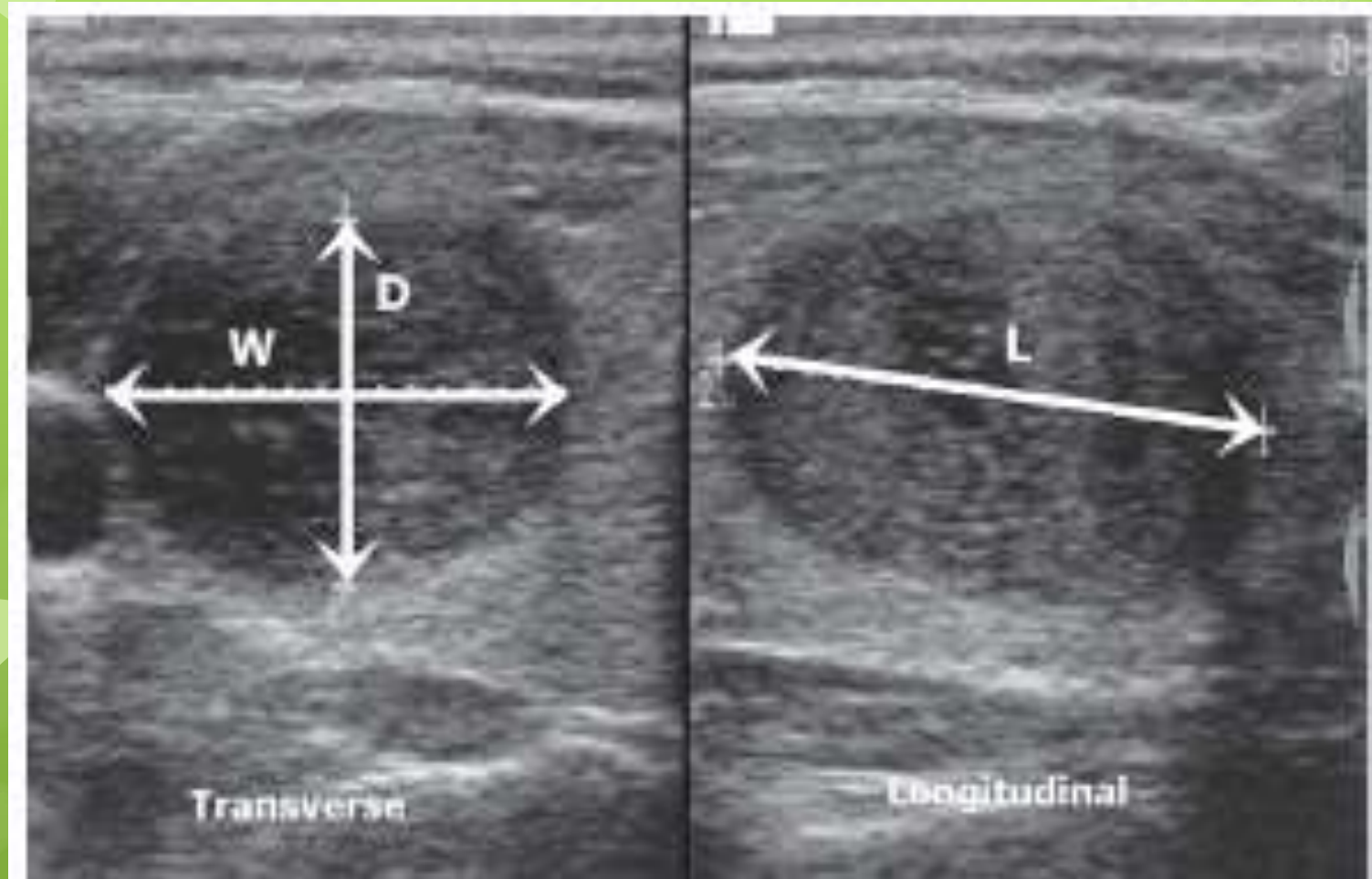
# Radionuclide Imaging: Thyroid Uptake



# Ultrasound of the Thyroid



# Ultrasound of the Thyroid



The background is a solid green gradient with several white butterfly silhouettes scattered across it. The butterflies are of various sizes and orientations, some appearing as simple outlines and others with more detail. The overall aesthetic is clean and modern.

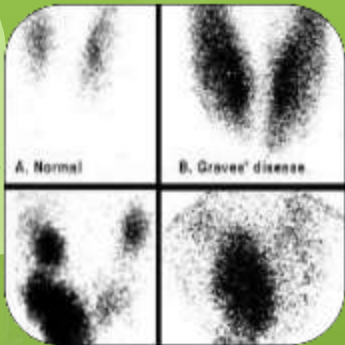
# Hyperthyroidism

# Definition of Terms



## Thyrotoxicosis

- State of thyroid hormone excess



## Hyperthyroidism

- Thyrotoxicosis due to excessive thyroid function

# Signs and Symptoms

**TABLE 335-7** SIGNS AND SYMPTOMS OF THYROTOXICOSIS (DESCENDING ORDER OF FREQUENCY)

## Symptoms

Hyperactivity, irritability, dysphoria  
Heat intolerance and sweating  
Palpitations  
Fatigue and weakness  
Weight loss with increased appetite  
Diarrhea  
Polyuria  
Oligomenorrhea, loss of libido

## Signs<sup>a</sup>

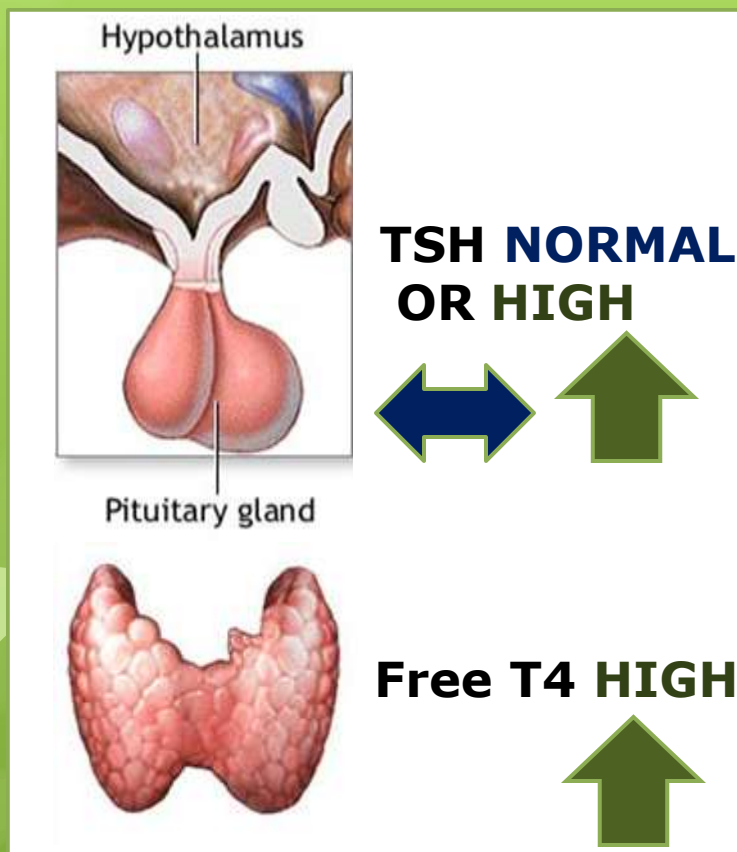
Tachycardia; atrial fibrillation  
in the elderly  
Tremor  
Goiter  
Warm, moist skin  
Muscle weakness, proximal  
myopathy  
Lid retraction or lag  
Gynecomastia

<sup>a</sup>Excludes the signs of ophthalmopathy and dermopathy specific for Graves' disease.

**Suspected  
Hyperthyroidism?**



**Measure TSH and Free T4 (FT4)**



### **TSH Dependent Cause**

#### **TSH Secreting Pituitary Adenoma**

- Pituitary MRI
- Transphenoidal Surgery
- Thyroid Ablation/Anti thyroids
- Somatostatin Analogues

### **TSH Independent Cause**

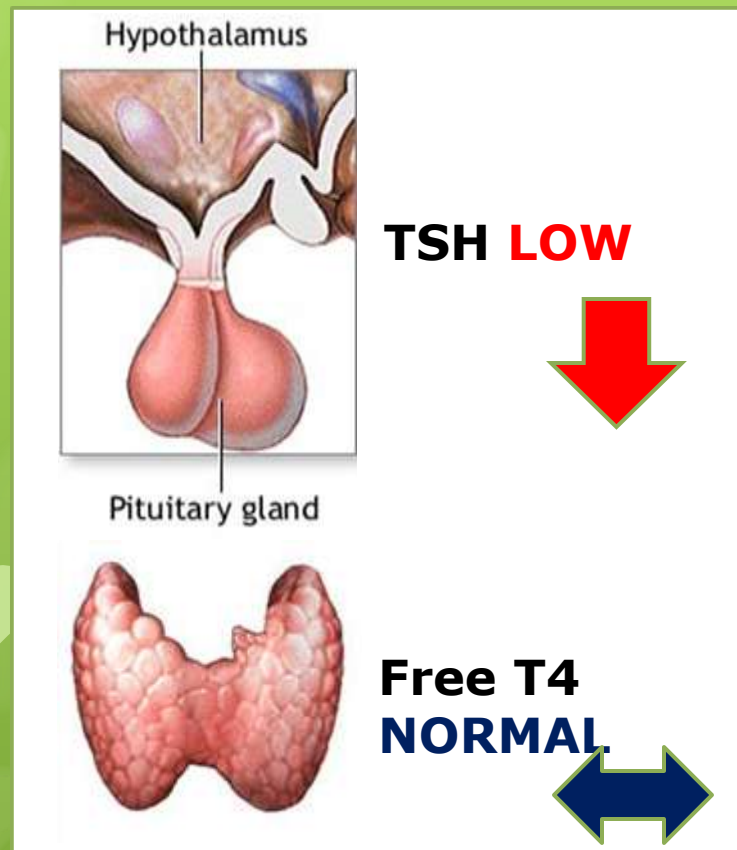
#### **Thyroid Hormone Resistance Syndrome**



**Suspected  
Hyperthyroidism?**

**Measure TSH and Free T4 (FT4)**

**Check Free T3 (FT3)**



**Free T3 High**

**Isolated T3 Toxicosis**

- 2-5%
- Treat as Hyperthyroidism

**Free T3 Normal**

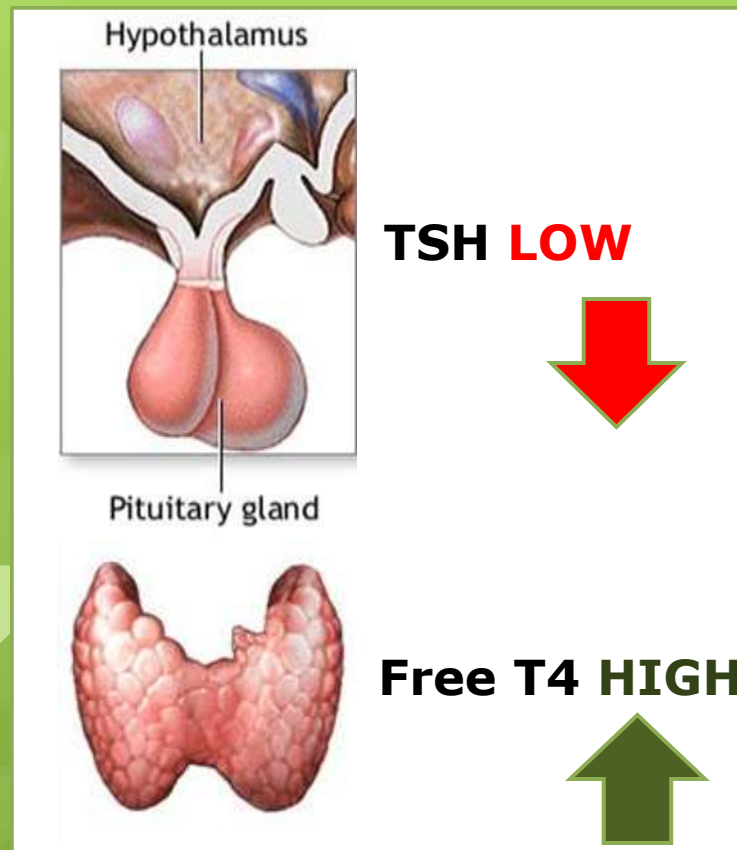
**Subclinical  
Hyperthyroidism**

- Repeat Thyroid function after a few months and watch out for Overt Hyperthyroidism

**Suspected  
Hyperthyroidism?**

**Measure TSH and Free T4 (FT4)**

**Thyroid Scan & Uptake**



**Diffuse Uptake**

Graves' Disease  
Chorionic Gonadotropin  
Induced Hyperthyroidism

**Increased Nodular Uptake**

Toxic Nodular Goiter

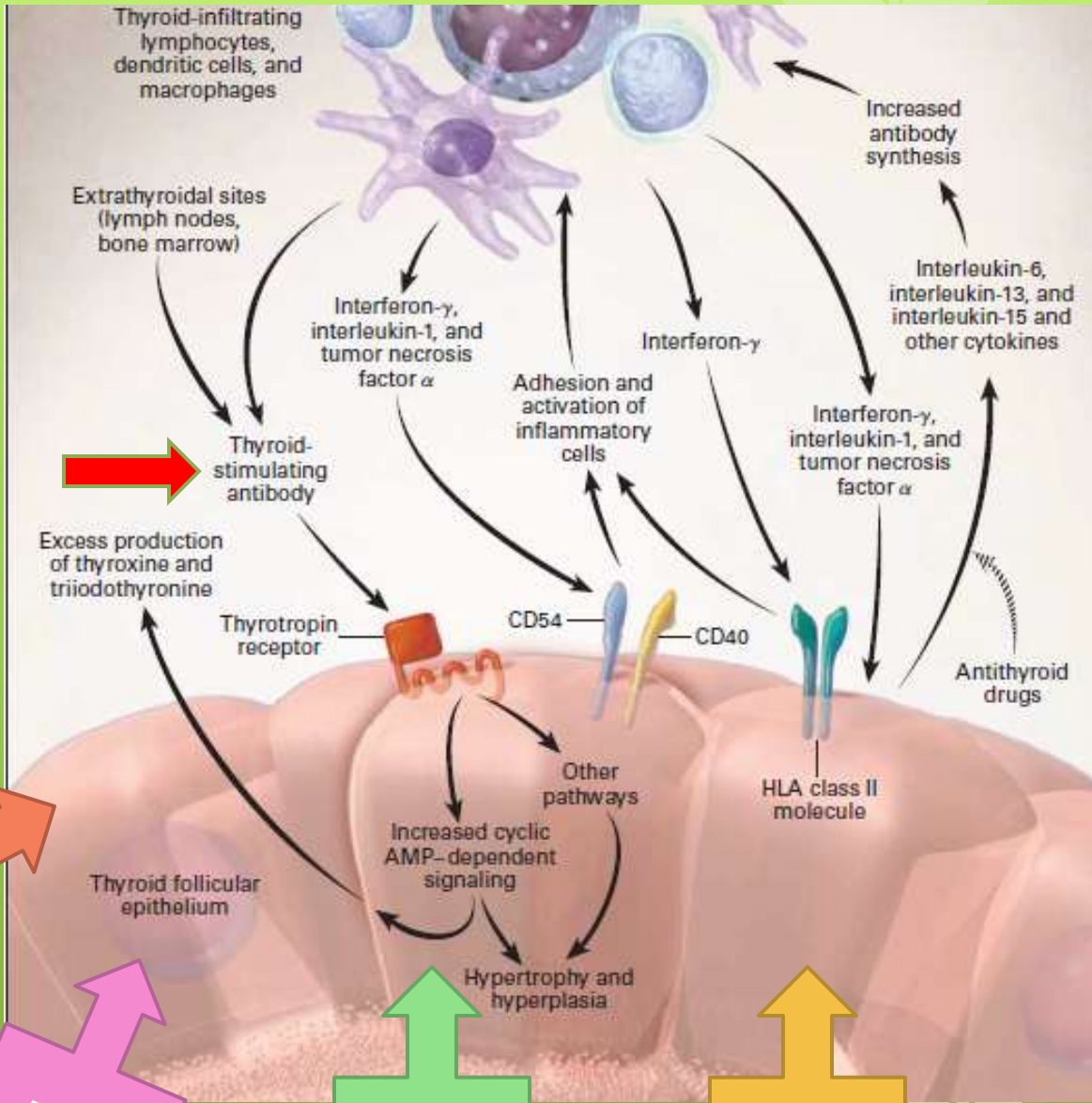
**Decreased Uptake**

- Thyroiditis
- Iatrogenic hyperthyroidism
- Struma ovarii

# Graves' Disease Pathogenesis

TSH-R stimulating antibodies (TRAB) causes hyperthyroidism

Inflammatory cells produces Cytokines such as IL-1, TNF alpha and Interferon alpha that triggers activation of other inflammatory cells, leading to a vicious cycle.



Smoking

Post partum

HLADR  
CTLA-4

stress



## Medical treatment

Thionamides:  
Propylthiouracil  
Methimazole  
High risk of recurrence  
Adverse effects:  
Hepatotoxicity,  
Agranulocytosis

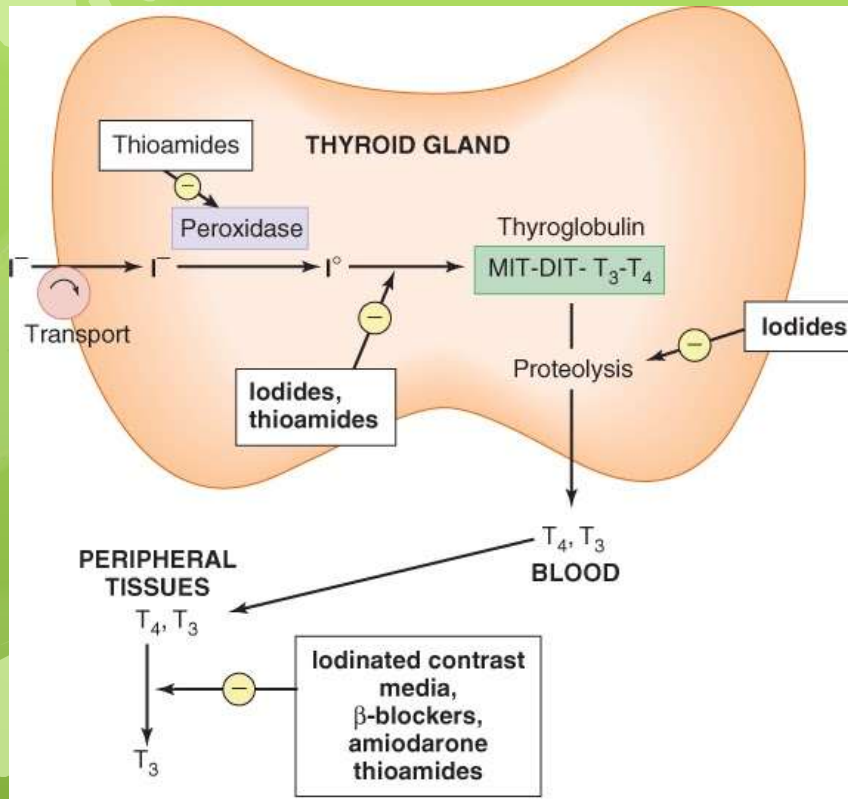
## Surgery

Subtotal or Near total thyroidectomy  
Risks of thyroid surgery:  
hypothyroidism,  
damage to recurrent laryngeal nerve,  
hypoparathyroidism

## Radioactive Iodine

Non invasive – capsule or liquid form  
Radiation Thyroiditis  
Avoid in pregnancy or breastfeeding  
Avoid in children  
Risk of hypothyroidism  
May worsen ophthalmopathy

# THIONAMIDES



- Inhibits oxidative process required for iodination of tyrosine groups
- Inhibits coupling of iodotyrosines to form  $T_3$  and  $T_4$
- PTU blocks peripheral conversion of  $T_4$  to  $T_3$

# Methimazole vs Propylthiouracil

Table 1

Comparison of characteristics of the thionamides methimazole and propylthiouracil in the treatment of Graves' disease

Characteristic	Methimazole	Propylthiouracil
Relative potency	10–50	1
Administration	Oral	Oral
Absorption	Nearly complete	Nearly complete
Binding to serum proteins	Negligible	80%–90%
Serum half-life (hours)	4–6	1–2
Volume of distribution (L)	40	20
Duration of action (hours)	> 24	12–24
Metabolism during liver disease	Decreased	Normal
Metabolism during kidney disease	Normal	Normal
Transplacental passage	Low	Even lower
Level in breast milk	Low	Even lower
Inhibition of T4/T3 conversion	No	Yes
Dosing <sup>a</sup>	1–2 times daily	2–3 times daily

Hegedus, Treatment of Graves Disease: Evidence Based and Emerging Modalities; Endocrinol Metab Clin N Am 38 (2009) 355–371



# THIONAMIDE USE

Drug  
initiation

- Monitor thyroid function every month 1<sup>st</sup> 3 months

2 weeks

- Decreased nervousness, palpitations
- Increased strength and weight gain

6 weeks

- Normalization of metabolic state
- Start dosage reductions

Monitoring  
Phase

- Maintenance dose: 5-10 mg MMI or 100-200 mg PTU
- Monitor TFT q2-3 mos

- Thyroid Gland Size
  - Decrease 1/3-1/2
  - Unchanged or enlarged remaining half
- Thyroid Function Tests pattern
  - TSH may remain subnormal for 6 months



## Lithium

- Alternative to thionamides

## Iodine

- Saturated solution of Potassium Iodide (SSKI), ipodate, iopanoic acid
- Wolff- Chaikoff effect
- Thyroid storm (give 1 hour after thionamides)
- Decrease vascularity pre-op

## Steroids

- Thyroid storm

## Beta Blockers

- Adjunct to treatment
- to control adrenergic symptoms, especially in the early stages before antithyroid drugs take effect

The background is a solid light green color with a pattern of white butterfly silhouettes scattered across it. The butterflies are of various sizes and orientations, some appearing more prominent than others.

# THYROID STORM

# Burch Wartofsky Score

- Temperature
- CNS
- GIT-Hepatic Dysfunction
- CVS
  - Tachycardia
  - CHF
  - Atrial Fibrillation

> 45 **Thyroid Storm**

25-44 **Impending**

< 25 **Unlikely**

Diagnostic parameters	Scoring points
<b>Thermoregulatory dysfunction</b>	
<i>Temperature</i>	
99–99.9	5
100–100.9	10
101–101.9	15
102–102.9	20
103–103.9	25
≥ 104.0	30
<b>Central nervous system effects</b>	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, extreme lethargy)	20
Severe (seizures, coma)	30
<b>Gastrointestinal-hepatic dysfunction</b>	
Absent	0
Moderate (diarrhea, nausea/vomiting, abdominal pain)	10
Severe (unexplained jaundice)	20
<b>Cardiovascular dysfunction</b>	
<i>Tachycardia</i> (beats/minute)	
90–109	5
110–119	10
120–129	15
≥ 140	25
<i>Congestive heart failure</i>	
Absent	0
Mild (pedal edema)	5
Moderate (bibasilar rales)	10
Severe (pulmonary edema)	15
<i>Atrial fibrillation</i>	
Absent	0
Present	10
<b>Precipitating event</b>	
Absent	0
Present	10

Scoring system: A score of 45 or greater is highly suggestive of thyroid storm; a score of 25–44 is suggestive of impending storm, and a score below 25 is unlikely to represent thyroid storm.

Medication	Dosage	Mechanism of action	Conditions of use
<b>I. Inhibition of new hormone production</b>			
Propylthiouracil	200–400 mg po q 6–8 h <sup>a</sup>	Inhibits new hormone synthesis; decreases T4-to-T3 conversion	First-line therapy
or			
Methimazole	20–25 mg po q 6 h <sup>a</sup>	Inhibits new hormone synthesis	First-line therapy
<b>II. Inhibition of thyroid hormone release</b>			
Potassium iodide <sup>b</sup> SSKI	5 drops po q 6 h	Blocks release of hormone from gland	Administer at least 1 hr after thionamide
Lugol's solution <sup>b</sup>	4–8 drops po q 6–8 h	Blocks release of hormone from gland	Administer at least 1 hr after thionamide
Sodium ipodate <sup>c</sup> (308 mg iodine/ 500 mg tab)	1–3 g po qd	Blocks release of hormone from gland; inhibits T4-to-T3 conversion	Administer at least 1 h after thionamide
Iopanoic acid <sup>c</sup>	1 g po q 8 h for 24 h, then 500 mg po q 12 h	Blocks release of hormone from gland; inhibits T4-to-T3 conversion	Administer at least 1 h after thionamide
<b>III. Beta-adrenergic blockade</b>			
Propranolol	60–80 mg po q 4 h or 80–120 mg q 6 h	Beta-adrenergic blockade; decreases T4-to-T3 conversion	
<i>Cardioselective agents:</i>			
Atenolol	50–200 mg po qd	Beta-adrenergic blockade	Use when cardioselective agents preferred
Metoprolol	100–200 mg po qd		
Nadolol	40–80 mg po qd		
<i>Intravenous agent:</i>			
Esmolol	50–100 µg/kg/min	Beta-adrenergic blockade	Use when oral agents contraindicated; Consider use in heart failure

Medication	Dosage	Mechanism of action	Conditions of use
IV. Supportive treatment			
Acetaminophen	325–650 po/pr q 4–6 h as needed	Treatment of hyperthermia	Preferred treatment over salicylates
Hydrocortisone	100 mg IV q 8 h	Decreases T4-to-T3 conversion; vasomotor stability	Use when patient hypotensive to treat possible concomitant adrenal insufficiency
V. Alternative Therapies			
Lithium carbonate	300 mg po q 8 h <sup>d</sup>	Blocks release of hormone from gland; inhibits new hormone synthesis	Used when thionamide or iodide therapy is contraindicated; lithium levels should be checked regularly
Potassium perchlorate	1 g po qd	Inhibits iodide uptake by thyroid gland	Used in combination with thionamide in treatment of Type II amiodarone-induced thyrotoxicosis
Cholestyramine	4 g po qid	Decreases reabsorption of thyroid hormone from enterohepatic circulation	Used in combination with thionamide therapy

The background is a solid light green color with a subtle gradient. It is decorated with numerous white butterfly silhouettes of various sizes and orientations, scattered across the frame. The butterflies are most prominent on the left and right sides, with some appearing as fainter, larger-scale patterns in the background.

# Hypothyroidism

# Clinical Manifestations

**TABLE 335-5 SIGNS AND SYMPTOMS OF HYPOTHYROIDISM (DESCENDING ORDER OF FREQUENCY)**

## Symptoms

- Tiredness, weakness
- Dry skin
- Feeling cold
- Hair loss
- Difficulty concentrating and poor memory
- Constipation
- Weight gain with poor appetite
- Dyspnea
- Hoarse voice
- Menorrhagia (later oligomenorrhea or amenorrhea)
- Paresthesia
- Impaired hearing

## Signs

- Dry coarse skin; cool peripheral extremities
- Puffy face, hands, and feet (myxedema)
- Diffuse alopecia
- Bradycardia
- Peripheral edema
- Delayed tendon reflex relaxation
- Carpal tunnel syndrome
- Serous cavity effusions



# Iodine Deficiency

- Most common cause of hypothyroidism WORLDWIDE
- Most common cause of preventable mental deficiency
  - Mild deficiency can lead to subtle reduction of IQ
- Prevalent in mountainous regions and in Central Africa, South America and Northern Asia
- The World Health Organization (WHO) estimates that about 2 billion people are iodine-deficient, based on urinary excretion data.
- Manifestations:
  - Goiter
  - Cretinism
    - Mental and growth retardation in children living in iodine deficient regions

## Iodine Deficiency Disorders



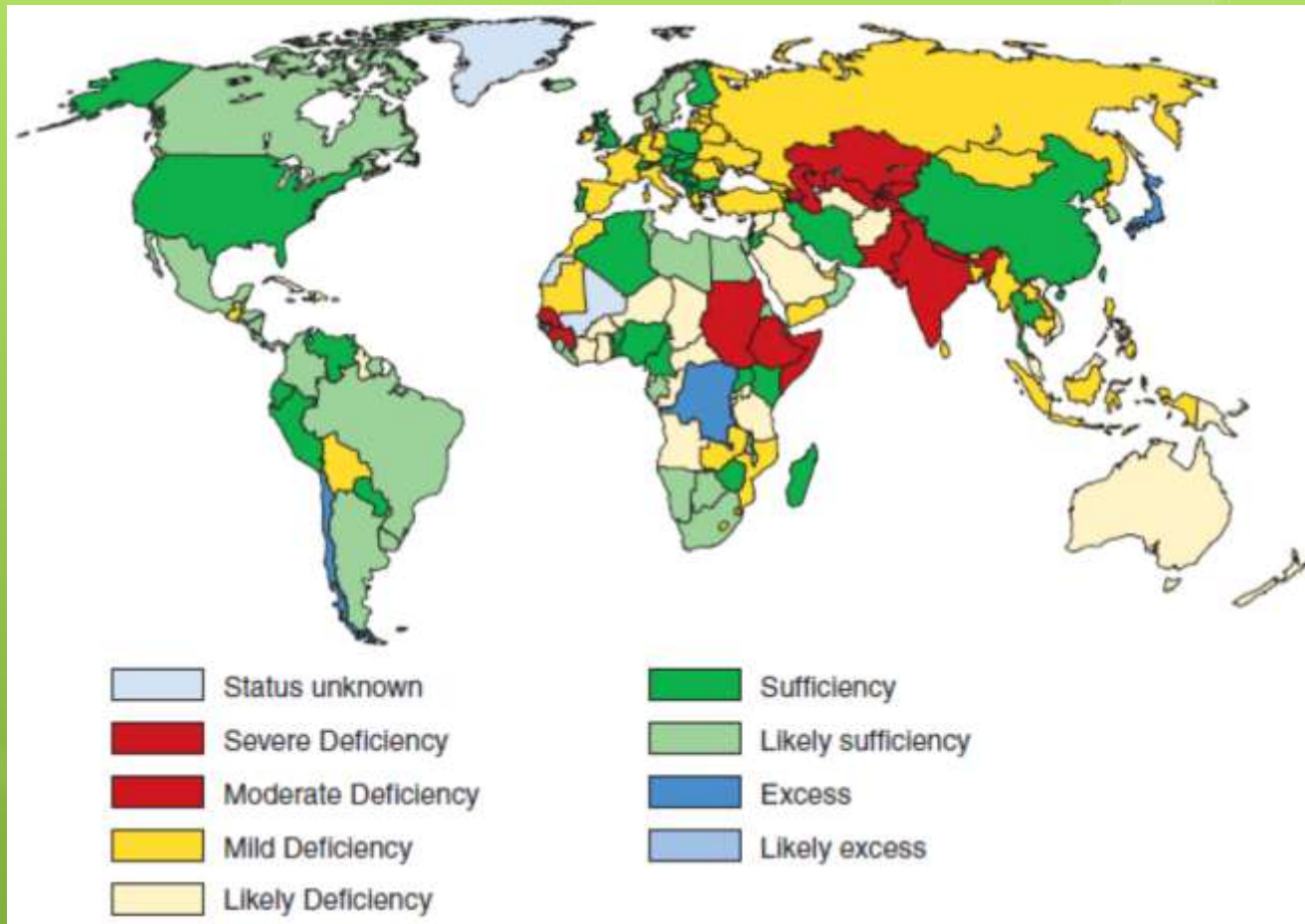
Goiter



Cretinism



# Iodine Deficiency



# Iodine Deficiency

- Recommended Daily Intake
  - Children 90-120 ug/d
  - Adults 150 ug/d
  - Pregnant 200 ug/d
- Oversupply of iodine, through supplements or foods can also worsen pre existing thyroid disease

**Table 1. Common Sources of Dietary Iodine**

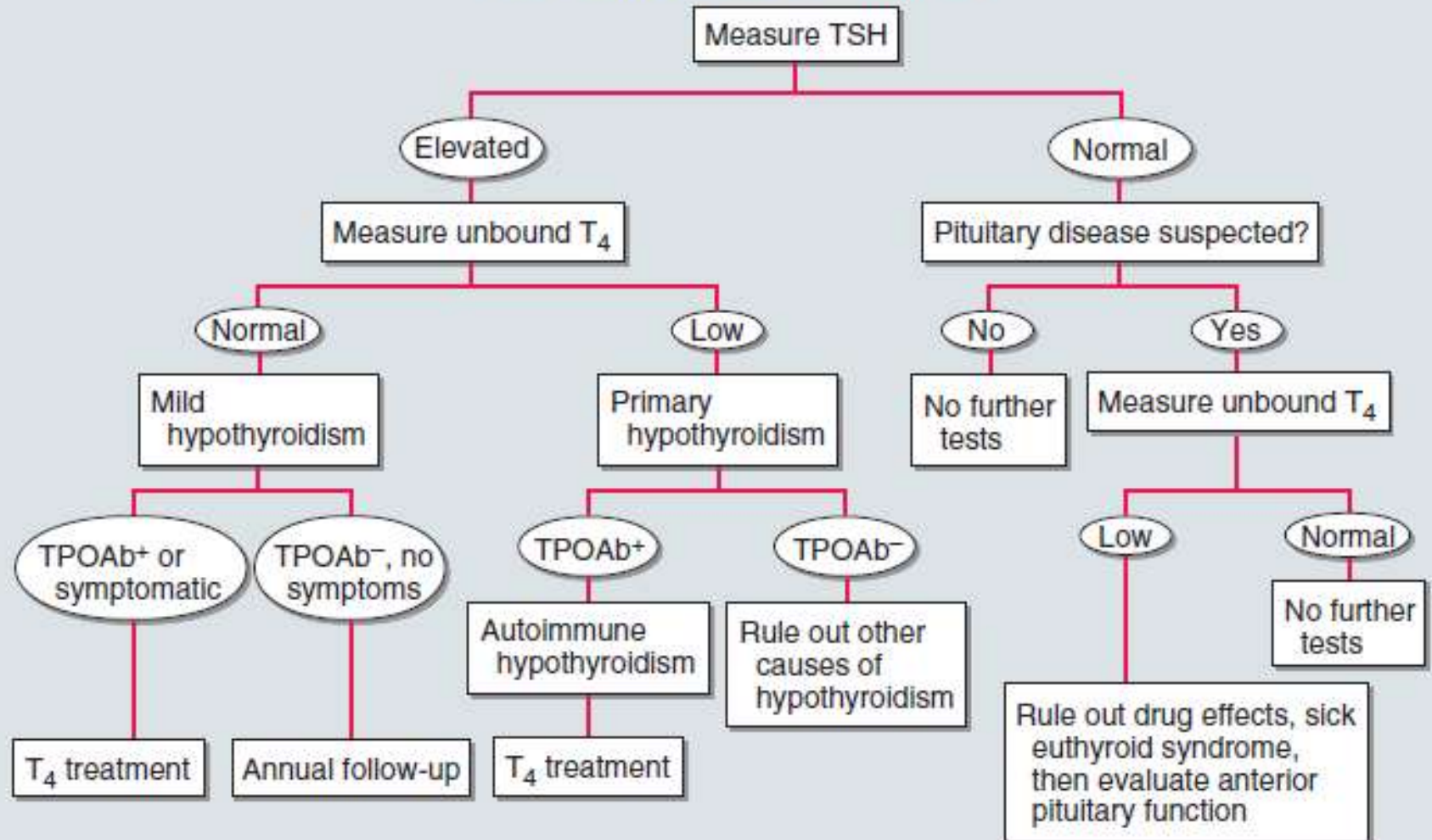
Breads	Iodized table salt
Cheese	Saltwater fish
Cow's milk	Seaweed (including kelp, dulce, nori)
Eggs	Shellfish
Frozen yogurt	Soy milk
Ice cream	Soy sauce
Iodine-containing multivitamins	Yogurt



**FIDEL – Fortification for Iodine Deficiency Elimination**

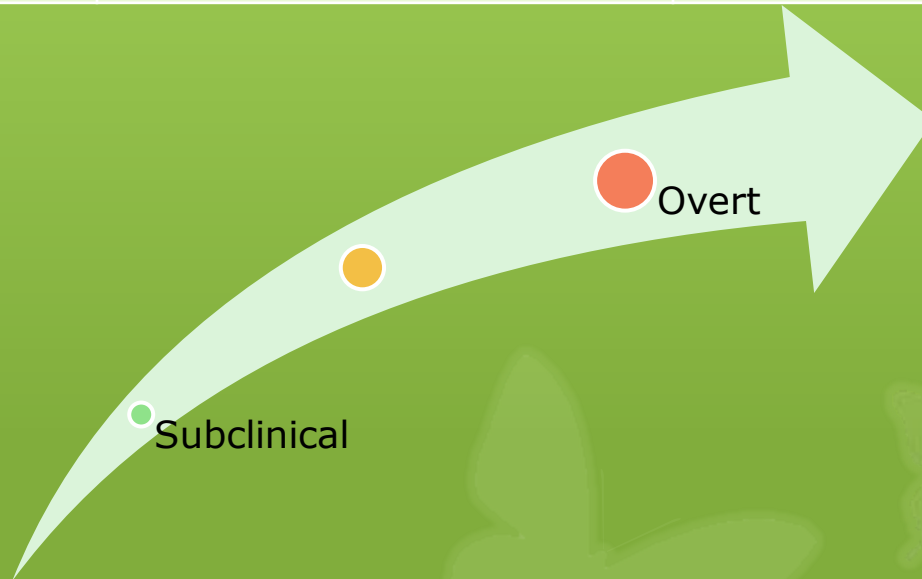
# Autoimmune Hypothyroidism

## EVALUATION OF HYPOTHYROIDISM



# Autoimmune Hypothyroidism

Histology	Hashimoto's or Goitrous thyroiditis	Atrophic Thyroiditis
Lymphocyte infiltration	Marked lymphocytic infiltration with germinal cell formation	Less pronounced
Thyroid follicles	Atrophy of thyroid follicles with absent colloid	Almost completely absent
Fibrosis	Mild to moderate	Extensive



# Autoimmune Hypothyroidism

- Lymphocytic infiltration: CD4+, CD8+, B cells
  - Thyroid cell destruction is primarily mediated by the CD8+ cytotoxic T cells
  - T cells produce cytokines, TNF, IL-1, and interferon have the following effects:
    - may render thyroid cells more susceptible to apoptosis
    - Impair thyroid function directly
    - Induce expression of other pro inflammatory molecules by the thyroid cells themselves.
  - Antibodies to Tg and TPO play secondary role by amplifying an ONGOING autoimmune response
  - 20% have TSH-R blocking antibodies which can cause hypothyroidism and thyroid atrophy

# Autoimmune Hypothyroidism

- Genetic factors
  - HLA-DR and *CTLA-4* polymorphisms account for approximately half of the genetic susceptibility to autoimmune hypothyroidism
  - Both of these genetic associations are shared by other autoimmune diseases (type 1 diabetes mellitus, Addison's disease, pernicious anemia, and vitiligo )
- Sex
  - Female preponderance: sex steroid effect on immune response vs X chromosome-related genetic factor
- Diet
  - A high iodine intake may increase the risk of autoimmune hypothyroidism by immunologic effects or direct thyroid toxicity.
- Infection
  - Congenital Rubella syndrome associated with high frequency of autoimmune hypothyroidism
  - Viral thyroiditis does not induce subsequent autoimmune thyroid disease

# Autoimmune Hypothyroidism

Start  
Levothyroxine  
replacement  
1.6-1.8  $\mu\text{g}/\text{kg}$  BW  
(100-150  $\mu\text{g}/\text{day}$ )

Check TSH every  
6-8 weeks

Adjust dose by 12.5  
to 25  $\mu\text{g}$  until TSH  
goal of Lower Half  
of Normal Range is  
achieved

- Special situations:

- Pregnancy: higher requirements; need to increase dose by 50% and reduce after delivery
- Elderly, CAD patients: starting dose 12.5 – 25  $\mu\text{g}/\text{day}$

The background is a solid green gradient, lighter at the top and darker at the bottom. It is decorated with numerous white butterfly silhouettes of various sizes and orientations, scattered across the frame. The word "THYROIDITIS" is centered in the lower half of the image.

# THYROIDITIS



## **Rare; Suppurative infection**

Associated with piriform sinus in children

Associated with longstanding goiter and degeneration in thyroid cancer in elderly

## **Laboratories:**

ESR and WBC elevated

**Thyroid Function Tests Normal**

# Acute Thyroiditis

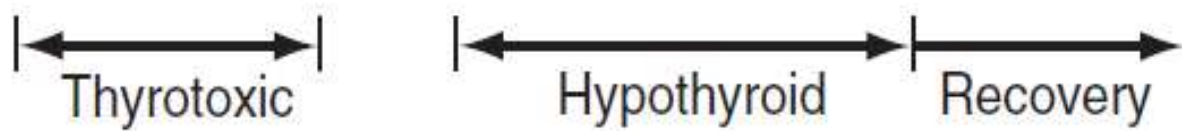
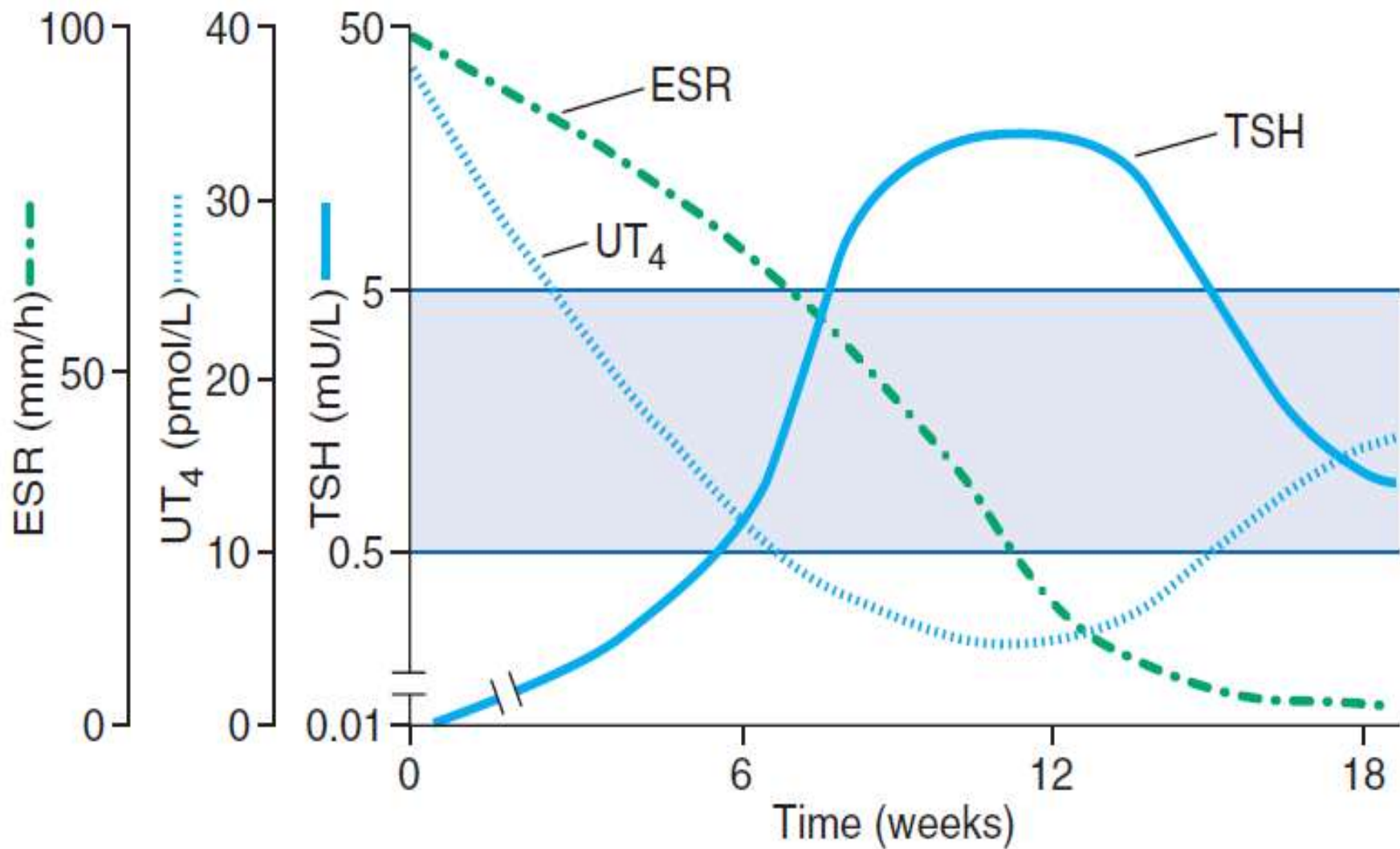
## **Clinical Manifestations:**

**Painful, tender thyroid**

With systemic symptoms presenting abruptly (fever, dysphagia)

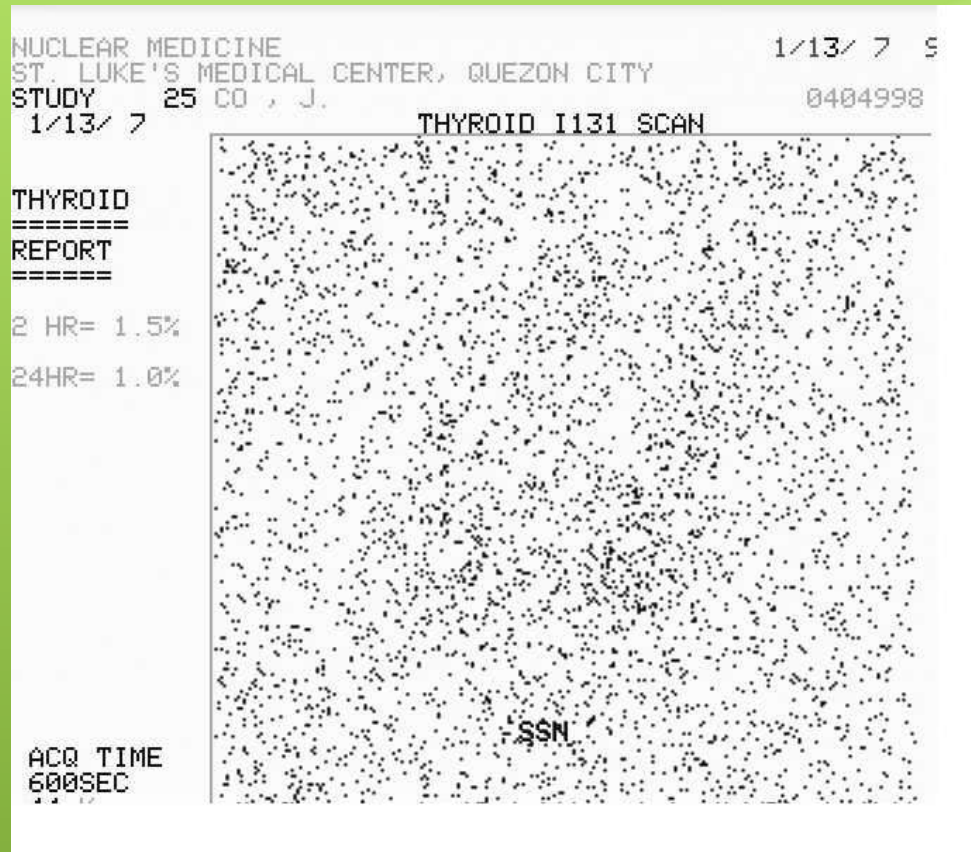
## **Treatment:**

Antibiotics with Surgical Drainage if necessary



**Clinical Phases**

# Thyroid Scan: Subacute Thyroiditis



Subacute in duration

Postpartum thyroiditis – 5% of women within 6 months post pregnancy

**With underlying autoimmune thyroid disorder**

**Laboratories:**

**Positive anti – TPO**

Normal ESR

Triphasic: thyroid function tests results depending on phase

## Silent Thyroiditis

**Clinical Manifestations:**

**Painless**

Symptoms related to phase

Shorter phases

**Treatment:**

Steroids not indicated

Beta Blockers or Levothyroxine as indicated

# CHRONIC THYROIDITIS

- Hashimoto's thyroiditis
- Riedel's thyroiditis
  - Rare; occurs in middle aged women
  - Dense extensive fibrosis with no thyroid dysfunction
  - Presents with painless goiter and compressive symptoms
  - Treatment: Surgical relief of compressive symptoms.

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**GOITER**

## **Diffuse Non Toxic, Colloid**

Endemic vs Sporadic

Iodine Deficiency

Inherited Defects in hormone synthesis

Goitrogens

Cassava root (thiocyanate), Cruciferae fam. (brussels sprouts, cabbage, cauliflower)

Thyroid Function Tests:

low T4, normal T3 and TSH

TPO antibodies

Do PFT and imaging studies if with obstructive symptoms

Ultrasound

# Simple Goiter

## **Women**

Greater prevalence of autoimmune disease and greater demands of iodine during pregnancy

## **Obstructive Symptoms**

Substernal Goiter

Pemberton's Sign

Iodine replacement

Suppressive therapy with levothyroxine:

Best response in young patients and soft goiter; regression seen in 3-6 months

Surgery:

Subtotal or near total surgery for obstructive symptoms

## **Solitary, autonomously functioning thyroid nodule**

Most have acquired somatic, activating mutations in the TSH-R leading to enhanced thyroid follicular cell proliferation and function. Less commonly, somatic mutations are identified in Gs

## **Thyroid scan**

Focal uptake in the hyperfunctioning nodule and diminished uptake in the remainder of the gland, as activity of the normal thyroid is suppressed.

# Toxic Adenoma

## **Mild thyrotoxicosis**

## **Radioiodine ablation**

$^{131}\text{I}$  is concentrated in the hyperfunctioning nodule with minimal uptake and damage to normal thyroid tissue

Surgery (enucleation/lobectomy)

Ethanol injection

Medical treatment is not an optimal long term treatment



# Toxic Adenoma



## Multi-Nodular Toxic Goiter

Pathogenesis of toxic MNG appears to be similar to that of nontoxic MNG; the major difference is the presence of functional autonomy in toxic MNG

Onset of Hyperthyroidism may have precipitating factor (iodine contrast)

- Low TSH, T4 normal or minimal increase, T3 elevated to a greater degree than T4
- Thyroid scan:  
Heterogeneous uptake with multiple regions of increased and decreased uptake; 24-h uptake of radioiodine may not be increased

## MNTG

- Goiter
  - Subclinical or mild hyperthyroidism
- Elderly presenting with AF, nervousness, tremor or weight loss

- Medical management or Radioiodine does not provide complete control of both goiter and hyperthyroidism
- Surgery provides definitive treatment of underlying thyrotoxicosis as well as goiter.



# THYROID CANCER

Most common malignancy of the endocrine system

# Well Differentiated

- Classified according to histologic features

- Differentiated

- Papillary

- Most common 70-90%

- Histology: Psammoma bodies, cleaved nuclei with an "orphan-Annie" appearance caused by large nucleoli, and the formation of papillary structures

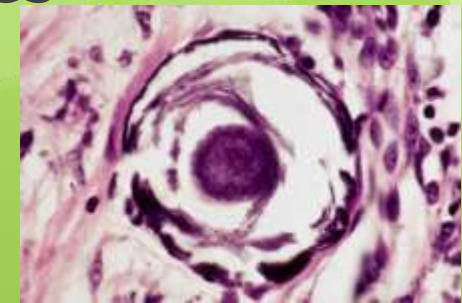
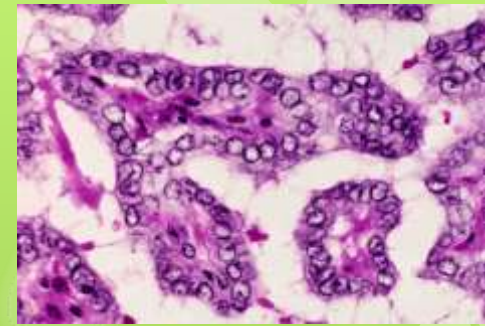
- Locally invasive

- Follicular

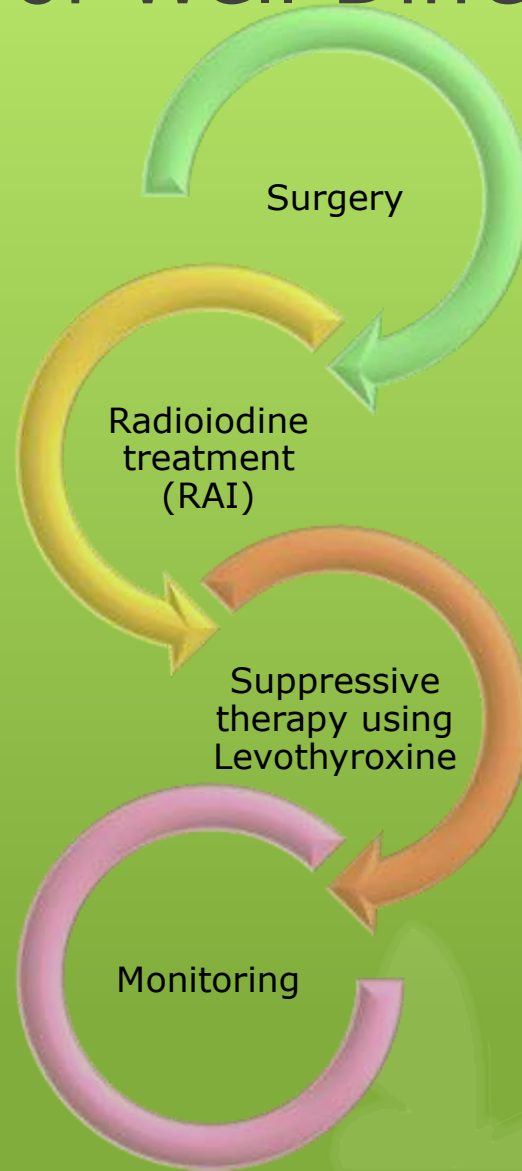
- more common in iodine-deficient regions.

- Difficult to diagnose by FNA because the distinction between benign and malignant follicular neoplasms rests largely on evidence of invasion into vessels, nerves, or adjacent structures

- Hematogenous spread



# Treatment of Well Differentiated



# Poorly Differentiated and others

- Poorly Differentiated

- Anaplastic

- Poor prognosis
    - Poor response to radioiodine treatment
    - Chemotherapy ineffective

- Others

- Medullary

- Association with Multiple Endocrine Neoplasia 2
    - Serum calcitonin is a marker of residual or recurrent disease

- Lymphoma

- Rapidly expanding thyroid mass
    - Highly sensitive to external radiation



Thank you

[www.medclerk.weebly.com](http://www.medclerk.weebly.com)